Learning about Colorectal Cancer
A Personalized Treatment Guide for Patients
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Learning About Colorectal Cancer: A Personalized Treatment Guide for Patients

Introduction

Welcome to Learning About Colorectal Cancer – A Personalized Treatment Guide for Patients.

The goal of this guide is help you learn about colorectal cancer (CRC), diagnosis, treatments options available to you, strategies to help you manage the disease while maintaining your well-being, and where to find support in your area.

Colour-coded, Personalized Treatment Section contains information on different combinations of chemotherapy and/or targeted therapy used to treat CRC. The guide also discusses current research and looks at future therapies in CRC.

For your convenience, you can find a Glossary at the end of this booklet, to help you better understand the medical terminology used in CRC. The words in the guide marked in italics can be found in the Glossary.

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

Knowing the Facts: Colorectal Cancer Statistics

CRC is the second leading cause of death from cancer in Canada in both men and women combined. CRC has a significant impact on death for men and women combined. This year an estimated 22,200 Canadians will be diagnosed with CRC and 8,900 will die from it. More than half of all new cases of CRC will be diagnosed in people 70 years of age and older. It is estimated that:

- 9,700 women will be diagnosed with CRC and 3,900 will die of it
- 12,500 men will be diagnosed with CRC and 5,000 will die of it
- On average, 426 Canadians will be diagnosed with CRC every week
- On average, 171 Canadians will die of CRC every week

What are the chances of getting or dying from CRC?

- In men: 1 in 14 is expected to develop CRC during their lifetime and 1 in 27 will die of it
- In women: 1 in 15 is expected to develop CRC during their lifetime and 1 in 31 will die of it
- Overall, colorectal cancer is the second-leading cause of cancer death in Canada
- Death from CRC continues to decline in both men and women due to improvements in treatments, especially chemotherapy. Screening for CRC can lower the risk of getting it and dying from it

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 (CRCs). 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, 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 CRC 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.

Screening for CRC can reduce both occurrence and death.

CRC grows in a predictable way, and when diagnosed at an early stage, it is often curable.
Cancer grades of the cancer.

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

### Stages and Grades of Colorectal Cancer

Once a CRC diagnosis is made, the cancer is usually described by a stage and grade. CRC 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 first began to grow. CRC is described by the following 5 stages:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>The abnormal cells are found only in the innermost layer (mucosa) of the colon or rectum. These abnormal cells may become cancerous and spread. Stage 0 CRC is also called carcinoma in situ.</td>
</tr>
<tr>
<td>I</td>
<td>The tumour (cancer) has grown into the inner wall of the colon or rectum, but has not grown through the wall.</td>
</tr>
<tr>
<td>II</td>
<td>The tumour (cancer) has grown more deeply into or through the wall colon or rectum, and may invade nearby tissues but has not spread to the lymph nodes.</td>
</tr>
<tr>
<td>III</td>
<td>Cancer involves the nearby lymph nodes, but not to other parts of the body.</td>
</tr>
<tr>
<td>IV</td>
<td>Cancer has spread to other parts of the body, such as the liver or lungs.</td>
</tr>
</tbody>
</table>

### 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 CRC, your treatment may include a combination of surgery, radiation therapy, chemotherapy and targeted 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.

Available treatments for CRC are described below.

#### Treatment option: Surgery

Surgery is the main treatment for CRC. 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 example, if the tumour is small and located in the rectum, the surgeon may perform a rectal resection and an end-to-end anastomosis. If the tumour is larger and located in the colon, the surgeon may perform an end-to-end anastomosis with a temporary colostomy to divert the flow of waste from the colon.

Cancer that has been treated and has come back after a period of time when the cancer could not be detected is called recurrence. The cancer may come back in the colon or rectum, or in another part of the body.

In addition to the cancer stage, it is also useful to determine the grade of the cancer, which is done by examining a biopsy sample from the tumour under a microscope. Examining how the cancer cells look and behave in comparison to normal cells will help determine the grade of the cancer, and enable your doctor to estimate how quickly the cancer may be growing. CRC has three grades:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Low)</td>
<td>Cancer is slow-growing, also referred to as well differentiated</td>
</tr>
<tr>
<td>2 (Moderate)</td>
<td>Cancer is intermediate growing, also known as intermediate differentiation</td>
</tr>
<tr>
<td>3 (High)</td>
<td>Cancer is faster growing, also referred to as poorly differentiated</td>
</tr>
</tbody>
</table>
the rectum heals and after about 2-3 months the colostomy can be removed (or reversed). The healthcare professional team will teach the patient how to manage a colostomy, which will allow the patient to continue to participate in everyday activities.\textsuperscript{1,2}

For some patients with CRC that has spread in a limited way to an area such as the liver, specialized surgery called partial liver resection for colorectal liver metastasis, may be an option to remove liver metastases if they are small or few in number.\textsuperscript{1,2}

Up to 30 percent of people may be cured if metastases in the liver can be completely removed (or resected).\textsuperscript{6}

**Treatment option: Radiation therapy**

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 aimed directly at the tumour. In brachytherapy, radioactive material is placed inside the tumour, making it possible to treat the cancer in a very focused manner.\textsuperscript{1,2,7,11}

During radiation therapy (also called radiotherapy), high doses of a special type of energy (radiation) are aimed at the area where the cancer is growing, destroying cells and making it impossible for them to grow and divide. While radiation therapy destroys cancer cells, which grow uncontrollably, it also can damage healthy cells nearby. The good news is that healthy cells are able to repair themselves after the therapy is complete.\textsuperscript{1,2,7,11}

Radiochemotherapy (also called chemoradiation) is chemotherapy (typically 5-FU or capecitabine) combined with radiation therapy. It is used before rectal cancer surgery to improve the chances of better tumour control, and reduce local recurrences (cancer from coming back).\textsuperscript{1,2,7,11}

While radiochemotherapy is a standard of care in Canada, not all patients with rectal cancer are considered candidates for this treatment before surgery. For example, patients who are at risk of severe side effects from the combined therapy which might prevent successful surgery, are generally excluded, and given radiation alone, as either standard fractionation or shorter-course radiotherapy.\textsuperscript{10}

Two radiotherapy options are available in Canada: short-course (25 Gy given in five fractions) and long-course (45 Gy given in 25 fractions).\textsuperscript{8,12,13} Both short-course radiation alone (25 Gy in five fractions) and long-course radiation therapy combined with chemotherapy (45–50 Gy in 25–28 fractions) have been shown to be effective in decreasing local recurrence risk for rectal cancer.\textsuperscript{14}

Radiation therapy 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 types of radiation dosage that might be necessary.\textsuperscript{1,2}

However, the opposite is true for the rectum, where local spread can readily contaminate the side wall of the pelvis. In addition, the small intestine is at a safe distance. This means that 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.\textsuperscript{1,2}

Possible side effects that may be experienced after radiation treatment include feeling of being more tired than usual, occasional 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 and usually within 1-2 weeks.\textsuperscript{1,2}

**Treatment option: Chemotherapy**

Commonly, drugs (medications) are usually used to treat the different stages of CRC. Chemotherapy is the use of anticancer medications, also called chemotherapy drugs, that are typically given by injection into a vein by intravenous or IV infusion, or sometimes as pills, to destroy cancer cells.\textsuperscript{12,45}

While chemotherapy drugs work to destroy cancer cells and help prevent cancer cells from growing and spreading, they also can damage healthy cells, and may cause side effects. However, damage to healthy cells is temporary and they will repair themselves after the treatment stops.\textsuperscript{12,45}

Some of the side effects that may be experienced include nausea, vomiting, stomatitis or mucositis (soresness in the mouth), loss of appetite, tiredness, alopecia (hair loss), diarrhea, neurotoxicity, an increased risk of infection, and bleeding. Your healthcare team will carefully monitor any side effects and provide medications that are effective in reducing the symptoms.\textsuperscript{1,2,45}

Chemotherapy treatment may be given before or after surgery or both. Different types of chemotherapy (neoadjuvant, adjuvant, and palliative) are described in the table below:\textsuperscript{1,2,45}

<table>
<thead>
<tr>
<th>Timing of chemotherapy treatment</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy / chemoradiation therapy</td>
<td>Given before surgery (preoperative) to decrease tumour size and control local spread. Chemoradiation therapy is chemotherapy combined with radiation therapy to shrink a rectal tumour.</td>
</tr>
<tr>
<td><strong>After surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>Given after surgery (post-surgical) to destroy any microscopic cancer cells left behind and therefore help to reduce the risk of the cancer coming back.</td>
</tr>
<tr>
<td>Palliative chemotherapy</td>
<td>Given to help slow down and control the cancer when the cancer has spread to distant organs. The goal is to control symptoms and extend life but ultimately, the cancer is not curable.</td>
</tr>
</tbody>
</table>
If surgical removal of the liver metastases is successful, additional chemotherapy is usually recommended after surgery (also sometimes referred to as ‘pseudo’-adjuvant chemotherapy).1,2,4,5

In some cases, chemotherapy may be recommended before surgery to the liver, if the cancer is only confined to the liver. This approach may be used to help a person who is a borderline candidate for surgery, because of the size or location of the liver metastases, to have successful surgery after the CRC metastases have been reduced in size by the chemotherapy.1,5,10

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.1,2,4,5

Description of all available chemotherapy and/or targeted therapy combinations for the treatment of different stages of CRC are described in the Personalized Treatment Section of this guide.

The most commonly used chemotherapy drugs to treat CRC are fluorouracil (5-FU) and leucovorin (LV) or folinic acid, which is added to increase the effectiveness of 5-FU. 5-FU has been used for many years and its effectiveness is proven. Other drugs used to treat CRC include oxaliplatin, irinotecan, capcitabine (this is 5-FU in pill form), bevacizumab (BEV), cetuximab, and panitumumab. Other than capcitabine, which is a pill and is taken by mouth, all other chemotherapy drugs are given into a vein (intravenously or IV) through a pump. The regimen involving continuous intravenous infusion, requires that patients have a central venous (into a vein) access catheter either with a “port-a-cath” which is a vascular access device surgically implanted underneath the skin and connected to one of the large blood vessels in the chest, or a peripherally inserted central catheter (PICC) which is inserted through a vein in the arm. The 5-FU infusion is then delivered through a portable chemotherapy pump at home (referred to as a home infusion pump). This pump is very small, and it fits into a pack that can be worn around the waist.1,2,4,10

Chemotherapy drugs interfere with the ability of fast growing cells (like cancer cells) to divide or multiply. Because most of body’s normal cells of an adult are not actively growing, they are less affected by chemotherapy, except for those of bone marrow (where the blood cells are made), the hair, and the lining of the digestive tract. Effects of chemotherapy on these and other normal tissues can cause side effects such as nausea, hair loss, and tiredness.1,2,4,5

There are several choices of chemotherapy for both primary and advanced or metastatic CRC, which are decided upon in discussion mainly with your medical oncologist, and tailored specifically to your situation.1,2,4,5

### Chemotherapy

#### For primary colon cancer

- **For people 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: LV (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 (Keodala®) (this is 5-FU in pill form, which is taken twice daily for 2 of every 3 weeks, for a planned total of 24 weeks.

#### For advanced or metastatic CRC

- **The most common chemotherapy combinations used to treat advanced or metastatic CRC**
  - 1. FOLFOX: LV (folinic acid) (Leucovorin®), fluorouracil (5-FU, Adrucil®), oxaliplatin (Eloxatin®) +/- BEV
  - 2. FOLIRI: LV (folinic acid) (Leucovorin®), fluorouracil (5-FU, Adrucil®), irinotecan (Camptosar®, CPT-11), +/- BEV
  - 3. Capecitabine (Xeloda®) taken instead of 5-FU combination treatments +/- BEV

- **For people after previous chemotherapy treatments have failed**
  - Cetuximab (Erbitux®), type of targeted therapy, may be taken alone, or in combination with irinotecan, for the treatment of non-mutated (wild type) KRAS metastatic CRC.

- **Second or third treatment choice for people for whom first choice treatment options did not work**
  - Panitumumab (Vectibix®), type of targeted therapy in the same class as cetuximab, also used for the treatment of patients with non-mutated KRAS after treatments containing fluoropyrimidines, oxaliplatin or irinotecan have failed.

All available chemotherapy therapies either alone or in combination for the treatment of different stages of CRC are described in the Personalized Treatment Section of this guide.
Treatment option: Targeted therapy

Targeted therapy is another treatment option available to help treat CRC. Targeted therapy drugs are designed to find and attack specific cancer cells while trying not to harm normal cells. Monoclonal antibody therapy is a type of targeted therapy used to treat CRC. This type of therapy uses antibodies made in the laboratory from a single type of immune system cell. These antibodies can find substances on cancer cells or normal substances that may help cancer cells grow, stick to these substances and destroy the cancer cells, block their growth, or stop them from spreading.12,14

The most commonly available targeted therapy drug options include bevacizumab (Avastin®), cetuximab (Erbitux®), and panitumumab (Vectibix®), all of which are monoclonal antibodies.13,19,20

Bevacizumab (Avastin®) is one of the targeted therapy drugs used for the treatment of metastatic cancer of the colon and rectum. Bevacizumab 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 tumour to grow larger. VEGF is important in the development of a blood supply in a growing tumour as this blood supply is essential for the tumour to grow and spread. Bevacizumab works by attaching to VEGF and stopping blood vessels from reaching a tumour. Without blood supply, the tumour dies. Bevacizumab also improves how chemotherapy drugs work by helping carry these drugs directly to the tumour. Bevacizumab is generally given in combination with other drugs, such as 5-FU, oxaliplatin, irinotecan and capecitabine.17,18

Cetuximab (Erbitux®)

Cetuximab (Erbitux®) works by targeting a protein called the epidermal growth factor receptor (EGFR) on the cancer cell. EGFR is found in about 80 percent of CRCs. EGFR helps cancer cells grow and survive by transmitting signals to these cells. Cetuximab attaches to these receptors, which cuts off this signal transmission to cancer cells and causes these cells to die. Cetuximab has also been shown to work even if EGFR is not found in an individual tumour. Cetuximab does not work for all patients. The effectiveness of cetuximab treatment will depend on whether or not the tumour has a mutation in the KRAS gene. If the tumour has the KRAS mutation, cetuximab is not effective, but if the tumour does not have the KRAS mutation, cetuximab may be effective. Cetuximab is active when given alone or in combination with other drugs, like irinotecan.11,15 For more information on testing for biomarkers, see section on Biomarker Testing of this guide.

Panitumumab (Vectibix®)

Panitumumab (Vectibix®), like cetuximab, also targets the EGFR. Panitumumab is usually used for metastatic CRC after other drugs have been tried and did not work. Also like cetuximab, panitumumab is effective only for tumours that do not have a specific mutation in the KRAS gene. For more information on testing for biomarkers, see section on Biomarker Testing of this guide.17,20

Biomarker Testing

CRC is one of the most commonly diagnosed cancers. Recent scientific advances in how it is treated have dramatically improved survival. One such advance is a better understanding of genes called KRAS and BRAF which led researchers to develop a way to personalize treatment for some patients with metastatic CRC.21

KRAS and BRAF are biomarkers, also called molecular markers, which are biological molecules found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A test for a particular biomarker, called biomarker testing, may be used to see how well the body responds to a treatment for a disease or condition.4

Biomarker testing is a form of personalized approach which is the opposite of a “one size fits all” approach as has been used before the discovery of biomarkers. With the “one size fits all” approach, all patients with the same type and stage of CRC got the same treatment. However, the discovery of biomarkers changed that, and now researchers know that no two patients’ tumours are exactly alike. Knowing the information about your tumour can help doctors decide which treatment is more likely to work than another.21

KRAS and BRAF mutations

Researchers found that KRAS gene is mutated (or changed) in about 40% of people with CRC. The other 60% of people with CRC have a non-mutated (also called wild-type) KRAS gene. A biomarker test, also known as KRAS mutation analysis, or “KRAS testing”, which is done on sample tissue from tumours removed during surgery, can tell if the tumour has this mutation.21

It is recommended that all patients with metastatic CRC get tested for the KRAS mutation. If KRAS mutation is found, then patients should not be treated with cetuximab (Erbitux®) or panitumumab (Vectibix®). These drugs do not work in tumours that have the KRAS mutation. However, not all people with the non-mutated (also called wild-type) KRAS tumours respond well to treatment with cetuximab or panitumumab either. Other tumour markers may be present than can give additional information as to what treatments will work best for these patients, but the research in this area is still ongoing.21,22,23

Talk to your doctor about biomarker testing to find a treatment that is right for you.
Personalized Treatment Section

Introduction: Combinations of chemotherapy and/or targeted therapy

The side effects of combinations of chemotherapy and/or targeted therapy used to treat CRC depend on the type, combination, and schedule of drugs used.
5-FU/Leucovorin/Oxaliplatin (FOLFOX-4)

What is it?
FOLFOX-4 is one of several chemotherapy combinations that include 5-fluorouracil (5-FU), leucovorin (LV or folinic acid), and oxaliplatin. FOLFOX treatment schedule differs in dosing and administration schedule of each drug and include FOLFOX-4, FOLFOX-6, modified FOLFOX-6 (mFOLFOX-6), or others.27-28

What is it used for?
Oxaliplatin plus 5-FU and LV chemotherapy combination or FOLFOX-4 is used is used for the adjuvant treatment of patients with stage II or III colon cancer after they have undergone a surgery to remove the tumour, and for metastatic CRC.27

How is it given?
The FOLFOX-4 is given into a vein (intravenously) or IM.27

How often is it given?
FOLFOX-4 combination is given every 2 weeks. Every patient is different; your doctor will determine what dose is right for you.27

FOLFOX-4 treatment schedule27,28

<table>
<thead>
<tr>
<th>Treatment Schedule</th>
<th>FOLFOX-4 combination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 1</strong></td>
<td>Oxaliplatin + LV: IV infusion over 2 hours</td>
</tr>
<tr>
<td></td>
<td>followed by 5-FU: IV bolus</td>
</tr>
<tr>
<td></td>
<td>followed by 5-FU: continuous IV infusion over 22 hours</td>
</tr>
<tr>
<td><strong>Day 2</strong></td>
<td>LV: IV infusion over 2 hours</td>
</tr>
<tr>
<td></td>
<td>followed by 5-FU: IV bolus</td>
</tr>
<tr>
<td></td>
<td>followed by 5-FU: continuous IV infusion over 22 hours</td>
</tr>
</tbody>
</table>

What are the possible side effects?27-31

- Alopecia
- Anemia
- Diarrhea
- Hepatotoxicity
- Hypersensitivity
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking FOLFOX-4, contact your healthcare professional.
Modified 5-FU/Leucovorin/Oxaliplatin (modFOLFOX-6)

What is it?
modFOLFOX-6 is one of several chemotherapy combinations that include 5-fluorouracil (5-FU), leucovorin (LV or folinic acid), and oxaliplatin. FOLFOX treatment schedule differ in dosing and administration schedule of each drug and include FOLFOX-4, FOLFOX-6, modified FOLFOX-6 (modFOLFOX-6), or others.25-26

What is it used for?
Oxaliplatin plus 5-FU and LV chemotherapy combination or modFOLFOX-6 is used for the adjuvant treatment of patients with stage II or III colon cancer after they have undergone a surgery to remove the tumour, and for metastatic CRC.27-30

How is it given?
The modFOLFOX-6 is given into a vein (intravenously or IV).29-30

How often is it given?
modFOLFOX-6 combination is given once every 2 weeks. Every patient is different; your doctor will determine what dose is right for you.29-30

modFOLFOX-6 treatment schedule30

<table>
<thead>
<tr>
<th>Day</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Oxaliplatin + LV IV infusion over 2 hours followed by 5-FU IV bolus</td>
</tr>
<tr>
<td></td>
<td>Once every 2 weeks for 12 cycles in adjuvant setting.</td>
</tr>
<tr>
<td></td>
<td>In the metastatic setting, the schedule depends on the response or tolerance to the therapy.</td>
</tr>
<tr>
<td>Day 2</td>
<td>5-FU: continuous IV infusion over 24 hours</td>
</tr>
</tbody>
</table>

What are the possible side effects?27-31

- Alopecia
- Anemia
- Diarrhea
- Hepatotoxicity
- Hypersensitivity
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking modFOLFOX-6, contact your healthcare professional.
5-FU/Leucovorin/Oxaliplatin (FOLFOX-6)

What is it?

FOLFOX-6 is one of several chemotherapy combinations that include 5-fluorouracil (5-FU), leucovorin (LV or folinic acid), and oxaliplatin. FOLFOX treatment schedule differs in dosing and administration of each drug and include FOLFOX-4, FOLFOX-6, modified FOLFOX-6 (modFOLFOX 6), or others.25-26

What is it used for?

Oxaliplatin plus 5-FU and LV chemotherapy combination or FOLFOX-6 is used to treat people with metastatic CRC.31

How is it given?

The FOLFOX-6 is given into a vein (intravenously or IV).31

How often is it given?

FOLFOX-6 is given every 2 weeks in combination. Every patient is different; your doctor will determine what dose is right for you.31

FOLFOX-6 treatment schedule31

| Day 1 | Oxaliplatin + LV IV infusion over 2 hours followed by 5-FU IV bolus followed by 5-FU continuous IV infusion over 22 hours |
| Day 2 | 5-FU continuous IV infusion over 24 hours |
|       | Once every 2 weeks |

What are the possible side effects?27-31

- Alopecia
- Anemia
- Diarrhea
- Hepatotoxicity
- Hypersensitivity
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking FOLFOX-6, contact your healthcare professional.
FOLFOX (any) + bevacizumab treatment schedule

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Bevacizumab combination</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BEV IV infusion over 30-90 minutes</td>
<td>Once every 2 weeks</td>
</tr>
<tr>
<td></td>
<td>followed by FOLFOX</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oxaliplatin IV infusion over 2 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LV IV infusion over 2 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>followed by 5-FU IV bolus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>followed by continuous infusion over 22 hours</td>
<td></td>
</tr>
</tbody>
</table>

Day 2

| 5-FU continuous IV infusion over 22 hours |

*Treatment on Day 2 will vary depending on the FOLFOX combination.

What are the possible side effects?

- Abdominal abscess
- Alopecia
- Anemia
- Arterial thromboembolism
- Diarrhea
- Gastrointestinal perforation
- Hepatotoxicity
- Hypersensitivity
- Hypertension
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Proteinuria
- Stomatitis/mucositis
- Thrombocytopenia
- Wound/healing complications

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking FOLFOX (any) + bevacizumab, contact your healthcare professional.
5-FU/Leucovorin/Oxaliplatin + Cetuximab (FOLFOX (any) + Cetuximab)

What is it?
FOLFOX is one of several chemotherapy combinations that include 5-fluorouracil (5-FU), leucovorin (LV or folinic acid), and oxaliplatin. FOLFOX treatment schedule differ in dosing and administration schedule of each drug and include FOLFOX-4, FOLFOX-6, modified FOLFOX-6 (modFOLFOX 6), or others. Cetuximab can be added to any FOLFOX combination.

What is it used for?
FOLFOX (any) + cetuximab combination is used to treat patients with EGFR-expressing metastatic CRC whose tumors have wild-type (non-mutated) KRAS gene.

How is it given?
FOLFOX (any) + cetuximab combination is given into a vein (intravenously or IV).

How often is it given?
FOLFOX (any) + cetuximab combination is given every 2 weeks. Every patient is different; your doctor will determine what dose is right for you.

What are the possible side effects?
- Alopecia
- Anemia
- Diarrhea
- Hepatotoxicity
- Hypersensitivity
- Infusion reactions
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Skin reactions (rash, acne, itching, nail changes, and infusion-related reactions)
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking FOLFOX (any) + cetuximab, contact your healthcare professional.

FOLFOX (any) + cetuximab treatment schedule

| Day 1 | Cetuximab: IV infusion over 2 hours for the initial dose. After that, weekly doses are given over 1 hour † followed after 1 hour by FOLFOX |
|       | FOLFOX Oxaliplatin + LV: IV infusion over 2 hours † followed by 5-FU IV bolus † followed by 5-FU, continuous IV infusion over 22 hours |
| Day 2* | 5-FU: continuous IV infusion over 22 hours |

*Treatment on Day 2 will vary depending on the FOLFOX combination.
5-FU/Irinotecan/Leucovorin (FOLFIRI)

What is it?
FOLFIRI is a combination therapy consisting of 5-fluorouracil (5-FU), irinotecan, and leucovorin (LV or folinic acid).

What is it used for?
Irinotecan plus 5-FU and LV combination chemotherapy regimens or FOLFIRI may be considered for the treatment of advanced or metastatic CRC.

How is it given?
FOLFIRI is given into a vein (intravenously or IV).

How often is it given?
FOLFIRI is given every two weeks.

FOLFIRI treatment schedule

<table>
<thead>
<tr>
<th>Day 1</th>
<th>FOLFIRI combination</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV</td>
<td>IV infusion over 2 hours</td>
<td></td>
</tr>
<tr>
<td>Irinotecan</td>
<td>IV infusion over 90 minutes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>† followed by</td>
<td></td>
</tr>
<tr>
<td>5-FU</td>
<td>IV bolus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>† followed by</td>
<td></td>
</tr>
<tr>
<td>5-FU</td>
<td>continuous IV infusion over 22 hours</td>
<td></td>
</tr>
</tbody>
</table>

| Day 2 | 5-FU | continuous IV infusion over 24 hours |

What are the possible side effects?
• Alopecia
• Anemia
• Diarrhea
• Hypersensitivity
• Nausea/vomiting
• Neutropenia
• Stomatitis/mucositis
• Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking FOLFIRI, contact your healthcare professional.
5-FU/Irinotecan/Leucovorin + Bevacizumab (FOLFIRI + Bevacizumab)

What is it?
FOLFIRI + bevacizumab is a combination therapy consisting of 5-fluorouracil (5-FU), irinotecan, leucovorin (LV or folic acid), and bevacizumab (BEV).26

What is it used for?
FOLFIRI + BEV combination is used for the treatment of advanced or metastatic CRC.26

How is it given?
FOLFIRI + BEV are given into a vein (intravenously or IV).26

How often is it given?
FOLFIRI + BEV combination is given every two weeks.26
FOLFIRI + cetuximab treatment schedule⁶

<table>
<thead>
<tr>
<th>Day 1</th>
<th>FOLFIRI + cetuximab combination</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Cetuximab: IV infusion over 2 hours initially, then weekly over 1 hour † followed after one hour by FOLFIRI</td>
<td>Once every 1 or 2 weeks</td>
</tr>
<tr>
<td>Day 1</td>
<td>FOLFIRI</td>
<td>* * Infusion reactions</td>
</tr>
<tr>
<td>Day 1</td>
<td>Irinotecan: IV infusion over 30-90 minutes † followed by LV: IV infusion over 2 hours † followed by 5-FU: IV bolus † followed by 5-FU: continuous IV infusion over 22 hours</td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td>5-FU: continuous IV infusion over 24 hours</td>
<td></td>
</tr>
</tbody>
</table>

What are the possible side effects?⁶

- Alopecia
- Anemia
- Diarrhea
- Hypersensitivity
- Infusion reactions
- Nausea/vomiting
- Neutropenia
- Stomatitis/mucositis
- Skin reactions (rash, acne, itching, nail changes, and infusion-related reactions)
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking FOLFIRI + cetuximab, contact your healthcare professional.
Fluorouracil (5-FU) + Leucovorin (or folinic acid) (5-FU/LV)

What is it?
5-FU/LV is a chemotherapy combination of fluorouracil (5-FU) and leucovorin (LV or folinic acid). 25-26

What is it used for?
For patients who cannot tolerate an aggressive chemotherapy regimen FOLFOX, XELOX, or FOLFIRI due to their age, physical condition, or other medical problems, there is another alternative. 15
5-FU/LV chemotherapy combination is a less toxic alternative, which is used as adjuvant treatment for people with stage II or III colon cancer after they have undergone a surgery to remove the tumour. It is also used in the treatment of advanced or metastatic CRC. 27,37

How is it given?
5-FU/LV is given into a vein (intravenously or IV). 27,37

How often is it given?
5-FU/LV combination is given once every 2 weeks. Every patient is different; your doctor will determine what dose is right for you. 27,37

5-FU/LV treatment schedule 27,37

| Day 1 | LV: IV infusion over 2 hours + followed by 5-FU: IV bolus + followed by 5-FU: continuous IV infusion over 22 hours |
| Day 2 | LV: IV infusion over 2 hours + followed by 5-FU: IV bolus + followed by 5-FU: continuous IV infusion over 22 hours |

Once every 2 weeks for 12 cycles in adjuvant setting.
In the metastatic setting, the schedule depends on the response or tolerance to the therapy.

What are the possible side effects? 27

- Alopecia
- Anemia
- Diarrhea
- Nausea/vomiting
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking 5-FU/LV, contact your healthcare professional.
Capecitabine (CAPECITABINE)

What is it?

Capecitabine belongs to a family of medications called the fluoropyrimidines (medications that interfere with the growth of cells that rapidly divide in the body, including cancer cells). Capecitabine is an inactive substance on its own. When capecitabine is taken, it is changed in the body, mostly within the tumour (cancer cells), to become the commonly used cancer medication called 5-FU. In some patients 5-FU will kill cancer cells and decrease the size of the tumour.25-26

Why is it used for?

Capecitabine is used as adjuvant treatment for people with stage II or III colon cancer after they have undergone a surgery to remove the tumour. It is also used in the treatment of advanced or metastatic CRC.38,39

How is it given?

Capecitabine is available as tablets that are taken by mouth, and swallowed whole with water. Your doctor will calculate the dose for you. You may need to take a combination of 150 mg and 500 mg tablets. To get the right dose it is very important that you identify the tablets correctly each time you take capecitabine. Taking the wrong tablets could result in an overdose (too much medication) or underdose (too little medication).39

How often is it given?

Capecitabine tablets are taken twice a day for 14 days.38,39

Capecitabine treatment schedule39

<table>
<thead>
<tr>
<th>Day 1-14</th>
<th>Capecitabine</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tablets taken twice a day (morning and evening doses) for 14 days within 30 minutes after the end of a meal (breakfast and dinner)</td>
<td>Taken in 21 day cycles - take capecitabine for 14 days and then stop taking it for 7 days, then start again</td>
</tr>
</tbody>
</table>

What are the possible side effects?28-39

- Anemia
- Diarrhea
- Hand-and-foot syndrome
- Nausea/vomiting
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking capecitabine, contact your healthcare professional.
Capecitabine/Oxaliplatin (CAPOX/XELOX)

What is it?
CAPOX/XELOX is a combination of two anticancer drugs: capecitabine and oxaliplatin.25-26

What is it used for?
CAPOX/XELOX is used in adjuvant treatment of advanced or metastatic CRC that has spread outside of the colon and/or rectum.43

How is it given?
CAPOX/XELOX combination is given as an intravenous infusion of an oxaliplatin followed by capecitabine tablets taken by mouth.43

How often is it given?
Capecitabine tablets are taken twice a day, and oxaliplatin is infused once every 3 weeks.43

CAPOX/XELOX treatment schedule

<table>
<thead>
<tr>
<th>CAPOX/XELOX combination</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td><em>Oxaliplatin</em> IV infusion over 2 hours</td>
</tr>
<tr>
<td>Day 1-14</td>
<td><em>Capecitabine</em> Tablets taken twice a day (morning and evening doses) for 14 days within 30 minutes after the end of a meal (breakfast and dinner)</td>
</tr>
</tbody>
</table>

What are the possible side effects?40

- Alopecia
- Anemia
- Diarrhea
- Hand-and-foot syndrome
- Hepatotoxicity
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking CAPOX/XELOX, contact your healthcare professional.
Capecitabine/Oxaliplatin + Bevacizumab (CAPOX/XELOX + Bevacizumab)

What is it?
CAPOX/XELOX + Bevacizumab is a chemotherapy combination of capecitabine, oxaliplatin and bevacizumab (BEV).41-45

What is it used for?
CAPOX/XELOX + BEV combination is used for advanced or metastatic CRC that has spread outside of the colon and/or rectum.41

How is it given?
Oxaliplatin and BEV are given into a vein (intravenously or IV). Capecitabine is a tablet and is taken by mouth.41

How often is it given?
Capecitabine tablets are taken twice a day, and oxaliplatin and BEV are given once every 3 weeks into a vein by intravenous infusion.41

CAPOX/XELOX + bevacizumab treatment schedule

Day 1
| Oxaliplatin: IV infusion over 2 hours |
| BEV: IV infusion over 90 minutes the first time, and 30 or 60 minutes after the second or third time |
| Treatment Schedule: Once every 3 weeks |

Day 1-14
| Capecitabine: Tablets taken twice a day (morning and evening doses) for 14 days within 30 minutes after the end of a meal (breakfast and dinner) |
| Treatment Schedule: 14 days and then stop taking it for 7 days, then start again |

What are the possible side effects?42
- Abdominal abscess
- Alopecia
- Anemia
- Arterial thromboembolism
- Diarrhea
- Gastrointestinal perforation
- Hand-and-foot syndrome
- Hepatotoxicity
- Hypertension
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia
- Wound/healing complications

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking CAPOX/XELOX + bevacizumab, contact your healthcare professional.
Irinotecan/Oxaliplatin (IROX)

What is it?  
IROX is a chemotherapy combination consisting of two drugs, irinotecan and oxaliplatin.  

What is it used for?  
IROX is used to treat advanced or metastatic CRC in patients who cannot use 5-fluoropyrimidine therapy such as 5-FU or capecitabine.  

How is it given?  
IROX is given into a vein (intravenously or IV).  

How often is it given?  
IROX is given once every 3 weeks.  

IROX treatment schedule

| Day 1 | Oxaliplatin + irinotecan IV bolus infusion | Once every 3 weeks |

What are the possible side effects?  
- Diarrhea  
- Nausea/vomiting  
- Neurotoxicity/neuropathy  
- Neutropenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking IROX, contact your healthcare professional.
Irinotecan + Cetuximab
(IRINOTECAN + Cetuximab)

What is it?
Irinotecan + cetuximab is a chemotherapy combination consisting of two anticancer drugs, irinotecan and cetuximab.\textsuperscript{25-26}

What is it used for?
This combination is used for the treatment of non-mutated KRAS metastatic CRC in patients who have been resistant to other chemotherapy regimens containing 5-FU, irinotecan or oxaliplatin.\textsuperscript{19}

How is it given?
Irinotecan + cetuximab are given into a vein (intravenously or IV).\textsuperscript{19}

How often is it given?
Irinotecan + cetuximab are given once every week.\textsuperscript{19,44}

Irinotecan + Cetuximab treatment schedule\textsuperscript{19,44,45}

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Cetuximab: IV infusion over 2 hours followed by Irinotecan: IV infusion over 60-90 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cetuximab: Once every week</td>
</tr>
<tr>
<td></td>
<td>Irinotecan: Once every 2 weeks</td>
</tr>
</tbody>
</table>

If you receive irinotecan with cetuximab in the same week, irinotecan will be given after the end of the cetuximab infusion.

What are the possible side effects?\textsuperscript{19,44}

- Anemia
- Diarrhea
- Hypersensitivity
- Infusion reactions
- Nausea/vomiting
- Neutropenia
- Skin reactions (rash, acne, itching, nail changes, and infusion-related reactions)
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking irinotecan + cetuximab, contact your healthcare professional.
**Cetuximab (CETUXIMAB)**

**What is it?**
Cetuximab is a monoclonal antibody that specifically recognizes and binds to the epidermal growth factor receptor (EGFR) found on the surface of certain tumor cells.19

**What is it used for?**
Cetuximab is used to treat EGFR-expressing metastatic CRC with non-mutated (wild-type) KRAS after failure of chemotherapy regimens containing fluoropyrimidine, oxaliplatin, and irinotecan.19

**What does it do?**
Cetuximab binds to the epidermal growth factor receptor (EGFR) found on the surface of certain tumor cells, and as a result of this binding, the tumor cell can no longer receive the messages it needs for growth, progression and metastasis.19

**How is it given?**
Cetuximab is given into a vein (intravenously or *IV*).19

**How often is it given?**
Cetuximab alone is given once a week.19

---

**Cetuximab treatment schedule**

| Day 1  | Cetuximab: IV infusion over 2 hours | Once every week |

**What are the possible side effects?**

- Diarrhea
- Hypersensitivity
- Infusion reactions
- Skin reactions (rash, acne, itching, nail changes, and infusion-related reactions)

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking cetuximab, contact your healthcare professional.
Panitumumab (PANITUMUMAB)

What is it?
Panitumumab is a monoclonal antibody that recognizes and attaches to CRC cells that express epidermal growth factor receptor (EGFR).

What is it used for?
Panitumumab is used to treat EGFR-expressing metastatic CRC with non-mutated (wild-type) KRAS after failure of chemotherapy regimens containing fluoropyrimidine, oxaliplatin, and irinotecan.

What does it do?
Panitumumab recognizes and attaches to CRC cells that express EGFR, preventing the cancer cells from growing and dividing.

How is it given?
Panitumumab is given into a vein (intravenously or IV).

How often is it given?
Panitumumab is given once every two weeks.

Panitumumab treatment schedule

<table>
<thead>
<tr>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panitumumab: IV infusion over 1 hour</td>
</tr>
<tr>
<td>Once every 2 weeks</td>
</tr>
</tbody>
</table>

What are the possible side effects?
- Anemia
- Diarrhea
- Hypersensitivity
- Skin rash

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking panitumumab, contact your healthcare professional.
Capecitabine + Bevacizumab (CAPECITABINE + Bevacizumab)

What is it?
Capecitabine + bevacizumab is a chemotherapy combination containing capecitabine and bevacizumab (BEV). 25-26

What is it used for?
Capecitabine + BEV combination is used to treat metastatic CRC that has spread outside of the colon and/or rectum. 25

How is it given?
Capecitabine is available as tablets that are taken by mouth, and swallowed whole with water. BEV is given into a vein (intravenously or IV). 25

How often is it given?
Capecitabine tablets are taken within 30 minutes after the end of a meal (breakfast and dinner), twice a day (morning and evening doses), and BEV is given once every 14 days. 25

Capecitabine + bevacizumab treatment schedule 42

<table>
<thead>
<tr>
<th>Day 1-14</th>
<th>Capecitabine</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tablets taken twice a day (morning and evening doses) for 14 days within 30 minutes after the end of a meal (breakfast and dinner)</td>
<td>Taken twice daily on day 1 through 14 followed by 7-day rest, every 3 weeks</td>
</tr>
<tr>
<td>Day 1</td>
<td>Bevacizumab: IV infusion over 90 minutes (about 30 or 60 minutes after the first or second time)</td>
<td>Once every 3 weeks</td>
</tr>
</tbody>
</table>

What are the possible side effects? 42
- Abdominal abscess
- Arterial thromboembolism
- Diarrhea
- Gastrointestinal perforation
- Hand-and-foot syndrome
- Hypersensitivity
- Hypertension
- Infusion reactions
- Nausea/vomiting
- Thrombocytopenia
- Wound/healing complications

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking Capecitabine + bevacizumab, contact your healthcare professional.
5-FU/Leucovorin/Irinotecan/Oxaliplatin (FOLFOXIRI)

What is it?
FOLFOXIRI is a chemotherapy combination treatment containing 5-fluorouracil (5-FU), leucovorin (LV or folinic acid), irinotecan and oxaliplatin.

What is it used for?
FOLFOXIRI is used to treat advanced or metastatic CRC.

How is it given?
FOLFOXIRI is given into a vein (intravenously or IV).

How often is it given?
FOLFOXIRI is given every 2 weeks.

FOLFOXIRI treatment schedule

<table>
<thead>
<tr>
<th>FOLFOXIRI combination</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 Oxaliplatin + Irinotecan + LV IV infusion over 2 hours followed by 5-FU continuous IV infusion over 48 hours</td>
<td>Once every 2 weeks</td>
</tr>
</tbody>
</table>

What are the possible side effects?
- Anemia
- Diarrhea
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking FOLFOXIRI, contact your healthcare professional.
5-FU/Leucovorin/Irinotecan/Oxaliplatin + Bevacizumab (FOLFOXIRI + Bevacizumab)

What is it?
FOLFOXIRI + bevacizumab is a chemotherapy combination treatment containing 5-fluorouracil (5-FU), leucovorin (LV or folic acid), irinotecan, oxaliplatin and bevacizumab (BEV).13,16

What is it used for?
FOLFOXIRI + BEV combination is used to treat advanced or metastatic CRC. Addition of BEV to FOLFOXIRI combination increases treatment effectiveness.47

How is it given?
FOLFOXIRI + BEV combination is given into a vein (intravenously or IV).47

How often is it given?
FOLFOXIRI + BEV is given once every 2 weeks.47

FOLFOXIRI + Bevacizumab treatment schedule47

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab BEV IV infusion (first infusion over 90 minutes, second infusion over 1 hour, and subsequent infusions over 30 minutes) † followed by FOLFOXIRI</td>
<td></td>
</tr>
<tr>
<td>FOLFOXIRI Oxaliplatin + irinotecan + LV IV infusion over 2 hours † followed by 5-FU continuous IV infusion over 48 hours</td>
<td></td>
</tr>
</tbody>
</table>

What are the possible side effects?47

- Abdominal abscess
- Anemia
- Arterial thromboembolism
- Diarrhea
- Gastrointestinal perforation
- Hypertension
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia
- Stomatitis/mucositis
- Thrombocytopenia
- Wound/healing complications

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking FOLFOXIRI + bevacizumab, contact your healthcare professional.
Irinotecan/Capecitabine/Oxaliplatin (IXO)

What is it?
IXO is a chemotherapy drug combination consisting of irinotecan, capecitabine and oxaliplatin.\textsuperscript{25-26}

What is it used for?
IXO is used to treat metastatic CRC.\textsuperscript{48}

How is it given?
Capecitabine is available as tablets that are taken by mouth, and swallowed whole with water. Irinotecan and oxaliplatin are given into a vein (intravenously or IV).\textsuperscript{48}

How often is it given?
Capecitabine tablets are taken twice a day for 14 days. Irinotecan and oxaliplatin are infused once every 3 weeks.\textsuperscript{48}

IXO treatment schedule\textsuperscript{29,48}

<table>
<thead>
<tr>
<th>IXO combination</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td><strong>Oxaliplatin</strong>: IV infusion over 2 hours followed by <strong>Irinotecan</strong>: IV infusion over 1 hour</td>
</tr>
<tr>
<td></td>
<td>Once every 3 weeks</td>
</tr>
<tr>
<td>Day 1-14</td>
<td><strong>Capecitabine</strong>: Tablets taken twice a day (morning and evening doses) for 14 days within 30 minutes after the end of a meal (breakfast and dinner)</td>
</tr>
<tr>
<td></td>
<td>Capecitabine is taken in 21 day cycles - take capecitabine for 14 days and then stop taking it for 7 days</td>
</tr>
</tbody>
</table>

What are the possible side effects?\textsuperscript{48}
- Anemia
- Diarrhea
- Nausea/vomiting
- Neurotoxicity/neuropathy
- Neutropenia

Please see the Glossary for definition of side effects appearing in italics. To help you manage your side effects, please see Managing Side Effects section.

Talk to your healthcare professional if you have these symptoms. This is not a complete list of side effects. If you have any unexpected effects while taking IXO, contact your healthcare professional.
Managing Side Effects

This section is designed to help you manage side effects which you may have in response to your treatment as described under “What are the possible side effects?” in the Personalized Treatment Section of this guide. For your convenience, side effects with the tips on how to manage them are listed in alphabetical order below.

A

Abdominal pain: Management of abdominal pain depends on their cause and severity, and can be controlled with over-the-counter medications. Changes in diet in a way that helps either slow or speed the intestinal activity can help control, and in some cases prevent abdominal cramps. Dairy, soy, fat or wheat gluten products are not tolerated well by patients following treatment for CRC. Your healthcare professional can assist you in choosing the right over-the-counter medication, and making changes to your diet to help control or prevent abdominal pain.

Allergic reaction: See “Hypersensitivity/Allergic reaction”.

 Alopecia (hair loss): Usually new hair should regrow in the weeks or months after treatment. In some cases, it might not regrow, which is more common after radiotherapy than after chemotherapy. To help you cope with the hair loss consider the following: You may wish to cut your hair before it starts falling out as the experience of losing the hair is sometimes worse than dealing with it once it’s gone; for women, plan ahead and shop for a wig before your hair is gone, especially if you wish to match your natural color; wearing hats or head scarves are good alternatives or a compliment to a wig; avoid exposure to the sun, and cover your head or use sunscreen on your scalp. Skin that has been covered with hair may be particularly sensitive to UV rays; ask your insurance company if they cover the cost of the wig; treat your new hair gently once it grows back, and avoid chemicals, bleach, peroxide or colors. Consider getting involved in a “Look Good… Feel Better” program, a community-based, free, national service that teaches female cancer patients beauty techniques to help restore their appearance and self-image during chemotherapy and radiation treatments. For more information go to www.lookgoodfeelbetter.org.

Anemia: Anemia is the most common cause of tiredness, weakness or fatigue. To help deal with these symptoms get plenty of rest by taking naps during the day, and go to bed earlier than usual. Eat a well-balanced diet, and ask to speak to a nutritionist, who will help you choose good, strengthening foods that appeal to you; try to stay active and take short walks as light exercise may help; restrict unnecessary activities, save your energy by doing the things that are really important, and let others help you by taking over some chores and tasks.

Arterial thromboembolism: See “Thromboembolism”.

D

Dehydration: Dehydration is the lack of sufficient fluid in the body. Cancer patients must have adequate fluid to remove toxins from the body as well as proteins released by dying cells. Take in as much fluid as possible on a daily basis, but do not drink products containing electrolytes (such as sports drinks) unless instructed to do so by your healthcare professional. In cases of severe dehydration, hydration therapy through IV is usually administered in the hospital setting.

Diarrhoea: Avoid foods high in fibre (fresh fruit, raw vegetables, whole grains, bran, nuts, and seeds). Eat frequent small meals of cooked fruits/vegetables, rice, lean meats, fish or chicken, bananas, applesauce, toast; Eliminate milk and milk products, caffeine and alcohol; Avoid greasy, spicy or sugary foods; Drink plenty of fluids by increasing fluid intake as much as you can (8-12 oz cups/day). Take anti-diarrheal medications as prescribed by your health care professional or according to package instructions; For more dietary tips, ask your healthcare professional to refer you to a dietician. Comfort measures include: Sitz baths (a warm water bath where the water covers only the hips and buttocks); Use soothing wipes; Use haemorrhoid barrier creams as needed.

F

Fever: See “Neutropenia”.

Fibroleukemia: See “Neutropenia”.

G

Gastrointestinal perforation: Treatment usually involves surgery to repair the perforation (hole). Sometimes, a small part of the intestine must be removed. A temporary colostomy (a surgical procedure that brings one end of the large intestine out through the abdominal wall, and allows stools moving through the intestine drain into a bag attached to the abdomen) or ileostomy (a surgery to remove part or all of your small intestine that is blocked or diseased) may be needed. Antibiotics alone can be used in rare cases to treat patients whose perforations have closed on their own.

Hand-and-foot syndrome: Apply moisturizer to hands and feet liberally and often. Sit or lie on padded surfaces of chairs or mattresses. Raise legs whenever possible with cushions. Place a pillow between knees or wear pyjamas (prevents rubbing legs during sleep). Wear loose-fitting clothes and loose-fitting comfortable shoes. Avoid the following: Exposure of hands and feet to heat such as hot water, vigorous rubbing to palms and soles when washing or applying moisturizers; activities that cause rubbing of skin surfaces, any unnecessary walking, jogging or vigorous exercise; and walking with bare feet. To alleviate discomfort try cold packs and other cold on the affected areas procedures (avoid cold packs if you are on oxaliplatin-based chemotherapy regimen as it may make the neuropathy symptoms worse), and over-the-counter pain medication (e.g. acetaminophen). To help soothe dry, irritated skin, apply Udderly Smooth® Udder Cream or Bag Balm® ointment 2-3 times a day.

Headache: Over-the-counter medications such as acetaminophen, ibuprofen or aspirin may be prescribed to treat headache. If you have a bleeding disorder, you should avoid aspirin. Always talk to your healthcare professional before taking any medications.

Hepatotoxicity: Treatment-related liver problems might occur. You may experience nausea, jaundice, swollen abdomen, pain in the upper abdomen, or mental confusion as a result of chemotherapy-induced liver damage. There is no treatment for liver damage once it occurs. Your healthcare professional will advise you to stop taking any medications that are processed through the liver, and may prescribe medications that help reduce the symptoms of liver damage such as a diuretic to reduce fluid accumulation or swelling by making you urinate out extra fluid. If your liver is not functioning properly avoid the following: alcohol, acetaminophen, medications that have caused liver dysfunction in the past, and medications to treat high blood cholesterol levels, such as atorvastatin or simvastatin. Talk to your healthcare professional before changing any medications.
**Hypersensitivity/allergic reaction:** Medications such as antihistamines, epinephrine and steroids can be used to treat allergic reactions. Severe reactions may require other therapy, such as corticosteroids, oxygen therapy, narcotics, or pulmonary rehabilitation for breathing difficulties/shortness of breath or intravenous fluids to boost blood pressure in anaphylactic shock. To help manage breathing difficulties, there are things you can do every day such as: relaxation techniques to control your breathing (meditation, yoga, or deep breathing exercises); promote oxygenation (air circulation) throughout your lungs to help prevent infection and pneumonia with breathing exercises or physical activity; use a spirometer, a device that makes you breathe slowly and deeply, to maintain oxygenation; find a kind of exercise that you can tolerate and do it daily; avoid smoking and smoke-filled environments; and reduce anxiety and manage stress.

It is difficult to predict which patients will develop an allergic reaction to their CRC therapies, which makes it difficult to prevent. If you develop a treatment-related allergic reaction, talk to your healthcare professional about available remedies that are right for you.

**Hypertension** (high blood pressure): High blood pressure can develop temporarily as a result of treatment for CRC. You may experience rapid pulse, fluid retention, headache, or other symptoms of high blood pressure. To help lower blood pressure, engage in regular aerobic exercise, weight reduction (if overweight) and salt restriction. If your blood pressure is still high after you tried these options, your healthcare professional may prescribe antihypertensive medications designed to lower blood pressure.

**Infection:** See “Neutropenia”.

**Infusion reactions:** See “Hypersensitivity/”.

**Mucositis:** See “Stomatitis/mucositis”.

**Nausea/vomiting:** The following tips can help you manage nausea and vomiting. **Eating tips:** If your treatment causes nausea, do not eat for at least 1 to 2 hours before treatment, or eat a light meal before your treatment; eat what appeals to you, and don’t force yourself to eat unappealing foods; in place of larger meals, eat more frequent and smaller meals and snacks before hunger sets in since feelings of hunger can make your nausea worse; avoid foods that have a strong odour, are high in fat, or are fried, spicy, or very sweet; rest after eating, sitting up rather than lying down; and if you have morning nausea, try eating dry foods like cereal, toast, or crackers, unless you have sores in your throat or mouth, or very little saliva.

**Drinking tips:** Limit drinks that leave you feeling bloated; drink slowly, with a straw if it helps you to drink more slowly; drink room-temperature liquids frequently, and in small amounts; and drink cool (not cold) re: may exacerbate neuropathy), clear, unsweetened juices or flat, light-coloured soft drinks without caffeine.

Foods that are easy on your stomach include canned fruit, cooked cereal, rice, noodles, potatoes, clear liquids (sports drinks, clear soft drinks such as ginger ale), tea, broth, and water.

If you are vomiting, avoid eating or drinking until it’s under control, then try small amounts of clear liquids and work up to a full liquid diet or a soft diet. If you have nausea and vomiting that is severe or lasts more than a day, or you can’t keep liquids down, contact your healthcare professional, and he or she may suggest antinausea medication or other treatment.

For more dietary tips, ask your healthcare professional to refer you to a dietitian.

**Neurotoxicity/neuropathy:** During infusion, wear a blanket to keep warm; Avoid activities that require you to go outdoors during cold weather, and if you go out, make sure you dress warmly; Cover your skin before you enter cold places; Don’t touch cold surfaces or objects, or wash your hands with cold water; Avoid breathing in deeply when exposed to cold air outside or to air conditioners; Do not use ice to soothe mouth sores or ease nausea; and Avoid eating frozen or cold foods, and drinking cold beverages or using ice.

**Neutropenia** (low white blood cell count): Rarely, cancer patients may experience neutropenia, which includes infections and fevers/fatal neutropenia, from chemotherapy or as a result of their underlying cancer. Depending on the cause of neutropenia, your healthcare professional will determine the treatment that is right for you. If the fever is determined to be related to an infection, treatment will be prescribed for the infection. For a bacterial infection, antibiotics are usually prescribed; for viral infections, the usual treatment is often rest and plenty of fluids, although antiviral drugs may be used to treat some viruses. If an infection-related fever is very high, over-the-counter medications such as acetaminophen, ibuprofen may be prescribed to reduce the fever and associated discomfort. If you have a bleeding disorder, you should avoid these medications. Always talk to your healthcare professional before taking any medications. While it may be difficult to prevent fevers resulting from infections due to neutropenia, some measures to help prevent infections may include: avoiding scratches and cuts via gentle handling of the skin, frequent hand-washing, patting skin dry rather than rubbing, thorough cooking of food, reducing human contact so as to reduce the potential of contracting an infection: and avoiding gardening and handling pets.

**P**

**Pain** (joint, muscle, bone, chest/thorax, abdomen, head/headache, or rectum): Medications can be used for pain relief, and are usually selected according to the needs of the patient. For some kinds of pain related to cancer: non-prescription over-the-counter medications such as acetaminophen, ibuprofen, may be sufficient. For other degrees and kinds of pain, prescription medications are used. Your healthcare professional will determine which type of medication is appropriate for your type of pain.

**Pulmonary embolism** : “Thromboembolism”.

**S**

**Skin rash:** See “Hypersensitivity/allergic reaction”.

**Skin reactions** (rash, itching, nail changes, and infusion-related reactions): See “Skin reaction/ acne”.

**Skin reaction/ acne:** For skin reactions, use lotions that do not contain alcohol to cool the skin. If your rash is a result of an allergic reaction to a drug, your healthcare professional may stop the drug. For minor, non-allergic skin reactions, your healthcare professional may recommend one of the following: corticosteroid cream to reduce help inflammation; antihistamine to help reduce symptoms of an allergic reaction; such as rash, hives and shortness of breath; analgesics, over-the-counter medications such as acetaminophen or aspirin, to help relieve pain associated with a rash. To help manage a rash: Wear loose, non-binding clothing; use mild soap without perfumes; dry your skin carefully after bathing; avoid harsh chemicals; protect your skin from the sun with sunscreens or long, loose clothing; try not to scratch, and talk to your healthcare professional about anti-acne medications.

**Stomatitis/mucositis:** For the treatment of stomatitis (mouth sores): Practice good oral care by frequently rinsing the mouth with saline/salt water and brushing teeth 2-3 times per day, mouthwashes (salt and soda mouthwash can help relieve mouth sores as well as medicated mouthwash; suck on ice chips to minimize the damage from chemotherapy drugs (avoid cold packs if you are on oxaliplatin-based chemotherapy regimen as it may make the neurotoxicity symptoms worse), avoid very hot foods, carbonated beverages, and eat soft foods until the sores heal. For the treatment of mucositis (inflammation of the mucosa) whether in the mouth, pharynx, esophagus, trachea, bowel, bladder or rectum: Avoiding irritation by keeping food or stools soft and preventing trauma of any kind: use local analgesic (pain-killing) mixtures, antibiotics or steroids; keep hydrated by taking in fluids; and eat foods low in fibre if you have bowel reaction.
Thrombocytopenia: Low platelet count. Platelets are the cells that form blood clots that stop bleeding. Low platelet count can cause bleeding. Check with your healthcare professional before taking any kind of medication, vitamin, or pill. Some medications like ASA (Aspirin) can affect blood clotting, and contribute to bleeding. To help prevent bleeding: Use a very soft toothbrush or cotton swab; blow your nose gently, and use a very soft tissue; try not to cut or nick yourself with any sharp items, and if you shave, switch to an electric razor; and avoid activities that could cause an injury, like contact sports.

Thromboembolism: If you are at risk for blood clot formation as a result of your CRC treatment, your healthcare professional will prescribe anticoagulant drug such as warfarin or heparin to help prevent blood clots.

For more information on description/symptoms, cause, remedy/treatment, and prevention of side effects, and ways to manage them, visit Colorectal Cancer Association of Canada website at www.colorectal-cancer.ca/en/treatments/addressing-effects/.

Talk to your healthcare professional if you have additional questions or need more information on your possible side effects and how to manage them.

**Colorectal Cancer Glossary**

*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 a normal cellular reactions but different enough to interfere with cell division and function). Also see Fluorouracil.

*5-FU* See 5-fluorouracil.

**A**

*Abdomen* The area of the body that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs.

*Abdominal* Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs.

*Abscess* An enclosed collection of pus in tissues, organs, or confined spaces in the body. An abscess is a sign of infection and is usually swollen and inflamed.

*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 or other therapy. Also see Neoadjuvant therapy.

*Alopecia* The lack or loss of hair from areas of the body where hair is usually found. Alopecia can be a side effect of some cancer treatments.

*Anemia* A condition in which the number of red blood cells is below normal, resulting in a reduction in the amount of oxygen that can be carried to the various body parts and tissues, causing fatigue or tiredness, weakness, trouble breathing, rapid heartbeat, dizziness, lightheadedness, inability to concentrate, or headache.

*Antibody* A protein made by plasma cells (a type of white blood cell) in response to an antigen (a substance that causes the body to make a specific immune response). Each antibody can bind to only one specific antigen. The purpose of this binding is to help destroy the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. Also see Monoclonal antibody.

*Arterial thromboembolism* The blocking of an artery by a clot of foreign material. This can be done as treatment to block the flow of blood to a tumour. Also called embolization.

**B**

*Bevacizumab* It is not chemotherapy but is given in combination with a specific type of chemotherapy. While chemotherapy attacks the tumour directly, bevacizumab which is a monoclonal antibody attacks the blood vessels that surround the tumour. In order to grow and spread, tumours need a constant supply of oxygen and other nutrients. Tumours get this supply by creating their own network of blood vessels. This process is called angiogenesis, and bevacizumab works by blocking angiogenesis. By preventing the growth of new blood vessels, bevacizumab helps starve the tumour of oxygen and other nutrients. This makes it hard for the tumour to grow.

*BEV* see Bevacizumab.

*Biomarker* Also called molecular marker, is a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. Also called molecular marker.

*Biomarker Testing* A test of blood, or other body fluid or tissues done to look for a biomarker of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition.
**Biopsy**: A procedure in which a sample of cancereous tissue is removed for analysis under the microscope to help precisely diagnose the type of cancer and its grade.

**Bolus**: A single dose of a drug or other substance given over a short period of time. It is usually given by infusion or injection into a blood vessel. It may also be given by mouth.

**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.

**BRAF** gene: A gene that makes a protein called B-RAF, which is involved in sending signals in cells and in cell growth. This gene may be mutated (changed) in many types of cancer, which causes a change in the B-RAF protein. This can increase the growth and spread of cancer cells.

**BRAF Mutation**: A mutation in the BRAF gene that makes patients with colorectal cancer non-responsive to treatments with cetuximab and panitumumab.

**Cancer**: A term to describe diseases in which abnormal cells divide uncontrollably and can invade nearby tissues. Also called malignancy.

**Capcitabine**: Belongs to a family of medications called the fluoropyrimidines (medications that interfere with the growth of cells that rapidly divide in the body, including cancer cells). Capcitabine is an inactive substance on its own. When capcitabine is taken, it is changed in the body, mostly within the tumour (cancer cells), to become the commonly used cancer medication called 5-fluorouracil (also known as 5-FU). In some patients 5-FU will kill cancer cells and decrease the size of the tumour.

**Carcinoma in situ**: Also called stage 0 cancer, it is a group of abnormal cells that are confined to the place in the body where they first formed, and do not spread. These abnormal cells may become cancerous and spread into nearby normal tissue. In the bowel, in-situ carcinoma is typically seen on the surface of a polyp.

**Cell**: The individual unit that makes up the tissues of the body. All living things are made up of one or more cells.

**Cetuximab**: A monoclonal antibody that recognizes and attaches to colorectal cancer cells that express epidermal growth factor receptor (EGFR); with non-mutated (wild-type) KRAS after failure of chemotherapy regimens containing fluoropyrimidine, oxaliplatin, and irinotecan; and prevents the cancer cells from growing and dividing.

**Chemoradiation**: Treatment that combines chemotherapy with radiation therapy. Also called chemoradiotherapy.

**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.

**Colorectal**: Having to do with the colon or the rectum.

**Colorectal cancer**: Cancer that develops in the colon (the longest part of the large intestine) and/or the rectum (the last several inches of the large intestine before the anus). Also referred to as CRC.

**CRC**: See Colorectal cancer.

**Diabetes**: A condition caused by the loss of too much water from the body. Severe diarrhea or vomiting can cause dehydration.

**Differentiation** (differentiated): In cancer, refers to how mature (developed or differentiated) the cancer cells are in a tumour. Differentiated tumour cells resemble normal cells and tend to grow and spread at a slower rate than undifferentiated or poorly differentiated tumour cells, which lack the structure and function of normal cells and grow uncontrollably.

**DNA**: The molecules inside cells that carry genetic information and pass it from one generation to the next. Also called deoxyribonucleic acid.

**EGFR**: The protein found on the surface of some cells and to which epidermal growth factor binds, causing the cells to divide. It is found at abnormally high levels on the surface of many types of cancer cells, so these cells may divide excessively in the presence of epidermal growth factor. Also called epidermal growth factor receptor, ErbB1, and HER1.

**Embolism**: A block in an artery caused by blood clots or other substances, such as fat globules, infected tissue, or cancer cells.

**Epidermal growth factor receptor** receptor: see EGFR

**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.

**Febrile neutropenia**: A condition marked by fever and a lower-than-normal number of neutrophils in the blood. A neutrophil is a type of white blood cell that helps fight infection. Having too few neutrophils increases the risk of infection. Also see Neutropenia.

**Fluoropyrimidines**: One of a group of substances used to treat cancer. A fluoropyrimidine is a type of antimetabolite drugs such as capcitabine and fluorouracil (5-FU).

**Fluorouracil**: Anticancer drug used to treat symptoms of cancer of the colon, breast, stomach, or pancreas. It is also used in a cream to treat certain skin conditions. Fluorouracil stops cells from making DNA and it may kill cancer cells. It is a type of antimetabolite which interferes with cell growth. Also called 5-fluorouracil and 5-FU.

**Gastrointestinal**: Refers to the stomach and intestines. Also called GI.

**Gastrointestinal perforation**: A hole that develops through the entire wall of the stomach, small intestine, large bowel, or gallbladder.

**Gene**: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein.

**Hand-and-foot syndrome**: A condition marked by pain, swelling, numbness, tingling, or redness of the hands or feet. It sometimes occurs as a side effect of certain anticancer drugs. Also called palmar-plantar erythrodysesthesia.
**Hepatotoxicity**: Poisonous or harmful to the liver. Hepatic refers to the liver, and toxicity is the extent to which something is poisonous or harmful.

**HIPEC**: See Hyperthermic Intraperitoneal Chemotherapy.

**Hypersensitivity**: An exaggerated response by the immune system to a drug or other substance. Also called an allergic reaction.

**Hypertension**: A blood pressure of 140/90 or higher. Hypertension usually has no symptoms. It can harm the arteries and cause an increase in the risk of stroke, heart attack, kidney failure, and blindness. Also called high blood pressure.

**Hyperthermic Intraperitoneal Chemotherapy** (or **HiPEC**): is used for cancers that are confined to the peritoneal (abdominal) cavity and are otherwise difficult to treat with other available treatments. HiPEC is a treatment option for patients whose cancers are difficult to treat such as those that spread to the lining surfaces of the peritoneal cavity from primary colorectal cancer. “Intraperitoneal” means that the treatment is delivered to the abdominal cavity, and term “Hyperthermic Chemotherapy” means that the solution containing chemotherapy (anticancer drugs) is heated to a temperature that is higher than normal body temperature.

**Immune system**: The complex group of organs and cells that defends the body against infections and other diseases.

**Inflammation**: Redness, swelling, pain, and/or a feeling of heat in an area of the body. This is a protective reaction to injury, disease, or irritation of the tissues.

**Infusion**: A method of injecting fluids, including drugs, into the bloodstream. Also called intravenous infusion.

**Intra-abdominal**: Inside the abdomen (the area of the body that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs).

**Intravenous**: Giving chemotherapy drug into a vein. Also called intravenously or IV.

**Irinotecan**: Anticancer drug that works by killing rapidly dividing cells, such as cancer cells.

**IV**: See Intravenous.

**K**

**KRAS gene**: A gene that may cause cancer when it is mutated (changed). The KRAS gene makes the KRAS protein, which is involved in cell signaling pathways, cell growth, and apoptosis (cell death). Agents that block the activity of the mutated KRAS gene or its protein may stop the growth of cancer. Also called K-ras gene.

**KRAS mutation**: A change (or mutation) in the KRAS gene, which when mutated can lead to cancer. A mutation in this gene makes patients with colorectal cancer non-responsive to treatments with cetuximab and panitumumab. Also see Gene and KRAS gene.

**Leucovorin**: Given together with anticancer drugs such as fluorouracil, to help lessen the toxic effects of these medications, thus “rescuing” the patient while permitting the anticancer activity of the drugs like FU. It also enhances the effects of fluorouracil and its derivatives by stabilizing the binding of the drug’s metabolite to its target enzyme, thus prolonging drug activity. Also called LV or folinic acid.

**Liver metastasis**: Cancer that has spread from the original (primary) tumour to the liver.

**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.

**LV**: See Leucovorin.

**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 maligns are involved in colorectal (bowel) cancers, the Stage automatically becomes 3 (or 4 if distant organs are also involved).

**M**

**Malignant**: Cancerous. Malignant cells can invade and destroy nearby tissue and spread to other parts of the body.

**Metastasis** (or metastases): The spread of cancer from one part of the body to another. A tumour formed by cancerous cells that have spread from its original location is called a “metastatic tumour” or a “metastasis” or the plural form, “metastases”, if there is more than one. The metastatic tumour contains cells that are like those which came from the original (primary) tumour.

**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.

**Mitomycin C**: Anticancer drug that damages DNA, preventing cell division, which leads to cancer cell death.

**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, including cancer cells. There are many kinds of monoclonal antibodies. Each monoclonal antibody is made to find one substance. Monoclonal antibodies are designed to target the malignant (cancerous) cells that form the tumour, and are used to treat some types of cancer. Also see Targeted therapy.

**Mucosa**: Also called mucous membrane is the moist, inner lining of some organs and body cavities such as the nose, mouth, lungs, and stomach. Glands in the mucus make mucous (a thick, slippery fluid).

**Mucocutaneous**: A complication of some cancer therapies in which the lining of the digestive system becomes inflamed. Often seen as sores in the mouth or stomatitis.

**Mucous membrane**: The moist, inner lining of some organs and body cavities (such as the nose, mouth, lungs, and stomach). Glands in the mucus produce mucus (a thick, slippery fluid). Also called mucosa.

**Mucous membrane**: The moist, inner lining of some organs and body cavities (such as the nose, mouth, lungs, and stomach). Glands in the mucus produce mucus (a thick, slippery fluid). Also called mucosa.

**Mutation**: Any change in the DNA of a cell. Mutations may be caused by mistakes during cell division, or they may be caused by exposure to DNA-damaging agents in the environment. Mutations can be harmful, beneficial, or have no effect. If they occur in cells that make eggs or sperm, they can be inherited. If mutations occur in other types of cells, they are not inherited. Certain mutations may lead to cancer or other diseases.

**N**

**Neoadjuvant therapy**: Treatment given before the primary surgical treatment. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, or other therapies. Neoadjuvant therapy is usually given to make the surgery easier and more effective. Also see Adjuvant therapy.

**Neurology** (or neurologic): Having to do with nerves or the nervous system.

**Neuropathy**: A nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse over time. Neuropathy may be caused by physical injury, infection, toxic substances, disease (such as cancer, diabetes, kidney failure, or malnutrition), or drugs, including anticancer drugs. Also called peripheral neuropathy.
Neurotoxicity: The tendency of some treatments to cause damage to the nervous system.

Neutropenia: A condition in which there is a lower-than-normal number of neutrophils (a type of white blood cell). See Febrile Neutropenia.

Oxaliplatin: Anticancer drug which attaches to the DNA (genetic material contained in the cell) and interferes with cell division, causing the eventual death of the cancer cell.

Palliative care: A specialized area of healthcare that focuses on relieving and preventing the suffering of patients, and is given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of palliative care is to prevent or treat as early as possible the symptoms of a disease, side effects caused by treatment of a disease, and psychological, social, and spiritual problems related to a disease or its treatment. Also called comfort care, supportive care, and symptom management. Unlike hospice care, palliative medicine is appropriate for patients in all disease stages, including those undergoing treatment for curable illnesses and those living with chronic diseases, as well as patients who are nearing the end of life.

Panitumumab: A monoclonal antibody that recognizes and attaches to colorectal cancer cells that express epidermal growth factor receptor (EGFR) with non-mutated (wild-type) KRAS after failure of chemotherapy regimens containing fluoropyrimidines, oxaliplatin, and irinotecan, and prevents the cancer cells from growing and dividing.

Partial liver resection for colorectal liver metastasis: Surgery to remove tissue or part of an organ, in this case a liver, to which cancer has spread.

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).

Protein: A molecule made up of amino acids that are needed for the body to function properly. Proteins are the basis of body structures such as skin and hair and of substances such as enzymes, cytokines, and antibodies.

Proteinuria: Higher-than-normal amount of protein in the blood.

Pseudo-adjuvant chemotherapy: Beyond partial liver resection, the rationale for pseudo-adjuvant chemotherapy lacks scientific evidence, despite some promising data.

Pulmonary: Having to do with the lungs.

Pulmonary embolism: A block in an artery of the lung caused by blood clots or other substances, such as fat globules, infected tissue, or cancer cells.

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 tumours. Also see External beam radiation therapy and brachytherapy.

Radioactive: A substance that gives off radiation.

Radiochemotherapy: Cancer treatment, in which chemotherapy (5-FU or capecitabine) combined with radiation therapy, is used before surgery to improve the chances of better tumour control and reduce local recurrences (cancer from coming back).

Recurrence: Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumour or to another place in the body. Also called recurrent cancer.

Recurrent cancer: See Recurrence.

Resistant cancer: Cancer that does not respond to treatment. The cancer may be resistant at the beginning of treatment, or it may become resistant during treatment. Also called refractory cancer.

Stomatitis: Inflammation (redness, swelling, pain, and/or a feeling of heat) or irritation of the mucous membranes in the mouth. Mucous membrane, also called mucosa, is the moist, inner lining of the mouth.

Targeted therapy: A type of treatment that uses drugs or other substances, such as monoclonal antibodies, to find and attack specific cancer cells. Targeted therapy may have fewer side effects than other types of cancer treatments.

Thromboembolism: Formation in a blood vessel of a clot (thrombus) that breaks loose and is carried by the blood stream to plug another vessel. The clot may plug a vessel in the lungs (pulmonary embolism), brain (stroke), gastrointestinal tract, kidneys, or leg. Thromboembolism is an important cause of morbidity (disease) and mortality (death), especially in adults. Treatment may involve anticoagulants (bloodthinners), aspirin, or vasodilators (drugs that relax and widen vessels).

Toxicity: The extent to which something is poisonous or harmful.

Toxin: A poison made by certain bacteria, plants, or animals, including insects.

Tumour: An abnormal mass of tissue that results when cells divide more than they should or do not die when they should. Tumours may be benign (not cancer), or malignant (cancer). Also called neoplasm.

Vascular endothelial growth factor: Also called VEGF, is a molecule that helps new blood vessels to form. The receptor is the part of the cell that receives the VEGF signal. Identifying these polymorphisms may help doctors to decide to use targeted therapies against VEGF for this subgroup of people with colon cancer.

VEGF: See vascular endothelial growth factor.

Wound: A break in the skin or other body tissues caused by injury or surgical incision (cut).
Canadian Resources for Patients


For more useful links to various resources, please visit Colorectal Cancer Association of Canada at www.colorectal-cancer.ca.

References


10. Wong R, Berry S, Spiholt K, et al. Preoperative or Postoperative Therapy for the Management of Patients with Stage II or III Rectal Cancer: Guideline Recommendations. A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO) Evidence-Based Series #2: Section 1, Report Date: July 15, 2008.


Ongoing Research and the Future of Treatment

Ongoing research in CRC has lead to advances in treatment and new ways to manage side effects related to treatment, which helped improved 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 CRC.

Ongoing research in CRC can be found in ClinicalTrials.gov, a registry and results database of federally and privately supported clinical trials conducted in the United States and around the world. By visiting ClinicalTrials.gov website at clinicaltrials.gov, you can find information about the purpose of a trial, who may participate in it, locations where it is being conducted, and phone numbers for more details. This information should be used together with advice from your healthcare professionals.

For more information about ongoing research and development in CRC, you can also visit Canadian Cancer Encyclopedia from the Canadian Cancer Society at info.cancer.ca or Colorectal Cancer Association of Canada at www.colorectal-cancer.ca.

Where to find Support…

If you or someone close to you has been newly diagnosed with CRC or in active treatment, you don’t have to go through this alone.

CRC support groups exist in several communities across Canada which 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.1,2

Help is available…

Canadian Cancer Society: For more information or to find a support group in your area, contact the Canadian Cancer Society by calling toll-free number at 1-888-939-3333, or visit the website www.cancer.ca and click on Support/Services tab.1,2

Colorectal Cancer Association of Canada: For information about support groups in your area, call toll-free number 1-877-50COLON (26566), or visit the website at www.colorectal-cancer.ca.1,2