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Survey

2018

Colon Cancer

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Colon Cancer

LEARNING that you have cancer can be overwhelming.

The goal of this book is to help you get the best care. It explains which cancer tests and treatments are recommended by experts in colon cancer.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 28 leading cancer centers. Experts from NCCN have written treatment guidelines for doctors who treat colon cancer. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of colon cancer in adults. Key points of the book are summarized in the related NCCN Quick Guide™. NCCN also offers patient resources on lung, melanoma, and many other cancer types. Visit NCCN. org/patients for the full library of patient books, summaries, and other patient and caregiver resources.

About





These patient guidelines for cancer care are produced by the National Comprehensive Cancer Network® (NCCN®).

The mission of NCCN is to improve cancer care so people can live better lives. At the core of NCCN are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). NCCN Guidelines® contain information to help health care workers plan the best cancer care. They list options for cancer care that are most likely to have the best results. The NCCN Guidelines for Patients® present the information from the NCCN Guidelines in an easy-to-learn format.

Panels of experts create the NCCN Guidelines. Most of the experts are from NCCN Member Institutions. Their areas of expertise are diverse. Many panels also include a patient advocate. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors.

For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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NCCN Foundation was founded by NCCN to raise funds for patient education based on the NCCN Guidelines. NCCN Foundation offers guidance to people with cancer and their caregivers at every step of their cancer journey. This is done by sharing key information from leading cancer experts. This information can be found in a library of NCCN Guidelines for Patients® and other patient education resources. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of cancer research, education, and progress of cancer therapies.

For more information about NCCN Foundation, visit NCCNFoundation.org.

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As an organization dedicated to helping patients, caregivers, and those impacted by colorectal cancer find trusted resources and information they need to make informed decisions about their health, we are proud to support this comprehensive resource. FightColorectalCancer.org



NCCN Guidelines for Patients®: Colon Cancer, 2018

Colon Cancer

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cancer

areas.

Presents the recommended care after colon cancer treatment.

Presents treatment options for colon cancer that has spread to the liver, lungs, or other

Treatment guide: Metastatic

How to use this book

Who should read this book?

This book is about treatment for colon cancer. It does not discuss rectal cancer. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It is a good starting point to learn what your options may be.

The treatment options are based on science and the experience of NCCN experts. However, their recommendations may not be right for you. Your doctors may suggest other options based on your health and other factors. If other options are given, ask your treatment team questions.

Are the book chapters in a certain order?

Early chapters explain concepts that are repeated in later chapters. Starting with **Part 1** may help. It explains what colon cancer is. It also explains how colon cancer is found and given a stage. Your treatment plan will be partly based on the cancer stage. Tests that help doctors plan treatment are described in **Part 2**.

An overview of treatments for colon cancer is presented in **Part 3**. Knowing what a treatment is will help you understand the treatment options presented in **Parts 4 and 5**. Recommendations for follow-up care are provided in **Part 6**, and **Part 7** lists the systemic therapy treatment options for advanced colon cancer. Tips for talking and deciding your options with your doctor are presented in **Part 8**.

Help! What do the words mean?

In this book, many medical words are included. These are words you will likely hear from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don't be discouraged as you read. Keep reading and review the information. Feel free to ask your treatment team to explain a word or phrase that you don't understand. Words that you may not know are defined in the text or in the *Dictionary. Acronyms* are also defined when first used and in the *Glossary*. One example is DNA for deoxyribonucleic acid.

Does this book include all options?

This book includes information for many people. You treatment team can point out what applies to you. They can also give you more information. While reading, make a list of questions to ask your doctors.

1 Colon cancer basics

- 8 The colon
- 10 How cancer works
- 11 Polyps
- 12 Cancer staging
- 12 Review



You've learned that you have colon cancer. It's normal to feel shocked and confused. This chapter will give you some basic information about cancer and how it affects the colon.

The colon

The colon is part of the digestive system. This system breaks down food for the body to use. After being swallowed, food moves through four organs known as the digestive tract. **See Figure 1.** First, food passes through the esophagus and into the stomach, where it is turned into a liquid. From the stomach, food enters the small intestine. Here, food is broken down into very small parts to allow nutrients to be absorbed into the bloodstream.

Food then moves into the large intestine, which turns unused food from a liquid into a solid by absorbing water. This solid, unused food is called feces or stool. The large intestine has four parts, including the colon. **See Figure 2**.

- Cecum. This pouch is the first part of the large intestine. Food comes here first after leaving the small intestine. It is around the size of a small orange. Sticking out from the cecum is a skinny tube called the appendix. It is closed at one end, and is about the size of a finger.
- Colon. The colon is the longest part of the large intestine. It is almost 5 feet long and has four parts: the ascending, transverse, descending, and sigmoid colon.
- **Rectum.** This is the last part of the large intestine, and is about 5 inches long.

Anus. The anus is the opening at the bottom of the rectum. This is where stool leaves the body.

The wall of the colon has four main layers. The names of the layers (from inner to outer) are the mucosa, submucosa, muscularis propria, and serosa or adventitia. Cancer starts in the inner layer and grows towards the outer layer. You don't need to remember the names of each layer, but having a general idea of the structure will be helpful to understand how colon cancer is staged.

Figure 1 The digestive tract

The digestive tract consists of four main parts. The esophagus moves food from your throat to your stomach. In the stomach, food is turned into a liquid. Nutrients from the liquid are absorbed into your body in the small intestine. The large intestine absorbs liquid from and pushes unused food out of the body.

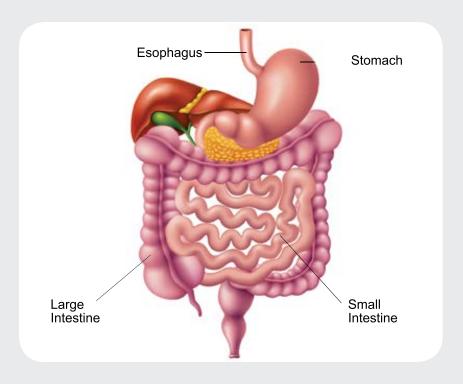
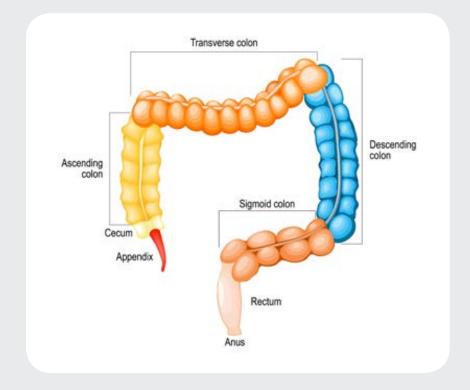


Figure 2 The colon

The colon is part of the large intestine. It is almost 5 feet long and has four sections: the ascending, transverse, descending, and sigmoid colon.



How cancer works

Your body is made of over 30 trillion cells. All cells have built-in rules that tell them how to act. These rules, or instructions, are called genes. Genes are a part of your DNA (deoxyribonucleic acid). Changes (called mutations) in genes cause normal cells to become cancer cells.

Cancer cells don't act like normal cells. **See Figure 3**. The three most important differences between cancer cells and normal cells are:

- Normal cells grow and then divide to make new cells when needed. They also die when old or damaged. Cancer cells make new cells that aren't needed and don't die quickly when old or damaged. Over time, cancer cells form a lump called a tumor.
- Normal cells listen to signals from nearby cells telling them to "stop" when they get too close. Cancer cells ignore the "stop" signals from nearby cells and invade nearby tissues.
- Normal cells stay in the area of the body where they belong. For example, stomach cells stay in the stomach. Cancer cells can travel to other parts of your body (metastasize). They can then grow and make more tumors in the new area of your body.

Figure 3 Key differences between normal cells and cancer cells



Polyps

A polyp is an overgrowth of cells that line the inner colon wall. While most colon polyps do not become cancer, almost all colon cancers start in a polyp. The two main shapes of polyps are called sessile and pedunculated. Pedunculated polyps are shaped like mushrooms and stick out from the colon wall. They have a stalk and round top. **See Figure 4**. Sessile polyps are flatter, don't stick out much from the colon wall, and don't have a stalk. **See Figure 5**.

Just like there are different shapes of polyps, there are also different types. This means that they look different under a microscope. Some types are more likely to turn into cancer than others. Polyps that are highly unlikely to turn into cancer include hyperplastic and inflammatory polyps.

The most common type of polyp is called an *adenoma*. Adenomas are considered "pre-cancer" because, while it may take many years, they can turn into cancer. This is the type to be concerned about. Serrated is a term for any polyp that has a saw-tooth pattern. Sessile serrated adenomas are rare but have been linked to cancer.

Polyps need to be removed and tested for cancer. Most polyps can be removed during a colonoscopy, using a minor surgical procedure called a polypectomy.

Figure 4 Pedunculated polyp

Pedunculated polyps (shown here) have a stalk and are mushroom-like in appearance.



Figure 5 Sessile polyp

Sessile polyps (shown here) don't have a stalk and can be harder to spot than pedunculated polyps.



Cancer staging | Review

Cancer staging

A cancer stage is a rating by your doctors of the extent of the cancer. It is used to plan which tests may be needed and which treatments are best for you. The AJCC (American Joint Committee on Cancer) TNM (tumor, node, metastasis) system is used to stage colon cancer.

In the AJCC system, the following key pieces of information about your cancer are used to give it a stage:

- > T: How far the cancer has grown through the colon wall
- > N: Whether any lymph nodes have cancer
- ➤ **M**: Whether the cancer has spread to areas far from the colon (metastasized)

The T, N, and M scores are combined to assign the cancer a stage. There are five stages of colon cancer. They are numbered 0, I (1), II (2), III (3), or IV (4). The stages are explained below.

Stage 0

These cancers are also called carcinoma in situ of the colon. The cancer is noninvasive. This means it has not grown beyond the first layer of the colon wall. You may not need more treatment if a polypectomy removed all of the cancer.

Stage I

The cancer has grown into either the second or third layer of the colon wall. There is no cancer in nearby lymph nodes or in areas far from the colon.

Stage II

The cancer has grown into, or beyond, the fourth layer of the colon wall. There is no cancer in nearby lymph nodes or in areas far from the colon.

Stage III

The cancer has spread from the colon to nearby lymph nodes or there are tumor deposits. Tumor deposits are small tumors in the fat around the colon.

Stage IV

The cancer has spread to areas far from the colon. Colon cancer often spreads to the liver and the lungs first.

Review

- The colon is the longest part of the large intestine and has four parts: the ascending, transverse, descending, and sigmoid colon.
- Cancer starts on the inside of the colon wall and grows toward the outside.
- Cancer cells form a tumor since they don't grow and die as normal cells do.
- Cancer cells can spread to other body parts through lymph or blood. This is called metastasis.
- Most colon cancers start in polyps called adenomas.
- The cancer stage is a rating of how much cancer there is in your body.

2 Treatment planning

14 **Health history** Physical exam 16 16 **Biopsy** 17 Colonoscopy 18 **Blood tests Imaging tests** 18 21 **Tumor marker testing** Review 22



Your doctors will make a treatment plan just for you. First, they need to gather information about your unique cancer and your general health. This chapter goes over the tests you may need to have done and other steps needed to create your treatment plan.

There are a number of tests that can provide your doctors with helpful information about which treatments might help you the most, and which treatments might be too harsh for you. The health tests you may have before treatment are described next. Some tests are for anyone with colon cancer, while others are for a select group.

Health history

Your medical history includes any health events and medicines you've taken in your life. It helps your doctors decide if you can have surgery. It also helps doctors decide if chemotherapy is a good treatment option for you.

Colon cancer and other diseases can run in families. For this reason, your doctor will ask about the medical history of your blood relatives. It's important to know who in your family has had what diseases and at what ages. You doctor may ask about the health of your siblings, your parents and their siblings, and your grandparents and their siblings.

Inherited cancer syndromes

Colon cancer often occurs for unknown reasons. Some people, however, are more likely to get colon cancer than the average person. This is because a gene mutation in their DNA was passed down to them from their parents. Because of this mutation, they have a disorder that increases their risk of getting colon cancer. This is called an inherited cancer syndrome. There are two main inherited cancer syndromes for colon cancer—Lynch syndrome and FAP (familial adenomatous polyposis).

Lynch syndrome is also called HNPCC (hereditary non-polyposis colon cancer). It's the most common type of inherited syndrome to cause colon cancer. It also increases the risk for other types of cancer. Only 3 to 5 out of every 100 people with colon cancer have Lynch syndrome.

FAP is a rare inherited syndrome that often leads to colon cancer. However, only 1 out of 100 people with colon cancer have FAP. FAP causes hundreds of polyps to form in the colon and rectum. You are likely to have cancer by age 50 if you have classic FAP. In a milder version called attenuated FAP, the disease causes fewer polyps and usually starts later in life.

If your doctor thinks you might have an inherited syndrome, you will likely be referred to a genetic counselor. A genetic counselor can talk with you about getting tested for syndromes related to colon cancer. To be tested, you must provide a sample of blood. Using the sample, a pathologist can test your genes for abnormal changes that cause these syndromes.

Physical exam

Doctors often perform a physical exam along with taking a medical history. A physical exam is a study of your body for signs of disease. To start, your basic body functions will be measured. These functions include your temperature, blood pressure, and pulse and breathing (respiration) rate. Your weight will also be checked.

During the exam, your doctor will listen to your lungs, heart, and gut. Your doctor will also look at and feel parts of your body. This is done to see if organs are of normal size, are soft or hard, or cause pain when touched. Cancer and other diseases can cause organs to become enlarged and hard.

Biopsy

A biopsy involves removing small pieces of tissue, which are sent to a pathologist for testing. A biopsy can be done during a colonoscopy. Sometimes a needle is used to do the biopsy. In this case, a CT scan or ultrasound may be used to help guide the needle into the tumor in order to remove the tissue sample.

Pathology report

A report will be written each time tissue is removed from your body and tested for cancer. The report is called a pathology report. Pathology reports are very important for planning the best treatment for you.

One important test result is the cancer grade. The cancer grade is a score assigned by the pathologist. He or she will rate the cancer based on how the cancer cells look. The score is a sign of how fast the cancer will likely grow and spread. Higher scores mean that the cancer will likely grow and spread fast.



SNAPSHOT

Lynch syndrome

- Also called HNPCC (hereditary nonpolyposis colorectal cancer)
- ✓ About 5 out of 100 people with colon cancer will also have Lynch syndrome
- People born with this syndrome are at high risk of getting colon cancer and some other cancers
- ✓ Caused by inherited mutations of the genes that fix damaged DNA, called MMR (mismatch repair) genes
- ✓ NCCN experts recommend testing all people with colon cancer for problems with the MMR genes. This helps determine who should be tested for Lynch syndrome.

Review your pathology report(s) with your doctor. Ask questions if you don't understand. This information can be complex. It's also a good idea to get a copy of your pathology report(s) and take notes.



SNAPSHOT

FAP (familial adenomatous polyposis)

- ✓ A rare, inherited condition that can cause hundreds to thousands of polyps to form in the colon
- ✓ The polyps start as non-cancerous (benign) growths, but over time they can turn into colon cancer
- ▼ There is a milder form called attenuated FAP, which doesn't cause as many polyps. People with this type usually get colon cancer a little later than people with classic FAP.

Colonoscopy

A colonoscopy is a procedure that allows your doctor to examine your colon for polyps and other diseases. A colonoscope is the device used for the test. Part of it looks like a thin tube. It has a light and camera. This part will be inserted into your anus and gently guided through your large intestine.

You may be put on a liquid diet for 1 to 3 days before the test. You may also take a laxative or an enema the night before. This will clean out your intestine. Right before the test, you may be given a sedative to lessen any pain. As shown in **Figure 6**, you will likely wear a hospital gown. The test will be performed while you lie on your side.

To see better, gas may be pumped into your intestine to make it bigger. You may be asked to shift a little to help your doctor guide the device. A picture of your colon will be viewed by your doctor on a screen. If a polyp is found, a cutting tool will be inserted through the tube to remove it.

A colonoscopy takes about 30 to 60 minutes. Afterward, you may stay for another hour for any drugs that were used to wear off. However, you'll still need someone to drive you home. The next day, you will likely feel normal. If you have severe pain, bloody stool, or weakness, contact your doctor.

Blood tests

Blood tests are used to look for signs of disease. A needle will be inserted into your vein to remove a sample of blood. The needle may bruise your skin and you may feel dizzy from the blood draw. Your blood sample will then be sent to a lab where a pathologist will test it. A pathologist is a doctor who's an expert in testing cells to find disease.

Complete blood count

A CBC (**c**omplete **b**lood **c**ount) measures the number of blood cells in a blood sample. It includes numbers of white blood cells, red blood cells, and platelets. Cancer and other health problems can cause low or high counts.

Chemistry profile

A blood test called a chemistry profile measures the amount of certain substances in the blood, such as metabolites, electrolytes, fats, and proteins. This test gives important information about how well your kidneys, liver, and other organs are working.

CEA blood test

When colon cancer spreads, it can cause high or low levels of chemicals in the blood. One example is a high CEA (carcinoembryonic antigen) level. CEA is normally low in healthy adults unless a woman is

pregnant. High CEA levels suggest the cancer has spread far.

Imaging tests

Imaging tests make pictures (images) of the insides of your body. They can show areas of the body that have cancer. This information helps your doctors stage the cancer and plan treatment. Certain imaging tests also reveal some features of a tumor and its cells.

A radiologist is a doctor who's an expert in reading images. Your radiologist will convey the imaging results to your cancer doctor. This information helps your doctor decide what the next steps of care should be.

Figure 6 Colonoscopy

A total colonoscopy is a procedure that allows your doctor to look for and remove any abnormal tissue from the colon. It involves inserting a thin device through the anus, up the rectum, and into the colon. The device has a light, a camera, and a cutting tool.

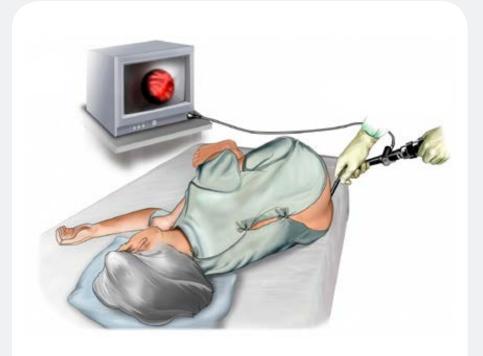


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Your treatment team will tell you how to prepare for these tests. You may need to stop taking some medicines and stop eating and drinking for a few hours before the scan. Tell your team if you get nervous when in small spaces. You may be given a sedative to help you relax.

Some imaging tests use contrast. Contrast is a dye that will be injected into your bloodstream. It makes the pictures clearer. Some people have an allergic reaction to the dye. Tell your doctor if you've had problems with contrast in the past.

CT with contrast

CT (computed tomography) takes many pictures of a body part using x-rays. A computer combines the x-rays to make one detailed picture. The picture is saved for later viewing by the radiologist. **See Figure 7**.

If the cancer has spread beyond the second layer of the colon wall, CT scans of your chest, abdomen, and pelvis are recommended. Contrast should be used. The radiologist will look for cancer in nearby and distant sites.

PET/CT

Sometimes CT is combined with PET (**p**ositron **e**mission **t**omography). When used together, it is called a PET/CT scan. PET/CT scan is not often used to plan treatment for colon cancer. There are three reasons why you may have a PET/CT scan:

- To show how big a tumor is if you have metastases
- To find metastases other than in the liver that would exclude surgery
- PET/CT may be an option if you can't receive contrast dye for CT or MRI



What to expect: CT scan

- ✓ You will lie face-up on a table that moves through a tunnel-like machine. See Figure 7.
- ✓ Contrast dye ("contrast" for short) will be used to see everything better.
- ✓ The dye will be injected into your vein and mixed with a liquid you drink.
- ✓ The contrast may cause you to feel flushed or get hives.
- ✓ You will be alone during the scan, but a technician will be nearby. You will be able to hear and talk to the technician.
- ✓ You may hear buzzing or clicking during the scan.
- ✓ Tell your doctor if you get nervous in tight spaces.

PET/CT may be done with one or two machines depending on the cancer center. For PET, a sugar radiotracer will first be injected into your body. The radiotracer is detected with a special camera during the scan. Cancer cells appear brighter than normal cells because they use sugar more quickly. PET can show even small amounts of cancer.

be used to help you stay in place. An MRI may cause your body to feel a bit warm. **See Figure 8**.

MRI

MRI (magnetic resonance imaging) uses a magnetic field and radio waves to make pictures. It is not often used to plan treatment for colon cancer. Your doctor may order an MRI if the CT scan was unclear. Contrast should be used. For stages II or III, CT without contrast may also be done if you can't receive CT contrast.

Getting an MRI is much like getting a CT. Except, you will need to wear a coil device. The device covers your body from below your chest to the top of your legs. It sends and receives radio waves. Straps may

Figure 7 CT scan

CT takes many pictures of a body part using x-rays. A computer combines the x-rays to make one detailed picture. The picture is saved for later viewing by the radiologist.



Tumor marker testing

Just like each person's DNA is unique, each person's cancer is unique. This means that a treatment that helps one person might not help you. To find out if certain treatments might help you, your doctor may offer you tumor marker testing. This is also called biomarker (short for biological marker) testing.

Tumor markers can be substances, like molecules or proteins, that are made by your body because you have cancer. Tumor markers can also be processes, such as the way your DNA "acts" that makes it unique. To find out if your cancer has any markers, the primary tumor removed during surgery is tested in a laboratory.

MMR deficiency

Some people have tumors that have developed a problem making them unable to fix damaged DNA. In normal cells, a process called MMR fixes errors that happen when the DNA divides and makes a copy of itself. If a cell's MMR system isn't working right, errors build up and cause the DNA to become unstable. This is called MSI (microsatellite instability).

There are two kinds of laboratory tests for this tumor marker. Depending on which method is used, if you have this genetic defect the result will either be MSI-H (microsatellite instability high) or dMMR (mismatch repair deficient). Both results mean the same thing.

NCCN experts recommend testing for this tumor marker in all people with colon cancer for two

Figure 8 MRI

MRI makes pictures of areas inside the body without using radiation. Not everyone with colon cancer will need an MRI. Your doctor may order it to help determine if you have colon or rectal cancer, or if results of other imaging tests were unclear.



2 Treatment planning

Tumor marker testing

important reasons. One reason is to determine if you should also be tested for Lynch syndrome. The other is to determine if treatment with certain immunotherapy drugs may help you.

KRAS and **NRAS** mutations

RAS is a family of genes that includes the HRAS, KRAS, and NRAS genes. Two of these genes—KRAS and NRAS—can play a role in colon cancer. Genes work as instruction manuals for making important proteins. Some people with colon cancer have abnormal KRAS or NRAS genes. As a result, the proteins these genes make are overactive and can help the cancer grow.

Some treatments for metastatic colon cancer do not work if the *RAS* genes are abnormal. For this reason, NCCN experts only recommend testing for *KRAS* and *NRAS* mutations if your colon cancer has spread to other parts of your body (metastasized).

BRAF mutation

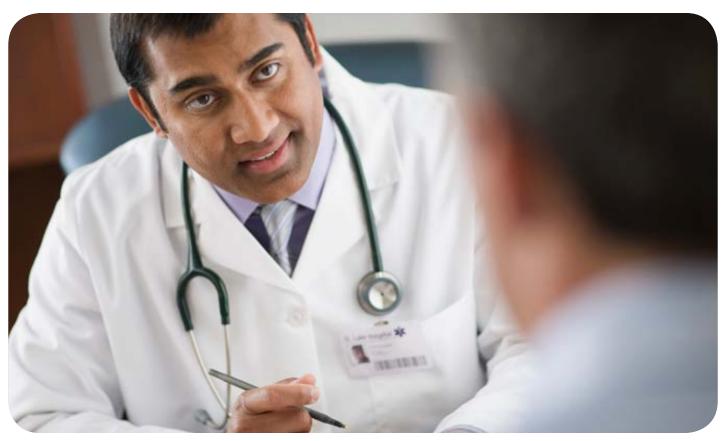
About 5 to 9 out of every 100 people with colon cancer have a mutation called *BRAF* V600E. Having this mutation may cause cancer cells to grow and spread more quickly than they normally would. NCCN experts recommend testing for this mutation in all patients with stage IV colon cancer. If cancer has spread to other parts of your body and you have this mutation, a type of targeted therapy called a *BRAF* inhibitor may help you when combined with chemotherapy and another targeted therapy.

Review

- A medical history is a report of all health events in your lifetime. It will include questions about your family's health to help assess if you have a syndrome related to colon cancer. Such syndromes include Lynch syndrome and FAP.
- Your doctor will examine your body for signs of disease. He or she will touch parts of your body to see if anything feels abnormal.
- Blood tests you may have include a CBC, chemistry profile, and CEA blood test.
- Imaging tests are a noninvasive way for your doctor to see how far the cancer has spread.
- A needle biopsy may be done to test for cancer in distant sites.
- Testing for defects with the MMR system is advised for all colon cancers. Testing for mutated KRAS, NRAS, and BRAF genes is recommended for colon cancer that has spread to other parts of the body.

3 Overview of cancer treatments

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This chapter describes the ways colon cancer is usually treated. Knowing what a treatment is will help you understand your treatment options listed in Parts 4 and 5. Not every person will receive every treatment described in this chapter.

Surgery

Some colon cancers grow beyond the polyp and into the colon wall. In many of these cases, surgery is a key part of treatment. This section describes the types of surgery used for colon cancer. You may have more than one type of surgery. Your treatment team will tell you how to prepare for and what to expect during surgery. You may need to stop taking some medicines to reduce the risk of severe bleeding. Eating less, changing to a liquid diet, or using enemas or laxatives will empty your colon for surgery. Right before surgery, you will be given general anesthesia.

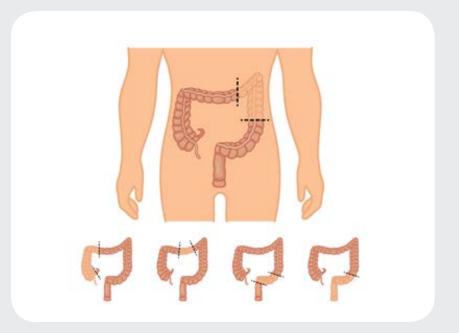
Colectomy

A colectomy is a surgery that removes the part of the colon with cancer. **See Figure 9**. After the cancerous part is removed, the two ends of the remaining colon are often joined back together. They are either sewn or stapled together.

Before surgery, the cancer site may be marked with a tattoo. The tattoo allows your surgeon to find the cancer site after the polyp has been removed.

Figure 9 Colectomy

Colon cancer is often removed with a surgery called colectomy. The surgery removes the part of the colon that has cancer. The two ends of the remaining colon are then attached to each other.



Marking isn't always needed. For example, marking isn't done if the cancer site can be easily found.

A colectomy can be done in two ways. The open method removes cancer tissue through a large cut in your abdomen. The minimally invasive method involves making a few small cuts. Tools are inserted through the cuts to see and remove part of your colon.

A colectomy can take 1 to 4 hours to complete. You may stay in the hospital for several days to recover. After surgery, you will be told what you can and can't eat to prevent discomfort and help healing.

After a colectomy, some people may have a procedure called a colostomy. A colostomy connects a part of the colon to the outside of the abdomen. This creates an opening in your abdomen that allows stool to pass through. If a colostomy is done, it is usually for a short period of time. It is rare for a colostomy not to be removed.

Lymphadenectomy

A lymphadenectomy is a surgery that removes lymph nodes. It is done at the same time as the colectomy. At least 12 lymph nodes near to the cancer site should be removed for cancer testing. All nodes that look abnormal should be removed, too.

Metastasectomy

Surgery to remove a metastasis is called a metastasectomy. Not all metastatic disease can be treated with surgery. The methods of surgery for metastasectomy vary based on where the cancer has spread.

Side effects of surgery

Surgery causes pain, swelling, and scars. Pain and swelling often fade away in the weeks following surgery. Scars from surgery don't fully fade away.

As with any surgery, there is a chance of complications. These include major blood loss, infection, heart attack, and blood clots. There can also be injury to nearby organs. Your surgical team will design care to prevent these risks.

Colectomy may cause certain side effects. Organs may push through weakened tissue (hernia). Scar tissue may block the colon. Food may leak out where the colon was reconnected.

Not all side effects of surgery are listed here. Please ask your treatment team for a complete list of common and rare side effects.

Chemotherapy

Chemotherapy ("chemo" for short) is treatment with drugs to kill cancer cells. Most chemotherapy drugs are liquids that are slowly injected into a vein. The drugs travel in your bloodstream to treat cancer throughout your body. Treatments that affect the whole body are called *systemic*. If you need chemotherapy, you are most likely to have a combination of two or three chemotherapy drugs. Combinations of chemotherapy drugs are called regimens. Regimens commonly used to treat colon cancer are shown in Guide 1. Keep the following things in mind:

The individual chemotherapy drugs and/ or regimens you are treated with depend (in part) on the type of tumor you have and other features of your cancer. There are other chemotherapy drugs and regimens not shown in Guide 2 that may be right for you.

Chemotherapy is given in cycles of treatment days followed by days of rest. This allows your body to recover before the next cycle. For example, you might receive chemotherapy every day for 1 week followed by 3 weeks with no chemotherapy. These 4 weeks make up one cycle. Cycles vary in length depending on which drugs are used. Often, a cycle is 14, 21, or 28 days long.

While most chemo drugs for colon cancer travel in the bloodstream through your whole body, chemo can also be given using HAI (hepatic arterial infusion). This method is sometimes used for colon cancer that has spread to the liver. Using a port or a pump, the drugs are funneled directly into the artery leading to the liver. NCCN experts advise that

Guide 1. Commonly used chemotherapy regimens

Regimen name	Drugs included in regimen
5-FU/LV	Fluorouracil, leucovorin
Capecitabine	Capecitabine (Xeloda®)
CAPEOX	Capecitabine (Xeloda®), oxaliplatin (Eloxatin®)
FOLFIRI	Leucovorin, fluorouracil, irinotecan (Camptosar®)
FOLFOX	Leucovorin, fluorouracil, oxaliplatin (Eloxatin®)
FOLFOXIRI	Leucovorin, fluorouracil, oxaliplatin (Eloxatin®), irinotecan (Camptosar®)
Irinotecan	Irinotecan (Camptosar®)
Trifluridine + tipiracil	Trifluridine, tipiracil (Lonsurf®)

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HAI should only be done at treatment centers with experience in this method.

Chemotherapy can be given in different settings. Many people get chemotherapy at cancer centers, in areas called infusion rooms. **See Figure 10**.



What to expect: Chemotherapy

- ✓ Side effects of chemotherapy depend on many things (drug type, dosage, length of treatment) and are different for everyone.
- ✓ Common side effects include nausea, not feeling hungry, diarrhea, hair loss, and mouth sores.
- ✓ Some chemotherapy drugs can damage your sensory nerves. Symptoms of this include numbness, tingling, and pain in fingers and toes.

Figure 10 Chemotherapy infusion room

Chemotherapy is often given in infusion rooms, which allow several people to receive treatment at the same time.



Targeted therapy

Targeted therapy is a type of cancer treatment that can target—and attack—specific kinds of cancer cells. Different targeted therapies work in different ways. One type stops the growth of new blood vessels into colon tumors. Without the blood they need to grow, cancer cells "starve" and die. A second type of targeted therapy for colon cancer stops the cancer cells from receiving signals to grow. Other types work in more than one way.

Targeted therapy is less likely to harm normal cells than chemotherapy. Targeted therapy drugs for colon cancer are listed in Guide 2. Ask your treatment team for a full list of common and rare side effects. Not everyone with colon cancer will benefit from treatment with a targeted therapy. In Parts 4, 5, and 7, information on who should receive these drugs is provided.

Guide 2. Targeted therapies

Generic name	Brand name	How it's given
Bevacizumab	Avastin [®]	Infusion
Ramucirumab	Cyramza [®]	Infusion
Ziv-aflibercept	Zaltrap®	Infusion
Cetuximab	Erbitux [®]	Infusion
Panitumumab	Vectibix [®]	Infusion
Regorafenib	Stivarga [®]	Pill
Vemurafenib	Zelboraf®	Pill



Targeted therapy

- ✓ Used to treat some colon cancers that have spread to other parts of the body and/or can't be removed with surgery.
- ✓ Not everyone with colon cancer will
- benefit from targeted therapy. For example, some targeted therapies will only work for people with (or without) a specific gene mutation.
- ✓ Most (but not all) targeted therapies for colon cancer are given by infusion. This means they are put directly into your bloodstream using an IV.

Immunotherapy

The immune system is your body's natural defense against infection and disease. A newer type of cancer treatment called immunotherapy increases the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells. Drugs called checkpoint inhibitors are a type of immunotherapy used to treat colon cancer.

Your immune system has important white blood cells called T cells. T cells' main job is to attack harmful things in your body, like bacteria, viruses, and cancer. They do this with the help of certain proteins on their surface. When T-cell proteins "meet" certain proteins on cancer cells, it is called an immune checkpoint. The T cell is "told" to leave the cancer cell alone instead of attacking it. Checkpoint inhibitors can stop the T-cell protein from meeting the cancer cell protein. This means that the T cells will do their job and attack the cancer cells.

Checkpoint inhibitors used for colon cancer are shown in Guide 3. Not everyone with colon cancer will benefit from treatment with immunotherapy. In Parts 4, 5, and 7, information on who should receive these drugs is provided.

Guide 3. Immunotherapy drugs

Generic name	Brand name	How it's given
Ipilimumab	Yervoy [®]	Infusion
Nivolumab	Opdivo®	Infusion
Pembrolizumab	Keytruda [®]	Infusion



Chemobrain is real! My brain does not work as quickly as it did before. I have to employ strategies, tactics and other people to help me remember things. I am still good at Jeopardy though!

EvelynSurvivor, Stage III colon cancer

Radiation therapy

Radiation therapy uses high-energy, highly focused rays to treat cancer. The rays damage DNA. This either kills the cancer cells or stops new cancer cells from being made.

Radiation therapy is not often used to treat colon cancer. You may receive radiation therapy as part of a clinical trial. Otherwise, Parts 4 and 5 explain when radiation therapy is an option.

External beam radiation

Most often, EBRT (external beam radiation therapy) is the method used to treat colon cancer. This method delivers radiation from outside your body using a large machine. **See Figure 11**. The radiation passes through your skin and other tissue to reach the tumor.

A planning session is needed to receive the best treatment. This session is called *simulation*. First, you will be guided and adjusted into the position needed for treatment. After this, pictures of the cancer sites will be made with an imaging test. Using the pictures, your radiation team will plan treatment. They will plan the best dose, number, and shape of radiation beams, and number of treatments.

Conformal techniques are used for colon cancer. These techniques shape the radiation dose to the cancer site to spare healthy tissue. However, some healthy tissue still gets radiated. The radiation dose is shaped with computer software and hardware added to the machine. The types of conformal radiation include:

➤ **3D-CRT** (three-dimensional conformal radiation therapy) delivers, from different angles, a photon beam that matches the shape of the tumor. Treatment is completed in about 6 weeks.



What are some side effects of radiation?

- Feeling tired and worn out
- Hair loss in the treated area
- Changes to urination and bowel movements
- Diarrhea
- Nausea/vomiting
- Late side effects can include infertility, sexual dysfunction, bowel dysfunction, reduced bone density, and second cancers
- Not all side effects are listed here. Ask your treatment team for a full list.
- IMRT (intensity-modulated radiation therapy) is a form of 3D-CRT that further modifies the beam's intensity during treatment. Treatment is completed in about 6 weeks. IMRT should be used only for a second treatment with radiation or for cancer in an uncommon site.
- SBRT (stereotactic body radiation therapy) treats cancer with very precise, high-dose photon beams. Receiving SBRT is much like

other conformal techniques except treatment is finished in about 5 visits. At this time, SBRT should only be used to treat colon cancer in the liver or lungs.

During treatment, you will lie on a table as you did for simulation. Devices may be used to keep you from moving. This helps to target the tumor. Radiation beams are aimed with help from ink marks on your skin or marker seeds in the tumor.

You will be alone in the treatment room. A technician will operate the machine from a nearby room. He or she will be able to see, hear, and speak with you at all times. As treatment is given, you may hear noises. You will not see, hear, or feel the radiation. One session can take less than 10 minutes.

Intraoperative radiation

IORT (intraoperative radiation therapy) delivers radiation inside your body at the time of an operation. Different methods can be used. However, the usual method involves a device that is placed where the tumor was. The radiation kills remaining cancer cells in the tissue that was near the tumor.

IORT can deliver a radiation dose similar to EBRT or deliver extra radiation. This extra radiation is called a *boost*. Some cancer centers do not have an IORT machine. In this case, a boost of radiation can be given with EBRT if technically feasible.

Figure 11 External beam radiation therapy

A large machine aims radiation at the tumor, passing through skin and other tissue to reach it.



Ablation

Surgery is the preferred way to remove colon cancer that has spread to the liver or lungs. Sometimes, however, a procedure called *ablation* may be used to treat small tumors in these areas. Ablation may be used by itself if surgery isn't possible, or it may be used in addition to surgery. Most available research is on a type of ablation called *radiofrequency ablation*. This method heats and kills cancer cells using high-energy radio waves.

Embolization

Embolization treats liver tumors with chemotherapy or radioactive beads. A catheter will be inserted into an artery in your leg and guided to the tumor. Once in place, the beads will be inserted into the blood vessel.

The beads block blood flow to the tumor. Without blood, the cancer cells "starve" and die. The chemotherapy or radiation further damage the cancer cells and cause the tumor to shrink.

This treatment is a type of arterially directed catheter therapy. If radiation beads are used, it's called selective internal radiation therapy. Embolization is an option for some people with liver metastases. It is given when chemotherapy is not an option.

clinical trials, the tests and treatments in this book are now widely used to help people with colon cancer.

Joining a clinical trial can have both upsides and downsides. **See Figure 12** for some things to consider when deciding to join a clinical trial. You will need to weigh the pros and cons and decide what is right for you.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to know that any progress is because of the treatment and not because of differences between patients.

To join, you'll need to review and sign a paper called an informed consent form. This form describes the study in detail. The study's risks and benefits should be described and may include others than those described above.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you're getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 8, *Making treatment decisions*.

Clinical trials

New tests and treatments aren't offered to the public as soon as they're made. They first need to be studied. A clinical trial is a type of research that studies how safe and helpful tests and treatments are. When found to be safe and helpful, they may become tomorrow's standard of care. Because of

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Review

- A colectomy is surgery that removes the part of the colon with cancer. A lymphadenectomy is the removal of lymph nodes, and a metastasectomy is the removal of metastases.
- Chemotherapy stops cancer cells from completing their life cycle so they can't increase in number.
- One type of targeted therapy stops the growth of new blood vessels into colon tumors. Without blood, cancer cells starve and die. A second type stops the cancer cells from receiving certain growth signals.
- Radiation kills cancer cells or stops new cancer cells from being made. It isn't often used to treat colon cancer.
- Ablation destroys small tumors by freezing or burning them. It isn't often used for colon cancer.
- Embolization treats cancer by blocking blood flow to the tumor and damaging cancer cells with chemotherapy or radiation. It is used for a very select group of people.
- Clinical trials give people access to new tests and treatments that otherwise can't usually be received. These new tests and treatments may, in time, be approved by the FDA (U.S. Food and Drug Administration).

Figure 12 Possible pros and cons of joining a clinical trial



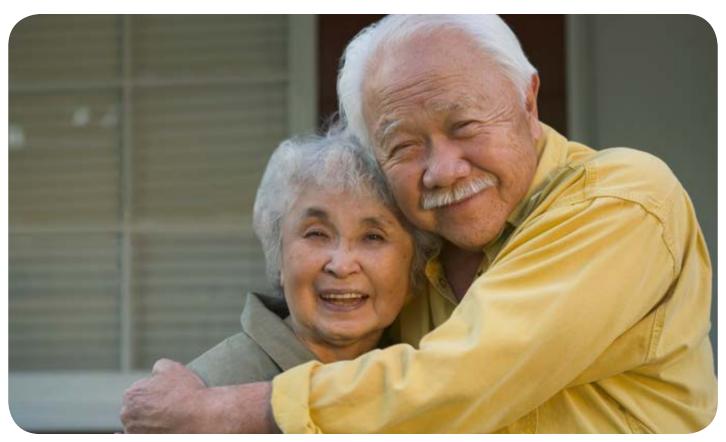
4

Treatment guide: Nonmetastatic cancer

35 Stage I

38 Stages II and III

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This chapter is a treatment guide for colon cancer that hasn't spread to areas far from the colon. The cancer may be only in the colon, or also in nearby organs or lymph nodes. The treatment options presented are partly based on the cancer stage.

Stage I

Stage I colon cancer means that the tumor has grown into either the second layer of the colon wall (a T1 tumor), or into the third layer of the colon wall (a T2 tumor). Some T1 tumors need to be treated. Treatment is based on the shape of the polyp and whether your doctor thinks cancer will return after it's been removed. The cancer is more likely to return if:

- ➤ The tumor was removed in more than one piece. This is called a *fragmented specimen*.
- There is cancer around the edge of the tissue that was removed. This means there might still be cancer leftover in the colon. This is called a positive surgical margin.
- The tumor cells look very different from normal cells under a microscope. This means that the cancer is likely to grow and spread more quickly than it normally would. These cells are called high grade.
- Cancer cells can be seen under a microscope in the tiny blood or lymph vessels of the tumor. This is called angiolymphatic invasion.
- There are small groups of cancer cells in the part of the tumor that was connected to the colon. This is called tumor budding.



After two years of being misdiagnosed and hopping from doctor to doctor, I was finally heard and seen by a doctor who ignored my age. Had it not been for this doctor I wouldn't be here. My tumor was the size of a grapefruit and just 2cm away from blocking my colon completely.

April, 33Survivor, Stage II colon cancer

Guide 4. Treatment for T1 tumors

Type of polyp	What are the options?
Low-risk pedunculated polyp	Watch-and-wait (no treatment)
Low-risk sessile polyp	Watch-and-wait (no treatment)Colectomy and lymphadenectomy
Any high-risk polyp	Colectomy and lymphadenectomy

Guide 5. Treatment for T2 tumors

Test results	What are the options?
The tumor can be treated with surgery and ISN'T blocking the gut	Colectomy + lymphadenectomy
The tumor can be treated with surgery and IS blocking the gut	 Colectomy + lymphadenectomy Colectomy + lymphadenectomy + diversion Diversion followed by colectomy + lymphadenectomy In some cases, stent followed by colectomy + lymphadenectomy

Guide 6. Follow-up care for stage I colon cancer

Type of care	When?	Advanced adenoma?		What's next?	
Colonogopy	One year after	No	→	Repeat colonoscopy in 3 years. If normal, repeat every 5 years after that	
Colonoscopy	treatment	Yes	-	Repeat colonoscopy in 1 year	
Imaging tests	If you don't have any symptoms, imaging tests aren't needed on a regular basis. Your doctor may order imaging tests if he or she thinks the cancer may have come back or spread.				

Stage I

T1 tumors

Guide 4 lists the treatment options for T1 tumors. T1 tumors haven't grown beyond the second layer of the colon wall. If you had a low-risk pedunculated polyp, a polypectomy likely removed all the cancer. You don't need more treatment, and you can start follow-up testing. For a low-risk sessile polyp, there are two options if the polyp was fully removed:

- Watch-and-wait (no treatment)
- Surgery

Either type of polyp may have high-risk features. In this case, surgery is recommended. The part of the colon with cancer and some lymph nodes should be removed.

T2 tumors

Guide 5 lists the treatment options for tumors rated as T2. These tumors haven't grown beyond the third layer of the colon wall. These tumors should be treated. If you are able to have surgery, a colectomy and lymphadenectomy are advised. It is very rare that surgery can't be done. If you can't have surgery, you may have chemotherapy if you're healthy enough. Radiation therapy may be added.

In very rare cases, a T2 tumor has grown so large that it blocks the flow of stool. There are four options when there is a blockage:

- A colectomy that unblocks your gut
- Removal of the cancer and a diversion within one operation. A diversion is a surgery that attaches the colon to the surface of the abdomen, and an ostomy pouch is needed.
- A diversion followed by a second operation to remove the cancer

A stent followed by a second operation to remove the cancer

The tissue that is removed from your body will be sent to a pathologist. The pathologist will assess how far the cancer has grown within the colon wall. He or she will also test for cancer in your lymph nodes. If the cancer stage doesn't change, you will not need more treatment. If the cancer stage changes to stage II or III, see Guide 9.

Follow-up care

Guide 6 lists follow-up testing for stage I colon cancer. Follow-up testing is started when there are no signs of cancer after treatment. It can be helpful for finding new cancer growth early.

A colonoscopy is recommended 1 year after treatment has ended. If results are normal, the next colonoscopy should be received in 3 years and then every 5 years. If an advanced adenoma is found, your next colonoscopy will be needed within 1 year. Advanced adenomas include polyps with a ruffled structure (villous), a polyp larger than the width of a AAA battery (>1 cm), or a polyp with pre-cancerous cells (high-grade dysplasia).

If you don't have any symptoms, imaging tests aren't needed on a regular basis. Your doctor may order imaging tests if he or she thinks the cancer may have come back or spread.

Stages II and III

Treatment before surgery

Guide 7 lists the options for treating stage II and III cancers before surgery. Some stage II and III cancers will need treatment before surgery. The medical term for treatment before surgery is neoadjuvant therapy. The aim of this treatment is to shrink a tumor so it can be fully removed during surgery.

Treatment before surgery is based on how far through the colon wall the cancer has grown. Tumors that are rated as T1, T2, T3, and T4a haven't grown through the colon wall to nearby organs. For these tumors, treatment before surgery isn't advised.

Tumors rated as T4b have grown through the colon wall to nearby structures. In this case, your doctor may want to use chemotherapy before surgery. FOLFOX or CAPEOX are recommended.

Primary treatment

Guide 8 presents the primary treatment options for stage II and III cancers. After any treatment you received before surgery, the next step is primary treatment. Primary treatment is the main treatment used to rid your body of cancer (usually surgery). Treatment options are based on whether the tumor can be removed with surgery.

Surgery is an option

If you are able to have surgery, a colectomy and lymphadenectomy are advised. In rare cases, a tumor has grown so large that it blocks the flow of stool. There are four options when there is a blockage.

One option is a colectomy that unblocks your gut. Another option is removal of the cancer and a diversion within one operation. A diversion is a surgery that attaches the colon to the surface of the abdomen, and a "bag" is needed. A third option

is a diversion followed by a second operation to remove the cancer. Last, some people can get a stent followed by a second operation to remove the cancer.

Pathology

The tissue that will be removed from your body will be sent to a pathologist. The pathologist will assess how far the cancer has grown within the colon wall. He or she will also test for cancer in your lymph nodes. Based on test results, a pathologic stage will be assigned.

Surgery isn't an option

It is very rare but you may be unable to have surgery. Surgery may not be possible because of where the cancer is. Some health issues also exclude surgery.

In this case, sometimes chemotherapy is given if you are healthy enough. The chemotherapy listed in Part 7 may be used. Other preferred options are radiation therapy with either infusional 5-FU or capecitabine. If neither is an option, a third option is bolus 5-FU/LV with radiation therapy.

For very invasive tumors, chemotherapy may shrink the tumor enough for surgery. IORT may be added. If you're still unable to have surgery, you may be treated with more cycles of chemotherapy.

Guide 7. Treatment before surgery

T stage	What are the options?
Colon tumors haven't grown to nearby sites (T1–T4a)	No treatment needed before surgery
Colon tumors have grown to nearby sites (T4b)	 Chemotherapy with FOLFOX or CAPEOX before surgery You can go straight to surgery

Guide 8. Primary treatment - stage II and III colon cancer The tumor CAN be removed with surgery

ls gut blocked?	Primary treatment options	What's next?
Tumor isn't blocking gut	Colectomy + lymphadenectomy	Treatment after surgery (see Guide 9)
Tumor is blocking gut	 Colectomy + lymphadenectomy Colectomy + lymphadenectomy + diversion Diversion followed by colectomy + lymphadenectomy Stent followed by colectomy + lymphadenectomy 	Treatment after surgery (see Guide 9)

The tumor CAN'T be removed with surgery

Treatment options	Result		What's next?	What's next?
Treatment listed in Part 7Infusional 5-FU + radiation	Tumor can now be removed with surgery	→	Colectomy + lymphadenectomy, with or without IORT	Treatment after surgery (see Guide 9)
Capecitabine + radiationBolus 5-FU/LV + radiation	Tumor still can't be removed with surgery	→	Start (or continue) treatment listed in Part 7	

Guide 9. Stages II and III: treatment after surgery

Stage	MMR status	Risk level	Treatment options
	MSI-H or dMMR	Any level	Watch-and-wait (no treatment)
Stage IIA	MSI-L or normal MMR	Low risk	 Watch-and-wait (no treatment) Chemotherapy with: Capecitabine 5-FU/LV
	MSI-L or normal MMR	High risk	 Watch-and-wait (no treatment) Chemotherapy with: Capecitabine 5-FU/LV FOLFOX regimen CAPEOX regimen
Stage IIB Stage IIC	Any status	Any level	 Watch-and-wait (no treatment) Chemotherapy with: Capecitabine 5-FU/LV FOLFOX regimen CAPEOX regimen
Stage III	Any status	Low risk	Chemotherapy with: CAPEOX regimen (3 months) (preferred) FOLFOX regimen (3–6 months) (preferred) Capecitabine (6 mo) 5-FU (6 mo)
Stage III		High risk	Chemotherapy with: CAPEOX regimen (3–6 months) (preferred) FOLFOX regimen (6 months) (preferred) Capecitabine (6 months) 5-FU (6 months)

Treatment after surgery

The options for treatment after surgery for stage II and III cancers are shown in Guide 9. Treatment after surgery is given when all visible cancer has been removed. The aim of this treatment is to kill any unseen cancer cells. Some people won't need any further treatment after surgery. If you do, it's best to have it as soon as possible for the best results.

Options for treatment after surgery (adjuvant treatment) depend on:

- The stage of your cancer
- If your tumor is dMMR/MSI-H (explained in Part 2, Treatment planning)
- If your cancer is at high risk of coming back (explained next)

The risk level is high if these conditions are met:

- Positive surgical margin is cancer within the normal-looking tissue around the tumor.
- Close surgical margin is cancer near the normal-looking tissue around the tumor.
- Unknown surgical margin is an unclear assessment of the normal-looking tissue around the tumor.
- Cancer grade 3 or 4 means the cancer cells are likely to grow and spread more quickly than they normally would.
- Angiolymphatic invasion is cancer spread into the tumor's lymph and blood vessels.
- Perineural invasion is cancer spread around or into the nerves.

- Limited lymphadenectomy means fewer than 12 lymph nodes were examined.
- Bowel obstruction means the tumor has grown large enough to block the gut.
- Localized perforation is the presence of holes in the colon caused by the tumor.

Review

- Stage I colon cancer has grown into the second layer of the colon wall (T1 tumors) or into the third layer (T2 tumors). Some T1 tumors may not need treatment after a polypectomy. Otherwise, T1 and T2 tumors may be treated with colectomy and lymphadenectomy.
- Surgery is advised for stages II and III colon cancer if you are able and willing to have it. You may receive chemotherapy before surgery if you have a T4b tumor. Chemotherapy after surgery may not be helpful for stage II cancers but is helpful for stage III.
- If you can't have surgery, chemotherapy is an option.
- Follow-up care is started when there are no signs of cancer. It includes tests to look for any new cancer and help for side effects. It also includes help to prevent or detect other diseases.

5 Treatment guide: Metastatic cancer

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Colon cancer spreads most often to the liver, sometimes to the lungs, and less often to the abdomen or other areas.

Cancer may have already spread to these areas by the time it is first diagnosed.

This is stage IV colon cancer. Or, after successful treatment and a cancer-free period, cancer may return and spread to areas far from the colon. This chapter discusses both of these scenarios.

Metastases at diagnosis

If cancer was found in areas far from the colon at the time you were first diagnosed with colon cancer, your cancer is stage IV. Because the cancer has spread (metastasized) to areas far from the colon, this stage is also called *advanced cancer* or *metastatic cancer*.

Cancer is in the liver or lungs

Treatment of metastatic colon cancer depends on whether surgery is possible. If it is, that is the best way to treat cancer that has spread to the liver or lungs. However, surgery will not be an option for most people. Your treatment team will determine if surgery is an option for you. Because surgery is not often possible, nonsurgical treatment is described first.

Nonsurgical treatment

The main treatment for stage IV colon cancer that cannot be removed with surgery is chemotherapy. The chemotherapy regimens that may be used are listed below. A targeted therapy drug may be given with the chemotherapy. The targeted therapy drugs panitumumab and cetuximab should only be used for left-sided tumors that have normal *KRAS* and *NRAS* genes.

- FOLFIRI with or without bevacizumab, panitumumab, or cetuximab
- FOLFOX with or without bevacizumab, panitumumab, or cetuximab
- CAPEOX with or without bevacizumab
- > FOLFOXIRI with or without bevacizumab

For some people, chemotherapy may greatly shrink the tumors. If they shrink enough, surgery may be an option. If your doctors think that surgery might be possible for you, the size of the tumor should be checked about every two months during chemotherapy.

If chemotherapy didn't shrink the tumors enough to be removed with surgery, you can continue systemic therapy. Systemic therapy may include a combination of chemotherapy, targeted therapy, and immunotherapy. The systemic therapy regimens that may be used are found in Part 7, *Treatment guide:* Systemic therapy.

If chemotherapy worked well enough and the cancer can now be removed with surgery, you will have surgery to remove the colon tumor and the tumors in the liver and/or lungs. You may have the surgeries at the same time or separately. If you were being treated with bevacizumab, it should be stopped 6 weeks before surgery. It increases your risk for stroke and bleeding, especially if you're older than 65. Bevacizumab can be re-started 6 to 8 weeks after surgery. Otherwise, it can slow healing.

After surgery, most people will need more chemotherapy. A targeted therapy may be given with chemotherapy. Chemotherapy received before and after surgery should not exceed 6 months.

Surgical treatment options

There are three options that include surgery to treat colon cancer that had spread to the liver or lungs at diagnosis (stage IV). Surgery is only an option if all the tumors can be totally removed. If your doctor thinks your liver will be too small after the part with cancer is removed, you may need to have it enlarged. This is done using a procedure called portal vein embolization. This blocks the blood vessel to the liver tumor, which causes the healthy part of the liver to grow larger.

The three treatment pathways also include chemotherapy, either before or after surgery. Instead of chemotherapy given by infusion (the most common way), putting the chemotherapy medicine directly into your liver using HAI may be an option. NCCN experts advise that HAI should only be received at treatment centers with experience in this method.

The three treatment options are described next and shown in Guide 10.

Option 1

This option starts with surgery to remove the part of the colon with cancer (colectomy). NCCN experts recommend surgically removing the liver and/or lung metastases at the same time, or later in a second surgery. Instead of removing the metastases with surgery, another option is to treat them using local therapy (image-guided ablation or SBRT). While surgery is preferred by NCCN experts to remove the metastases, local therapy may be appropriate for patients with many small metastases. After surgery, you will likely have a CT scan (with contrast) of your chest, abdomen, and pelvis.

The next phase of this treatment option is chemotherapy. FOLFOX and CAPEOX are preferred regimens, but capecitabine and 5-FU/LV are options as well. Six months of chemotherapy is preferred.

Option 2

This option starts with chemotherapy. FOLFOX or CAPEOX are preferred regimens, but FOLFIRI is an option as well. There are pros and cons to starting with chemotherapy.

Some of the advantages include:

- You may receive early treatment of possible cancer not yet found.
- Knowing your response to chemotherapy early can help with treatment planning.
- If the cancer grows while taking chemotherapy, you can avoid local treatment.

Some of the disadvantages include:

- Fat may build up in your liver and your liver may swell.
- You may become unable to have surgery if the cancer grows or shrinks too much.
- Injury to small blood vessels may occur in your liver.

After 2 to 3 months of chemotherapy, the next step is surgery to remove the part of the colon with cancer (colectomy) and to remove the metastases. These can be done together during one operation or separately in two operations. After surgery, you will likely have a CT scan (with contrast) of your chest, abdomen, and pelvis.

Sometimes, more chemotherapy will be given after surgery. FOLFOX and CAPEOX are preferred regimens, but capecitabine and 5-FU/LV are options as well. Together, chemotherapy given before and after surgery should not exceed 6 months.

Option 3

Option 3 starts with surgery (colectomy), followed by 2 to 3 months of chemotherapy. FOLFOX and CAPEOX are preferred regimens, but FOLFIRI is an option as well. After chemotherapy, surgery to remove the metastases will be done. After surgery, you will likely have a CT scan (with contrast) of your chest, abdomen, and pelvis.

Sometimes, more chemotherapy will be given after surgery. FOLFOX and CAPEOX are preferred regimens, but capecitabine and 5-FU/LV are options as well. Together, chemotherapy given before and after surgery should not exceed 6 months.

Cancer is in the abdomen

About 17 out of 100 people with metastatic rectal cancer will also form tumors in the *peritoneum*. The peritoneum is the thin layer of tissue that lines the abdomen and covers most of the abdominal organs. The goal of treatment for most abdominal/peritoneal metastases is to relieve or prevent symptoms. The main treatment is systemic therapy.

Tumors growing in or around the intestines can cause what's called a *bowel obstruction*. A bowel obstruction is a blockage of the small or large intestine by something other than stool (feces). If the intestines are blocked, stool is prevented from moving and leaving the body. If the cancer isn't causing a bowel blockage, you would begin treatment with systemic therapy. See Part 7, *Treatment guide: Systemic therapy*. If the cancer is (or is expected to) block the bowel, you will first need care to unblock the bowel before beginning systemic therapy. This can be done using one of several surgical techniques, or with a mesh metal tube called a stent.



The visiting Oncologist, told me
I was terminal. No chance of
survival. Liver involvement was too
large. Because of our rural area,
my treatment team was my family
and research was the internet. We
were fortunate to find a cancer
center and surgeon who saved my
life.

- Elaine

Survivor, Stage IV colon cancer

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Guide 10. Surgical options for stage IV colon cancer

Option 1

Surgery options		Chemotherapy options
 Colectomy and metastasectomy, with or without local treatment Colectomy and local treatment 	→	FOLFOX (preferred)CAPEOX (preferred)Capecitabine5-FU/LV

Option 2

Chemotherapy options		Surgery		Chemotherapy options
FOLFOX (preferred)CAPEOX (preferred)FOLFIRI	→	Colectomy + metastasectomy	→	FOLFOX (preferred)CAPEOX (preferred)Capecitabine5-FU/LV

Option 3

Surgery		Chemotherapy options		Next surgery		Chemotherapy options
Colectomy	→	FOLFOX (preferred)CAPEOX (preferred)FOLFIRI	→	Metastasectomy	→	FOLFOX (preferred)CAPEOX (preferred)Capecitabine5-FU/LV

Metastases at recurrence

Sometimes, during the course of follow-up care, testing shows that cancer has come back. One sign that cancer may have returned is if your CEA blood test levels are getting higher each time your blood is tested. In this case, your doctor will likely do a physical exam, a colonoscopy, and a CT scan with contrast of your chest, abdomen, and pelvis. Or, your doctor may find cancer far from the colon during a follow-up imaging test.

If cancer returns, it is called a recurrence or recurrent cancer. There are different types of recurrent colon cancer, described below.

- Local recurrence means that the cancer has returned to the colon.
- Regional recurrence means that the cancer has returned to the lymph nodes or other tissues near the colon.
- Distant recurrence means that the cancer has returned and has spread to areas far from the colon, such as the liver or lungs. Because the cancer has spread to areas far from where

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it started (metastasized), this is also called metastatic cancer.

This section is about the last type of recurrence described above—distant recurrence. Distant recurrence of colon cancer is not the same as metastatic disease discovered at diagnosis, although both are considered metastatic cancer. There are differences in how these types of cancer are treated.

Treatment of a distant recurrence of colon cancer depends on whether surgery is possible. If it is, that is the best treatment option. However, surgery will not be an option for most people. Your treatment team will determine if surgery is an option for you. Because surgery is not often possible, nonsurgical treatment is described first.

Nonsurgical treatment

Colon cancer that returned and spread to the liver or lungs, and that cannot be removed with surgery, is treated with systemic therapy. Systemic therapy may include chemotherapy, targeted therapy, or immunotherapy (or a combination of these). If you've had chemotherapy with FOLFOX or CAPEOX within the past 12 months, there are four possible systemic therapy options. These are described next and shown in Guide 11. Systemic therapy options for everyone else are discussed in Part 7, *Treatment guide: Systemic therapy*.

FOLFOX or CAPEOX within last 12 months

Chemotherapy with FOLFIRI or irinotecan are options. A targeted therapy drug may be added. Bevacizumab is the preferred targeted therapy, but ziv-aflibercept and ramucirumab are also options. If the tumor has normal *KRAS/NRAS* genes, adding panitumumab or cetuximab to chemotherapy FOLFIRI or irinotecan is another option.

If the tumor has a *BRAF* V600E mutation, treatment with irinotecan, vemurafenib, and either cetuximab or panitumumab is an option. For tumors that are dMMR/

MSI-H, you will likely be treated with pembrolizumab alone, or with nivolumab (with or without ipilimumab).

For some people, chemotherapy may greatly shrink the tumors. If they shrink enough, surgery may be an option. If your doctors think that surgery might be possible for you, the size of the tumor should be checked about every two months during chemotherapy.

Surgery still not an option

If chemotherapy didn't shrink the tumors enough to be removed with surgery, you can continue systemic therapy. The systemic therapy regimens that may be used are found in Part 7, *Treatment guide: Systemic* therapy.

Surgery is now an option

If chemotherapy worked well enough and the cancer can now be removed with surgery, you will have surgery to remove the tumor(s). You may have the surgeries at the same time or separately. If you were being treated with bevacizumab, it should be stopped 6 weeks before surgery. It increases your risk for stroke and bleeding, especially if you're older than 65. Bevacizumab can be restarted 6 to 8 weeks after surgery. Otherwise, it can slow healing.

After surgery, most people will need more systemic therapy, although the regimen may be different from what you had before surgery. However, no further treatment will be an option for some people. When there are no signs of cancer, you can resume follow-up care and monitoring for the return of cancer.

You had chemotherapy with FOLFOX or CAPEOX within the past 12 months

Treatment options	May be given with	Notes
Chemotherapy with FOLFIRI regimen	Bevacizumab (preferred)Ziv-afliberceptRamucirumab	
Chemotherapy with irinotecan	Bevacizumab (preferred)Ziv-afliberceptRamucirumab	
Chemotherapy with FOLFIRI regimen	CetuximabPanitumumab	For normal KRAS/NRAS genes only
Chemotherapy with irinotecan	CetuximabPanitumumab	For normal KRAS/NRAS genes only
Nivolumab	Ipilimumab	For dMMR/MSI-H tumors only
Pembrolizumab		For dMMR/MSI-H tumors only
Irinotecan + cetuximab + vemurafenib		BRAF V600E mutation positive
Irinotecan + panitumumab + vemurafenib		BRAF V600E mutation positive

Surgical treatment options

There are two options that include surgery to treat colon cancer that had spread to the liver or lungs at recurrence. Surgery is only an option if all the tumors can be totally removed. If your doctor thinks your liver will be too small after the part with cancer is removed, you may need to have it enlarged. This is done using a procedure called portal vein embolization. This blocks the blood vessel to the liver tumor, which causes the healthy part of the liver to grow larger.

The treatment pathways also include chemotherapy, either before or after surgery. Instead of chemotherapy given by infusion (the most common way), putting the chemotherapy medicine directly into your liver using HAI may be an option. NCCN experts advise that HAI should only be received at treatment centers with experience in this method.

The treatment options are described next and shown in Guide 12.

Option 1

This option starts with surgery to remove the metastases. Instead of removing the metastases with surgery, another option is to treat them using local therapy (image-guided ablation or SBRT). While surgery is preferred by NCCN experts to remove the metastases, local therapy may be appropriate for patients with many small metastases. After surgery, you will likely have a CT scan (with contrast) of your chest, abdomen, and pelvis.

The next phase of this treatment option is chemotherapy. FOLFOX and CAPEOX are preferred regimens if you haven't had any chemotherapy before, but capecitabine and 5-FU/LV are options as well. If you have had chemotherapy before, a watch-and-wait approach (no treatment) is an option. This is preferred by NCCN experts for people who had previous chemotherapy that included oxaliplatin. Another option is to begin a systemic therapy regimen in Part 7, Treatment guide: Systemic therapy.

Option 2

This option starts with chemotherapy to try to shrink the metastases. FOLFOX or CAPEOX are preferred regimens, but capecitabine and 5-FU/LV are options as well. After 2 to 3 months of chemotherapy, the next step is surgery to remove the metastases. After surgery, you will likely have a CT scan (with contrast) of your chest, abdomen, and pelvis.

Treatment after surgery is based on the success of treatment before surgery. If the chemotherapy you had before surgery worked, you can restart that treatment or take FOLFOX. Together, chemotherapy given before and after surgery should not exceed 6 months. A third option is taking a watch-and-wait approach (no treatment).

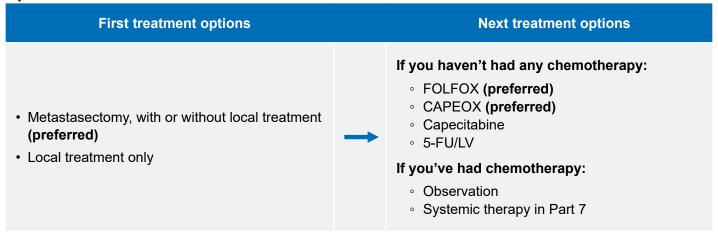
If chemotherapy before surgery didn't work, you have two options. One option is to begin a systemic therapy regimen in Part 7, *Treatment guide: Systemic*

therapy. The other option is taking a watch-and-wait approach (no treatment).

After surgery, most people will need more systemic therapy. However, no further treatment will be an option for some people. When there are no signs of cancer, you can resume follow-up care and monitoring for the return of cancer.

Guide 12. Surgical options for metastases at recurrence

Option 1



Option 2

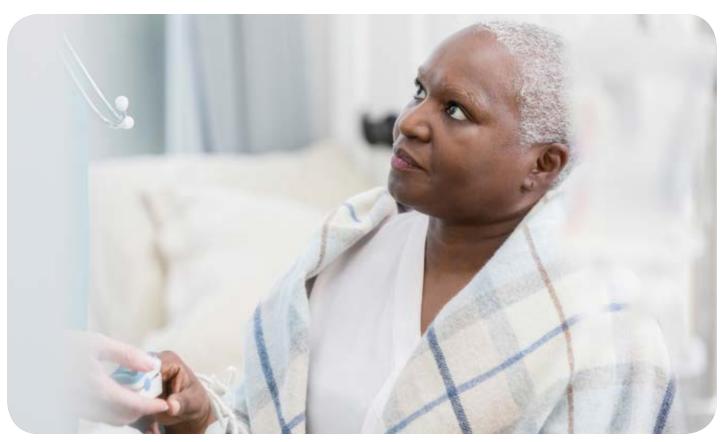
First treatment options		Next treatment options		Chemotherapy	
FOLFOX (preferred)CAPEOX (preferred)Capecitabine5-FU/LV	→	 Metastasectomy, with or without local treatment (preferred) Local treatment only 	→	If chemotherapy worked: Restart same chemotherapy regimen FOLFOX regimen Observation If chemotherapy didn't work: Systemic therapy in Part 7 Observation	

Review

- Cancer that has spread to areas far from where it started is called a metastasis. Colon cancer most often spreads to the liver, and sometimes the lungs.
- Metastases may already be present when you first learn that you have colon cancer. This is stage IV colon cancer. Metastases may also occur if the cancer re-appears during follow-up care.
- Some colon cancers with metastases can be treated with surgery. Local therapy may be used along with surgery or be used by itself. Chemotherapy should also be part of treatment.
- Most colon cancers with metastases cannot be treated with surgery. In most cases, chemotherapy is advised. Targeted therapy may be added.

6 Follow-up care

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- 54 Help with side effects
- 55 Living healthy
- 56 Review



Follow-up care starts when there are no signs of cancer after treatment. It is also called survivorship care. In addition to monitoring for the return of cancer, follow-up care includes managing side effects, staying connected with your primary care doctor, and living a healthy lifestyle.

Monitoring for the return of cancer

Staying alert for the return of cancer is just as important as treating it. If cancer does come back, catching it early will give you the best chance of beating it. The tests recommended by NCCN experts to monitor for the return of colon cancer are described below and shown in Guide 13.

Follow-up care for stage II, III, or IV colon cancer is also explained on the next page.

Guide 13. Follow-up cancer care

Follow-up test	Stage I	Stage II, III, and IV
Medical history and physical exam	Not needed on a regular basis if you don't have symptoms	Every 3–6 months for first 2 years, then every 6 months for 3 more years
CEA blood test	Not needed on a regular basis if you don't have symptoms	Every 3–6 months for first 2 years, then every 6 months for 3 more years
CT of chest, abdomen, and pelvis	If you don't have any symptoms, imaging tests aren't needed on a regular basis. Your doctor may order imaging tests if he or she thinks the cancer may have come back or spread.	Stage II and III: Every 6–12 months for 5 years Stage IV: Every 3–6 months for first 2 years, then every 6–12 months for 3 more years
Colonoscopy	 Colonoscopy one year after treatment If no advanced adenoma, repeat in 3 years, then every 5 years If advanced adenoma, repeat in 1 year 	No prior total colonoscopy: 3–6 months after treatment Prior total colonoscopy: 1 year after treatment If no advanced adenoma, repeat in 3 years, then every 5 years If advanced adenoma, repeat in 1 year

- Medical history and physical exams. Get this care every 3 to 6 months for the first 2 years, then every 6 months for another 3 years.
- CEA blood tests are mainly used to detect the return of cancer. CEA levels should be tested every 3 to 6 months for 2 years. If results are normal for 2 years, get tested every 6 months for another 3 years.
- CT scans may help find metastases. Scans of your chest, abdomen, and pelvis are advised. Get these scans every 3 to 6 months for the first 2 years, then every 6 to 12 months for 3 more years. CT should be done with both IV and oral contrast. CT images may be unclear or not possible. In this case, MRI of the abdomen and pelvis with non-contrast CT of the chest is an option. PET/CT is not recommended.
- Ongoing colonoscopies are also part of follow-up care. You may never have had a total colonoscopy if your gut was blocked. If so, get a colonoscopy within 3 to 6 months after treatment. If you had a total colonoscopy before, get tested 1 year after treatment. You'll need a colonoscopy less often if results are normal. The next test is advised in 3 years. If these results are normal, get tested every 5 years. If an advanced adenoma is found, another colonoscopy within 1 year is advised. Advanced adenomas include polyps with a ruffled structure (villous), a polyp larger than the width of a AAA battery (>1 cm), or a polyp with pre-cancerous cells (high-grade dysplasia).

Your primary care doctor

After finishing cancer treatment, your primary care doctor will play an important role in your care. Your cancer doctor and primary doctor should work together to make sure you get the follow-up care you need. Your oncologist should develop a survivorship care plan that includes:

- A summary of all cancer-related treatment(s) you've had (surgeries, chemotherapy, radiation, etc.)
- A description of the late- and long-term sideeffects you could have
- Recommendations for monitoring for the return of cancer
- Information on when your care will be transferred to your primary care physician. The plan should also outline specific responsibilities for both your cancer doctor and your PCP (primary care physician).
- Recommendations on your overall health and well-being.

Help with side effects

- If you have diarrhea often, or if you can't control your peeing or bowel movements (incontinence), the following things may help:
 - Anti-diarrheal agents
 - Laxatives
 - Changing your diet
 - Strengthening your pelvic floor

- Wearing protective undergarments
- The chemotherapy drug oxaliplatin can cause nerve damage to your fingers and toes. This means that you may have cramping, tingling, or pain in these areas. If you have painful nerve damage, a drug called duloxetine may provide some relief.
- If you have an ostomy, you may want to join an ostomy support group. Another option is to see a health care provider that specializes in ostomy care, such as an ostomy nurse. To prevent damage to the ostomy, it's a good idea to consult with an ostomy professional before undertaking any vigorous physical activity.

Living healthy

There are a few steps you can take that will make a big difference in your overall health.

- Keep up with other aspects of your health. This includes:
 - Getting screened for other types of cancer.
 Your primary care doctor should tell you what cancer screening tests you should have based on your gender, age, and risk level.
 - Getting other recommended health care for your age and gender, such as blood pressure screening, hepatitis C screening, and immunizations (such as the flu shot).
- Maintain a healthy body weight. The best ways to do this are:

Figure 13

Experts recommend eating a healthy diet, especially one that includes a lot of plant-based foods (veggies, fruits, and whole grains).



- Exercising at a moderate intensity for at least 30 minutes most days of the week. If you have an ostomy or nerve pain, your doctor may recommend doing low-intensity exercise or exercising fewer days per week.
- Eating a healthy diet with lots of plant-based foods.
- Drinking little to no alcohol. This means no more than 1 drink/day for women, and no more than 2 drinks/day for men.
- If you are a smoker, quit! Your doctor will be able to provide (or refer you for) counseling on how to stop smoking.

Review

- Follow-up care should address both your physical and emotional well-being.
- Monitoring for the return of stage II, III, and IV colon cancer includes having regular physical exams, CT scans, colonoscopies, and CEA blood tests.
- Your cancer doctor and primary care doctor should work together to make sure you get the follow-up care you need. The recommended care for you should be laid out in a survivorship care plan.
- ➤ It's very important to live a healthy lifestyle after cancer. This means drinking less alcohol, eating a healthy diet, exercising, quitting smoking, and keeping up with other aspects of your health.

Figure 14

Cutting back on alcohol is an important part of staying healthy. Experts recommend no more than 1 drink per day for women, and no more than 2 drinks per day for men.



Treatment guide: Systemic therapy

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60	Irinotecan
62	FOLFOXIRI
64	5-FU and capecitabine
66	Least toxic regimens
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This chapter presents the systemic therapy pathways used to treat advanced colon cancer. If one regimen doesn't work or stops working, there are other options that may work for you. These are called second- and third-line regimens. Some of the options depend on what treatment you've had before.

Oxaliplatin

Guide 14 maps a treatment path that starts with oxaliplatin. If you see a chemotherapy regimen that has "OX" in it (for example, FOLFOX or CAPEOX), that means the regimen includes oxaliplatin.

FOLFOX and CAPEOX are the two options for first-line treatment. Bevacizumab may be added to either regimen. Cetuximab or panitumumab can be added to FOLFOX to treat tumors with normal *KRAS/NRAS* genes that are in the left side of the colon.

Oxaliplatin can harm your nervous system. Stopping oxaliplatin—but not the other drugs—after 3 months of use may prevent harm. Keep taking the other drugs for 6 months. If the cancer progresses, oxaliplatin may be restarted if it was stopped due to side effects. You should only restart if the side effects have ended.

Capecitabine in the CAPEOX regimen can cause a side effect known as hand-foot syndrome. Symptoms include redness, swelling, and pain on the palms of the hands, bottoms of feet, or both. Sometimes blisters appear. Your dose of capecitabine may be changed at the earliest signs of hand-foot syndrome.

Second-line options

An oxaliplatin-based regimen may not prevent the cancer from getting worse. If this happens, you have several options:

Chemotherapy:

- FOLFIRI regimen, with or without targeted therapy. The targeted therapies cetuximab and panitumumab should only be added if you have normal KRAS/NRAS genes.
- Irinotecan, with or without targeted therapy.
 The targeted therapies cetuximab and
 panitumumab should only be added if you
 have normal KRAS/NRAS genes. For people
 with a BRAF V600E mutation, vemurafenib
 and either cetuximab or panitumumab are
 given with irinotecan.

> Immunotherapy:

- Pembrolizumab (only for dMMR/MSI-H tumors)
- Nivolumab, with or without ipilimumab (only for dMMR/MSI-H tumors)

Third-line and beyond

If the cancer progresses again, one of the secondline treatments may be an option. If not, your options include:

- Chemotherapy with trifluridine and tipiracil
- Targeted therapy with regorafenib
- Joining a clinical trial
- Supportive care for relief from symptoms

Guide 14. Oxaliplatin pathway

First-line regimens		Notes	
FOLFOX ±	Bevacizumab		
	Cetuximab	For left-side tumors with normal KRAS/NRAS genes	
	Panitumumab	For left-side tumors with normal KRAS/NRAS genes	
CAPEOX ±	Bevacizumab		
Second-line regimens		Notes	
	Bevacizumab		
	Ziv-aflibercept		
FOLFIRI ±	Ramucirumab		
	Cetuximab	Only for normal KRAS/NRAS genes	
	Panitumumab	Only for normal KRAS/NRAS genes	
	Bevacizumab		
	Ziv-aflibercept		
	Ramucirumab		
Irinotecan ±	Cetuximab	Only for normal KRAS/NRAS genes	
	Panitumumab	Only for normal KRAS/NRAS genes	
	Cetuximab and vemurafenib	For people with the BRAF V600E mutation	
	Panitumumab and vemurafenib	For people with the BRAF V600E mutation	
Pembrolizumab		Only for dMMR/MSI-H tumors	
Nivolumab ±	Ipilimumab	Only for dMMR/MSI-H tumors	
Third-line regimens and beyond			
Some second-line regimens if not received before		Join a clinical trial	
Regorafenib		Best supportive care	
Trifluridine + tipiracil			

Irinotecan

Guide 15 maps a treatment path that starts with FOLFIRI. If you see a chemotherapy regimen that has "IRI" in the name (for example, FOLFIRI OR FOLFOXIRI), it means that the regimen includes irinotecan.

Targeted therapy with bevacizumab, cetuximab, or panitumumab may be given with FOLFIRI. Cetuximab and panitumumab should only be given for people with left-side tumors and normal KRAS/ NRAS genes.

Irinotecan should be used with caution and at a low dose if you have Gilbert's disease or high bilirubin levels in your blood. Gilbert's disease impairs the liver from correctly processing bilirubin.

Second-line options

FOLFIRI may not prevent the cancer from getting worse. If this happens, you have several options:

- Chemotherapy:
 - FOLFOX regimen, with or without bevacizumab
 - CAPEOX regimen with bevacizumab
 - Irinotecan and a targeted therapy. The targeted therapies cetuximab and panitumumab should only be added if you have normal KRAS/NRAS genes. For people with a BRAF V600E mutation, vemurafenib and either cetuximab or panitumumab are given with irinotecan.
- Immunotherapy:
 - Pembrolizumab (only for dMMR/MSI-H tumors)

Nivolumab, with or without ipilimumab (only for dMMR/MSI-H tumors)

Third-line and beyond

If the cancer progresses again, one of the secondline treatments may be an option. If not, your options include:

- Chemotherapy with trifluridine and tipiracil
- Targeted therapy with regorafenib
- Joining a clinical trial
- Supportive care for relief from symptoms

Guide 15. Irinotecan pathway

First-line regimens		Notes
FOLFIRI ±	Bevacizumab	
	Cetuximab	For left-side tumors with normal KRAS/NRAS genes
	Panitumumab	For left-side tumors with normal KRAS/NRAS genes
Sec	cond-line regimens	Notes
FOLFOX ±	Bevacizumab	
CAPEOX +	Bevacizumab	
Irinotecan +	Cetuximab	Only for normal KRAS/NRAS genes
	Panitumumab	Only for normal KRAS/NRAS genes
	Cetuximab and vemurafenib	For people with the BRAF V600E mutation
	Panitumumab and vemurafenib	For people with the BRAF V600E mutation
Pembrolizumab		Only for dMMR/MSI-H tumors
Nivolumab ±	Ipilimumab	Only for dMMR/MSI-H tumors
Third-line regimens and beyond		
Some second-line regimens if not received before		Join a clinical trial
Regorafenib		Best supportive care
Trifluridine + tipiracil		

FOLFOXIRI

Guide 16 maps a treatment path that starts with the FOLFOXIRI regimen. This regimen includes leucovorin, fluorouracil, oxaliplatin, and irinotecan. It is an intense regimen and will be too harsh for some people. Bevacizumab (a targeted therapy) may be given with FOLFOXIRI.

Second-line options

FOLFOXIRI may not prevent the cancer from getting worse. If this happens, there are several options:

- Chemotherapy:
 - Irinotecan and a targeted therapy.
 The targeted therapies cetuximab and panitumumab should only be added if you have normal KRAS/NRAS genes. For people with a BRAF V600E mutation, vemurafenib and either cetuximab or panitumumab are given with irinotecan.
 - Trifluridine + tipiracil
- Targeted therapy with regorafenib
- Immunotherapy:
 - Pembrolizumab (only for dMMR/MSI-H tumors)
 - Nivolumab, with or without ipilimumab (only for dMMR/MSI-H tumors)

Cetuximab or panitumumab may be options for tumors with normal *KRAS/NRAS* genes. Cetuximab or panitumumab may be received with irinotecan. If you're unable to take irinotecan, you may take panitumumab or cetuximab alone.

Third-line and beyond

If the cancer progresses again, one of the secondline treatments may be an option. Other options include:

- Joining a clinical trial
- Supportive care for relief from symptoms

Guide 16. FOLFOXIRI pathway

First-line regimens		Notes
FOLFOXIRI ±	Bevacizumab	
Second-line regimens		Notes
	Cetuximab	Only for normal KRAS/NRAS genes
	Panitumumab	Only for normal KRAS/NRAS genes
Irinotecan +	Cetuximab and vemurafenib	For people with the BRAF V600E mutation
	Panitumumab and vemurafenib	For people with the BRAF V600E mutation
Regorafenib		
Trifluridine + tipiracil		
Pembrolizumab		Only for dMMR/MSI-H tumors
Nivolumab ±	Ipilimumab	Only for dMMR/MSI-H tumors
Third-line regimens and beyond		
Some second-line regimens if not received before		
Join a clinical trial		

• Best supportive care

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5-FU and capecitabine

Guide 17 maps a treatment path that starts with two intense but less harsh regimens. One of the first-line regimens is 5-FU/LV. This regimen includes fluorouracil and leucovorin. Receiving 5-FU by infusion is preferred over bolus injection. The second option is capecitabine. Bevacizumab may be added to either regimen.

The side effects of these regimens aren't usually as bad as those caused by oxaliplatin or irinotecan. So, if the cancer progresses, you should start supportive care if the side effects were too harsh. If not too harsh, second-line options may be of help.

Second-line options

If the cancer progresses, there are several options:

- Chemotherapy with:
 - FOLFOX regimen, with or without bevacizumab
 - CAPEOX regimen, with or without bevacizumab
 - FOLFIRI regimen, with or without a targeted therapy
 - Irinotecan, with or without a targeted therapy
 - Irinotecan and oxaliplatin, with or without bevacizumab
- Immunotherapy:
 - Pembrolizumab (only for dMMR/MSI-H tumors)
 - Nivolumab, with or without ipilimumab (only for dMMR/MSI-H tumors)

Third-line and beyond

If the cancer progresses again, there are multiple options. Some of the second-line treatments may be an option if not received before. Other options include:

- Chemotherapy:
 - Irinotecan, with or without a targeted therapy.
 The targeted therapies cetuximab and
 panitumumab should only be added if you
 have normal KRAS/NRAS genes. For people
 with a BRAF V600E mutation, vemurafenib
 and either cetuximab or panitumumab are
 given with irinotecan.
 - Trifluridine + tipiracil
- Targeted therapy with regorafenib
- Joining a clinical trial
- Supportive care for relief from symptoms

Guide 17. 5-FU and capecitabine pathway

First-line options		Notes
5-FU/leucovorin ±	Bevacizumab	
Capecitabine ±	Bevacizumab	
Seco	ond-line options	Notes
FOLFOX ±	Bevacizumab	
CAPEOX ±	Bevacizumab	
	Bevacizumab	
FOLFIRI ±	Ziv-aflibercept	
	Ramucirumab	
	Bevacizumab	
Irinotecan ±	Ziv-aflibercept	
	Ramucirumab	
Irinotecan + oxaliplatin ±	Bevacizumab	
Pembrolizumab		Only for dMMR/MSI-H tumors
Nivolumab ±	Ipilimumab	Only for dMMR/MSI-H tumors
Third-line and beyond options		Notes
	Cetuximab and vemurafenib	For people with the BRAF V600E mutation
Irinotecan ±	Panitumumab and vemurafenib	For people with the BRAF V600E mutation
IIIIOtecan ±	Cetuximab	Only for normal KRAS/NRAS genes
	Panitumumab	Only for normal KRAS/NRAS genes
Regorafenib		
Trifluridine + tipiracil		
Some second-line regimens if not received before		
Join a clinical trial		
Best supportive care		

Least toxic regimens

Chemotherapy can be very harsh on your body and can have many unpleasant side effects. The negative effects of chemotherapy are worse with some drugs and regimens more than others. Your treatment team will consider whether certain regimens would be too harsh for you. If this is the case, there are regimens that may be less harmful to you. These are shown in Guide 18.

Chemotherapy with 5-FU and leucovorin (with or without bevacizumab) is an option. Another option is capecitabine with or without bevacizumab. Targeted therapy (cetuximab or panitumumab) may be an option. These drugs treat tumors with normal *KRAS/NRAS* genes that are in the left side of the colon. If the tumor is dMMR or MSI-H, treatment with immunotherapy may be an option.

If your ability to do activities improves with one of the regimens shown in Guide 18, your doctor may recommend that you continue treatment with one of the stronger regimens described earlier in this chapter. If you are not able to tolerate the regimens shown in Guide 18, beginning supportive care is an option. Supportive care isn't meant to treat the cancer, but rather to help with symptoms and make you more comfortable.

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Guide 18. Least toxic systemic therapy options

Treatment options	Regimens that may be used	Notes
Chemotherapy	5-FU + leucovorinCapecitabine	
Chemotherapy + targeted therapy	5-FU + leucovorin + bevacizumabCapecitabine + bevacizumab	
Targeted therapy	CetuximabPanitumumab	Only for left-sided tumors with normal <i>KRAS/NRAS</i> genes
Immunotherapy	NivolumabPembrolizumabNivolumab + ipilimumab	Only for dMMR/MSI-H tumors

Review

- There are five pathways used to treat advanced colon cancer.
- The oxaliplatin pathway starts with either FOLFOX or CAPEOX.
- The irinotecan pathway starts with FOLFIRI.
- The FOLFOXIRI pathway starts with both oxaliplatin and irinotecan.
- ➤ The 5-FU/LV and capecitabine pathway starts with intense but less harsh regimens.
- The least toxic pathway starts with regimens likely to be the least harmful to you.

8 Making treatment decisions

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- 69 Questions to ask your doctors
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- 75 Review



Having cancer is very stressful. While absorbing the fact that you have cancer, you have to learn about tests and treatments. In addition, the time you have to accept a treatment plan feels short. Parts 1 through 7 described the cancer and treatment options. This chapter aims to help you make decisions that are in line with your beliefs, wishes, and values.

It's your choice

The role each person wants in choosing his or her treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. But, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which option to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. Most patients do. In shared decision-making, you and your doctors share information, weigh the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you are likely to get a higher quality of care and be more satisfied. You'll likely get the treatment you want, at the place you want, and by the doctors you want.

Questions to ask your doctors

You may meet with experts from different fields of medicine. Strive to have helpful talks with each person. Prepare questions before your visit and ask questions if the person isn't clear. You can also take notes and get copies of your medical records.

It may be helpful to have your spouse, partner, family member, or a friend with you at these visits. A patient advocate or navigator might also be able to come. They can help to ask questions and remember what was said. Suggested questions to ask include:

What's my diagnosis and prognosis?

It's important to know that there are different types of cancer. Cancer can greatly differ even when people have a tumor in the same organ. Based on your test results, your doctors can tell you which type of cancer you have. He or she can also give a prognosis. A prognosis is a prediction of the pattern and outcome of a disease. Knowing the prognosis may affect what you decide about treatment.

1.	Where did the cancer start? In what type of cell? Is this cancer common?
2.	What is the cancer stage? Does this stage mean the cancer has spread far?
3.	Is this a fast- or slow-growing cancer?
4.	What tests do you recommend for me?
5.	Where will the tests take place? How long will the tests take and will any test hurt?
6.	What if I am pregnant?
7.	How do I prepare for testing?
8.	Should I bring a list of my medications?
9.	Should I bring someone with me?
10.	How often are these tests wrong?
11.	Would you give me a copy of the pathology report and other test results?
12.	Who will talk with me about the next steps? When?

What are my options?

There is no single treatment practice that is best for all people. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

- 1. What will happen if I do nothing?
- 2. Can I just carefully monitor the cancer?
- 3. Do you consult NCCN recommendations when considering options?
- 4. Are you suggesting options other than what NCCN recommends? If yes, why?
- 5. Do your suggested options include clinical trials? Please explain why.
- 6. How do my age, health, and other factors affect my options? What if I am pregnant?
- 7. Which option is proven to work best?
- 8. Which options lack scientific proof?
- 9. What are the benefits of each option? Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
- 10. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?
- 11. How do you know if treatment is working?
- 12. What are my options if my treatment stops working?
- 13. What can be done to prevent or relieve the side effects of treatment?

What does each option require of me?

Many patients consider how each option will practically affect their lives. This information may be important because you have family, jobs, and other duties to take care of. You also may be concerned about getting the help you need. If you have more than one option, choosing the option that is the least taxing may be important to you:

1.	Will I have to go to the hospital or elsewhere? How often? How long is each visit?
2.	What do I need to think about if I will travel for treatment?
3.	Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?
4.	How do I prepare for treatment? Do I have to stop taking any of my medicines? Are there foods I will have to avoid?
5.	Should I bring someone with me when I get treated?
6.	Will the treatment hurt?
7.	How much will the treatment cost me? What does my insurance cover?
8.	Will I miss work or school? Will I be able to drive?
9.	Is home care after treatment needed? If yes, what type?
10.	How soon will I be able to manage my own health?
11.	When will I be able to return to my normal activities?

What is your experience?

More and more research is finding that patients treated by more experienced doctors have better results. It is important to learn if a doctor is an expert in the cancer treatment he or she is offering.

- 1. Are you board certified? If yes, in what area?
- 2. How many patients like me have you treated?
- 3. How many procedures like the one you're suggesting have you done?
- 4. Is this treatment a major part of your practice?
- 5. How many of your patients have had complications?

Weighing your options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another. Some ways to decide on treatment are discussed next.

2nd opinion

The time around deciding a treatment is very stressful. People with cancer often want to get treated as soon as possible. They want to make their cancer go away before it spreads farther. While cancer can't be ignored, usually there is time to think about and choose which option is best for you.

You may wish to have another doctor review your test results and suggest a treatment plan. This is called getting a 2nd opinion. You may completely trust your doctor, but a 2nd opinion about which option is best can help.

Copies of the pathology report, a DVD of the imaging tests, and other test results need to be sent to the doctor giving the 2nd opinion. Some people feel uneasy asking for copies from their doctors. However, a 2nd opinion is a normal part of cancer care.

When doctors have cancer, most will talk with more than one doctor before choosing their treatment. What's more, some health plans require a 2nd opinion. If your health plan doesn't cover the cost of a 2nd opinion, you have the choice of paying for it yourself.

If the two opinions are the same, you may feel more at peace about the treatment you accept to have. If the two opinions differ, think about getting a 3rd opinion. A 3rd opinion may help you decide between

your options. Choosing your cancer treatment is a very important decision. It can affect your length and quality of life.

Support groups

Besides talking to health experts, it may help to talk to other people who have walked in your shoes. At support groups, you can ask questions and hear about the experiences of other people with colon cancer. Find a support group at the websites listed on the next page.

Compare benefits and downsides

Every option has benefits and downsides. Consider these when deciding which option is best for you. Talking to others can help identify benefits and downsides you haven't thought of. Scoring each factor from 0 to 10 can also help since some factors may be more important to you than others.

Websites

American Cancer Society

cancer.org/cancer/colonandrectumcancer/detailedguide/index

Cancer Support Community

cancersupportcommunity.org

Colorectal Cancer Alliance

ccalliance.org

Fight Colorectal Cancer

FightColorectalCancer.org

National Cancer Institute (NCI)

cancer.gov/types/colorectal

National Coalition for Cancer Survivorship

canceradvocacy.org/toolbox

NCCN for Patients®

nccn.org/patients

66

As a caregiver I provide comfort and support where no one else can, being the foundation my wife needs for her treatment and her care.

FrederickCaregiver

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- ➤ Getting a 2nd opinion, attending support groups, and comparing benefits and downsides may help you decide which treatment is best for you.

Glossary

77 Dictionary

81 Acronyms

abdomen

The belly area between the chest and pelvis.

ablation

Treatment using radiofrequency or cold to destroy cancer cells.

adenocarcinoma

Cancer in cells that line organs and make fluids or hormones.

adenoma

The most common type of polyp and is the most likely to form cancer cells. Also called adenomatous polyps.

adjuvant treatment

Treatment that is given to lower the chances of the cancer returning.

adventitia

The outer layer, in some places, of the colon wall.

angiolymphatic invasion

Cancer has spread into the tumor's lymph or blood vessels.

anus

The opening at the end of the digestive system that allows stool to pass out of the body.

bilirubin

A substance in the body that causes bodily fluids to be yellow.

biopsy

Removal of small amounts of tissue or fluid to be tested for disease.

bolus

A fast injection of a drug.

boost

An extra dose of radiation to a specific area of the body.

cancer grade

How closely the cancer cells look like normal cells.

cancer stage

Rating of the growth and spread of tumors.

carcinoembryonic antigen (CEA)

A protein that gets released by some tumors and can be detected in blood as a tumor marker.

carcinoma in situ

Cancer that has not grown into tissue that could allow cancer cells to spread. It is a noninvasive cancer.

catheter

A flexible tube inserted in the body to give treatment or drain fluid from the body.

chemotherapy

Drugs that stop the life cycle of cells so they don't increase in number.

clinical stage

The rating of the extent of cancer based on tests before treatment.

clinical trial

Research on a test or treatment to assess its safety or how well it works.

colectomy

Surgery to remove a part of the colon.

colon

The hollow organ in which eaten food turns from a liquid into a solid form.

colonoscope

A thin, long tube with a light and camera used to see the colon.

colonoscopy

Insertion of a thin tool into the colon to view or remove tissue.

colostomy

Surgery to connect a part of the colon to the outside of the abdomen and that allows stool to drain into a bag.

complete blood count (CBC)

A test of the number of blood cells.

computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the inside of the body.

contrast

A dye put into your body to make clearer pictures during imaging tests.

deoxyribonucleic acid (DNA)

A very thin and long molecule that contains genetic code. Also called the "blueprint of life."

diagnosis

To identify a disease.

digestive system

A set of organs in the body that changes food into small parts for the body to use as energy.

embolization

Blockage of blood flow to a tumor with beads that emit either chemotherapy or radiation.

endoscopic polypectomy

Surgery to remove a polyp during a colonoscopy.

enema

Injection of liquid into the rectum to clear the bowel.

epithelium

Tissue that lines the colon wall.

esophagus

The tube-shaped digestive organ between the mouth and stomach.

external beam radiation therapy (EBRT)

Treatment with radiation received from a machine outside the body.

familial adenomatous polyposis (FAP)

An inherited medical condition that increases the odds of colon cancer.

gene

Coded instructions in cells for making new cells and controlling how cells behave.

general anesthesia

A controlled loss of wakefulness from drugs.

hereditary non-polyposis colon cancer (HNPCC)

An inherited medical condition that increases the odds of colon cancer. Also called Lynch syndrome.

hives

Itchy, swollen, and red skin caused by the body ridding itself of an invader.

hyperplastic polyp

A polyp that grows fast and is often found in the last part of the colon.

imaging test

A test that makes pictures of the insides of the body.

inflammatory bowel disease

A medical condition that causes the intestine to swell.

inflammatory polyp

A polyp that often grows after the intestine swells.

infusion

A method of giving drugs slowly through a needle into a vein.

intensity-modulated radiation therapy (IMRT)

Radiation therapy that uses small beams of different strengths based on the thickness of the tissue.

intraoperative radiation therapy (IORT)

Radiation therapy that is given inside the body at the end of an operation.

invasive cancer

Cancer cells have grown into the second layer of the colon wall.

lamina propria

Connective tissue within the mucosa of the colon wall.

large intestine

The digestive organ that prepares unused food for leaving the body.

laxative

Drugs used to clean out the intestines.

lymph

A clear fluid containing white blood cells.

lymph node

Small groups of special disease-fighting cells located throughout the body.

lymphadenectomy

Surgery to remove lymph nodes.

magnetic resonance imaging (MRI)

A test that uses a magnetic field and radio waves to make pictures of the insides of the body.

medical history

All health events and medications taken to date.

metastasectomy

Surgery to remove cancer that has spread far from the first tumor.

metastasis

The spread of cancer cells from the first (primary) tumor to a distant site.

microsatellite instability (MSI)

Errors in a small DNA part that happen when DNA is making a copy of itself.

microsatellite instability-high (MSI-H)

The presence of 2 or more MSI markers.

mismatch repair deficient (dMMR)

Abnormal changes in genes that contain instructions for making proteins that fix errors in DNA.

mismatch repair (MMR) proteins

Proteins that correct DNA errors that occur when copies of DNA are being made.

mucosa

The first, inner layer of the colon wall.

mucus

A sticky, thick liquid that moisturizes or lubricates.

muscularis mucosae

A thin layer of muscle within the mucosa of the colon wall.

muscularis propria

The third layer of the colon wall made mostly of muscle.

mutation

An abnormal change in the instructions within cells for making and controlling cells.

needle biopsy

Removal of tissue or fluid samples from the body with a needle.

neoadjuvant treatment

Treatment given before the main treatment used to cure disease. Also called preoperative treatment.

noninvasive cancer

Cancer cells have not grown into the second layer of the colon wall.

observation

A period of testing for cancer growth.

parietal peritoneum

The outer layer of tissue lining around the abdomen.

pathologic stage

A rating of the extent of cancer based on tests given after treatment.

pathologist

A doctor who's an expert in testing cells and tissue to find disease.

pedunculated polyp

A polyp shaped like a mushroom with a stalk.

pelvis

The area between the hip bones.

perineural invasion

Spread of cancer into nearby nerves.

physical exam

A review of the body by a health expert for signs of disease.

polyp

An extra growth of tissue from the epithelium of the colon wall

portal vein embolization

The blood vessel to the liver tumor is blocked causing the healthy part of the liver to grow larger.

positron emission tomography (PET)

Use of radioactive material to see the shape and function of body parts.

positron emission tomography/computed tomography (PET/CT)

A test that uses radioactive material and x-rays to view the shape and function of organs and tissues.

primary tumor

The first mass of cancer cells in the body.

prognosis

The pattern and outcome of a disease.

progression

The growth or spread of cancer after being tested or treated.

radiation therapy

The use of high-energy rays to destroy cancer cells.

radiologist

A doctor who specializes in reading imaging tests.

rectum

An organ in the digestive system that holds stool until expelled from the body.

recurrence

The return of cancer after a cancer-free period.

serosa

The outer layer, in some places, of the colon wall that makes fluid so that organs can slide against one another; also called the visceral peritoneum.

sessile polyp

A polyp that is flat.

side effect

An unplanned physical or emotional response to treatment.

small intestine

The digestive organ that absorbs nutrients from eaten food.

stereotactic body radiation therapy (SBRT)

Radiation therapy that uses precise, high-dose beams.

stool

Unused food passed out of the body; also called feces.

submucosa

The second layer of the colon wall made mostly of connective tissue.

subserosa

A thin layer of connective tissue that makes fluid.

supportive care

Treatment for the symptoms or health conditions caused by cancer or cancer treatment.

surface receptor

A protein found in the membrane of cells.

surgical margin

The normal tissue around the edge of a tumor that is removed during surgery.

targeted therapy

Drugs that stop the action of molecules that start the growth of cancer cells.

three-dimensional conformal radiation therapy (3D-CRT)

Radiation therapy that uses beams that match the shape of the tumor.

total colonoscopy

Insertion of a thin tool into the colon to view the entire colon and, if needed, remove tissue.

tumor budding

A group of 5 or fewer cancer cells separate from the main tumor.

tumor deposit

The presence of tiny tumors where the lymph drains from the tumor.

ultrasound

A test that uses sound waves to take pictures of the insides of the body.

villous polyp

A polyp with a ruffled structure.

Acronyms

3D-CRT

three-dimensional conformal radiation therapy

AJCC

American Joint Committee on Cancer

CBC

complete blood count

CEA

carcinoembryonic antigen

CT

computed tomography

dMMR

mismatch repair deficient

DNA

deoxyribonucleic acid

EBRT

external beam radiation therapy

FAP

familial adenomatous polyposis

FDA

U.S. Food and Drug Administration

HAI

hepatic arterial infusion

HNPCC

hereditary non-polyposis colon cancer

IMRT

intensity-modulated radiation therapy

IORT

intraoperative radiation therapy

MMR

mismatch repair

MRI

magnetic resonance imaging

MSI

microsatellite instability

MSI-H

microsatellite instability-high

MSI-L

microsatellite instability-low

NCCN®

National Comprehensive Cancer Network®

PET

positron emission tomography

PET/CT

positron emission tomography/computed tomography

SBRT

stereotactic body radiation therapy

TNM

tumor, node, metastasis

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For disclosures, visit www.nccn.org/about/disclosure.aspx.

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Abramson Cancer Center at the University of Pennsylvania Philadelphia, Pennsylvania 800.789.7366 pennmedicine.org/cancer

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City of Hope National Medical Center Los Angeles, California 800.826.4673 cityofhope.org

Dana-Farber/Brigham and Women's Cancer Center Massachusetts General Hospital Cancer Center Boston, Massachusetts 877.332.4294 dfbwcc.org massgeneral.org/cancer

Duke Cancer Institute Durham, North Carolina 888.275.3853 dukecancerinstitute.org

Fox Chase Cancer Center Philadelphia, Pennsylvania 888.369.2427 foxchase.org

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Robert H. Lurie Comprehensive Cancer Center of Northwestern University Chicago, Illinois 866.587.4322 cancer.northwestern.edu

Mayo Clinic Cancer Center Phoenix/Scottsdale, Arizona Jacksonville, Florida Rochester, Minnesota 800.446.2279 • Arizona 904.953.0853 • Florida 507.538.3270 • Minnesota www.mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center New York, New York 800.525.2225 mskcc.org

Moffitt Cancer Center Tampa, Florida 800.456.3434 moffitt.org

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Roswell Park Comprehensive Cancer Center Buffalo, New York 877.275.7724 roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine St. Louis, Missouri 800.600.3606 siteman.wustl.edu

St. Jude Children's Research Hospital The University of Tennessee Health Science Center Memphis, Tennessee 888.226.4343 • stjude.org 901.683.0055 • westclinic.com Stanford Cancer Institute Stanford, California 877.668.7535 cancer.stanford.edu

University of Alabama at Birmingham Comprehensive Cancer Center Birmingham, Alabama 800.822.0933 www3.ccc.uab.edu

UC San Diego Moores Cancer Center La Jolla, California 858.657.7000 cancer.ucsd.edu

UCSF Helen Diller Family Comprehensive Cancer Center San Francisco, California 800.689.8273 cancer.ucsf.edu

University of Colorado Cancer Center Aurora, Colorado 720.848.0300 coloradocancercenter.org

University of Michigan Rogel Cancer Center Ann Arbor, Michigan 800.865.1125 mcancer.org

The University of Texas MD Anderson Cancer Center Houston, Texas 800.392.1611 mdanderson.org

University of Wisconsin Carbone Cancer Center Madison, Wisconsin 608.265.1700 uwhealth.org/cancer

Vanderbilt-Ingram Cancer Center Nashville, Tennessee 800.811.8480 vicc.org

Yale Cancer Center/ Smilow Cancer Hospital New Haven, Connecticut 855.4.SMILOW yalecancercenter.org

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