

NCCN
NCCN
GUIDELINES
FOR PATIENTS®

2018

Please complete
our online survey at
NCCN.org/patients/survey

Rectal Cancer

Presented with support from:



Available online at NCCN.org/patients



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 rectal cancer.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 28 of the world's leading cancer centers. Experts from NCCN® have written treatment guidelines for doctors who treat rectal 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 rectal cancer in adults. Key points of the book are summarized in the related [NCCN Quick Guide™](#). NCCN also offers patient resources on lung, melanoma, prostate, and many other cancer types. Visit [NCCN.org/patients](https://www.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.

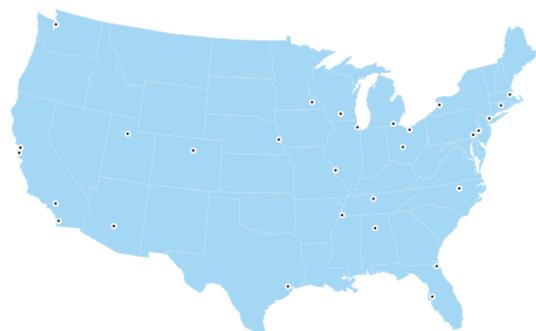
For more information about the NCCN Guidelines, visit [NCCN.org/clinical.asp](https://www.nccn.org/clinical.asp).

Dorothy A. Shead, MS
*Director, Patient
Information Operations*

Laura J. Hanisch, PsyD
*Medical Writer/Patient
Information Specialist*

Erin Vidic, MA
Medical Writer

Rachael Clarke
*Guidelines Data and
Layout Coordinator*



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](https://www.nccnfoundation.org).

© 2019 National Comprehensive Cancer Network, Inc. Based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Rectal Cancer (Version 3.2018, August 7, 2018).

All rights reserved. NCCN Guidelines for Patients® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. No one, including doctors or patients, may use the NCCN Guidelines for Patients® for any commercial purpose and may not claim, represent, or imply that the NCCN Guidelines for Patients® that has been modified in any manner is derived from, based on, related to or arises out of the NCCN Guidelines for Patients®. The NCCN Guidelines are a work in progress that may be redefined as often as new significant data become available. NCCN makes no warranties of any kind whatsoever regarding its content, use, or application and disclaims any responsibility for its application or use in any way.

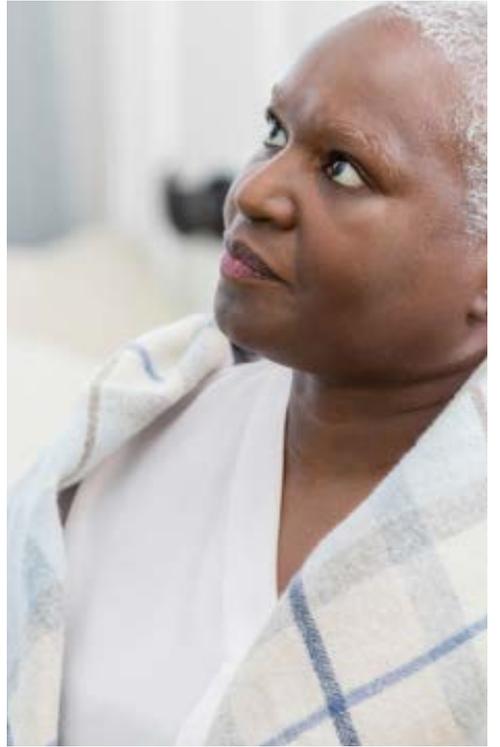
National Comprehensive Cancer Network (NCCN) • 3025 Chemical Road, Suite 100 • Plymouth Meeting, PA 19462 • 215.690.0300

Endorsed and sponsored in part by



Fight Colorectal Cancer

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



Contents

6	How to use this book	68	Part 7 Making treatment decisions Offers tips for choosing the best treatment.
7	Part 1 Rectal cancer basics Explains what cancer is and how it affects the rectum.	77	Dictionary
13	Part 2 Treatment planning Describes the health care needed before rectal cancer treatment.	81	Acronyms
22	Part 3 Overview of cancer treatments Describes the treatments used to cure and control rectal cancer.	82	NCCN Panel Members for Rectal Cancer
33	Part 4 Treatment guide: Nonmetastatic cancer Presents treatment options for rectal cancer that hasn't spread to distant sites.	83	NCCN Member Institutions
48	Part 5 Treatment guide: Metastatic cancer Presents treatment options for rectal cancer that has spread to the liver, lungs, or other sites.	84	Index
57	Part 6 Treatment guide: Systemic therapy Presents the order of drug options for advanced rectal cancer.		

Who should read this book?

This book is about rectal cancer treatment. It does not address colon 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.

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 rectal cancer is. It also explains how rectal cancer is found and given a stage. It is important to know the stage of the cancer. 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 rectal cancer is presented in **Part 3**. Knowing what a treatment is will help you understand your options. Treatment options are presented in **Parts 4 through 6** partly based on the cancer stage. Tips for talking and deciding your options with your doctor are presented in **Part 7**.

Does this book include all options?

This book includes information for many people. Your 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.

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.

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**.

1

Rectal cancer basics

-
- 8 The rectum

 - 10 How cancer works

 - 11 Polyps

 - 12 Cancer staging

 - 12 Review



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

The rectum

The rectum 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 rectum. **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. It holds stool until it leaves the body.

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

The wall of the rectum 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 rectal 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.

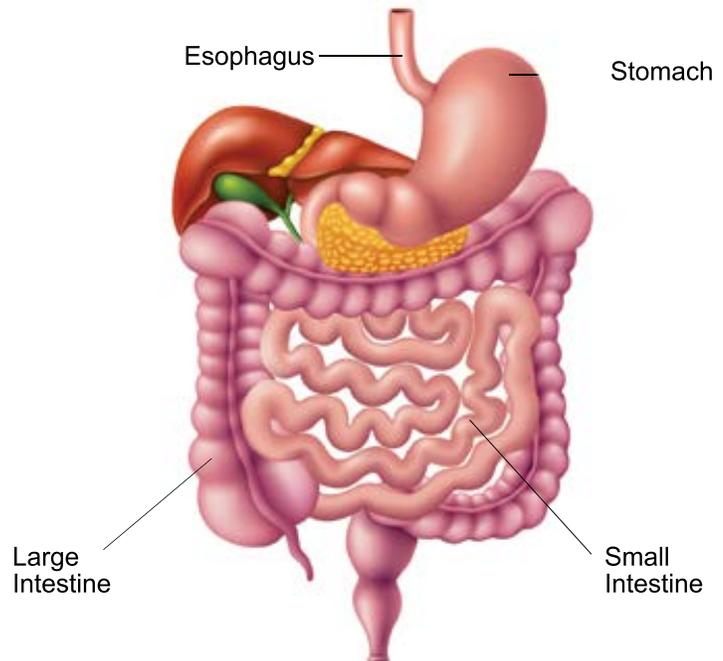
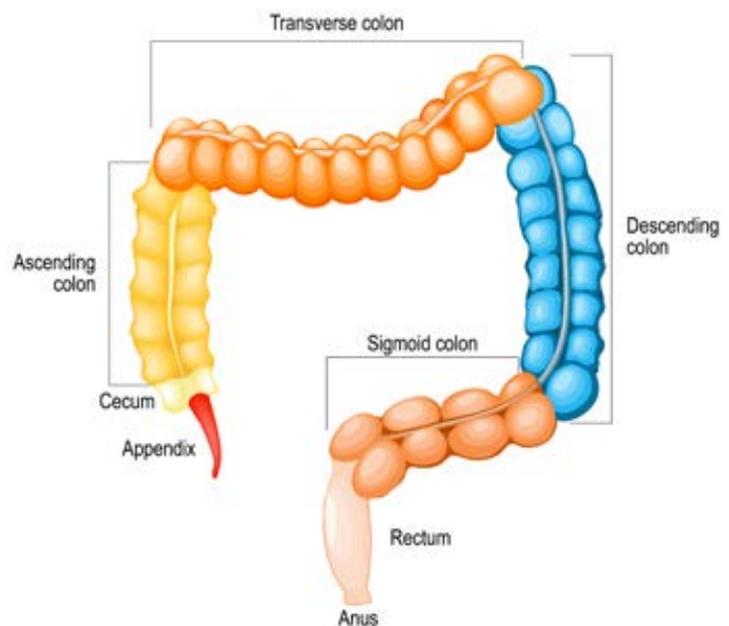


Figure 2 The rectum

The rectum is about 5 inches long and forms the last part of the large intestine. Stool is held in the rectum until it leaves the body through the anus.



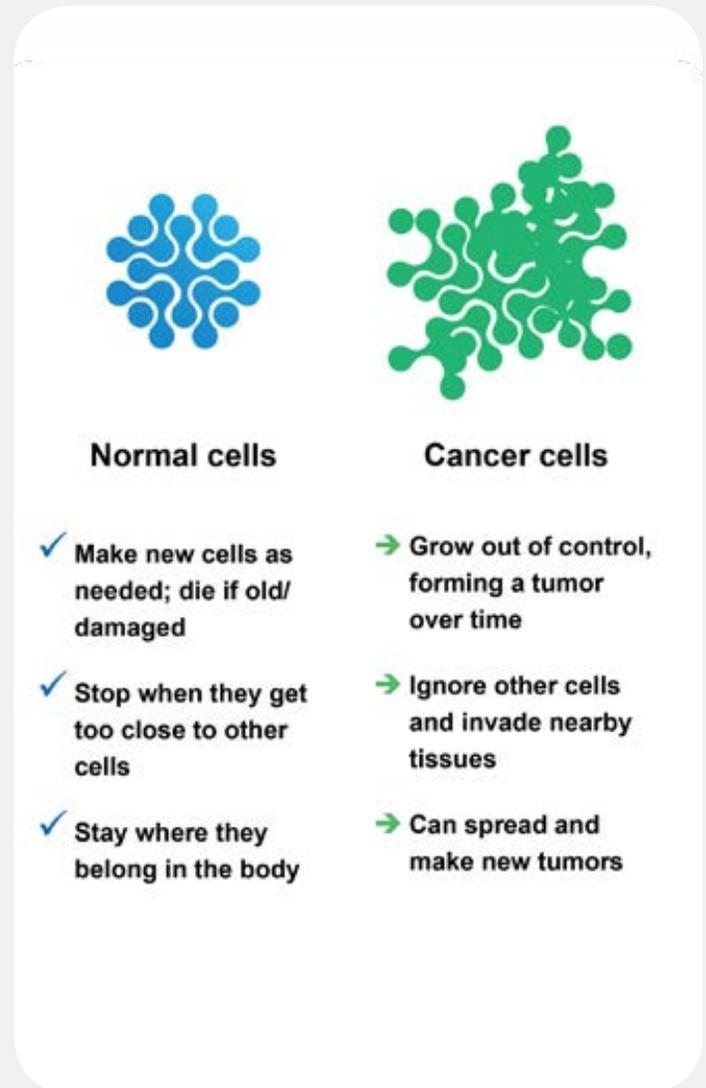
How cancer works

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 (**d**eoxyribonucleic **a**cid). Changes (called mutations or alterations) 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 rectal wall. While most rectal polyps do not become cancer, almost all rectal 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 rectal wall. They have a stalk and round top. **See Figure 4.** Sessile polyps are flatter, don't stick out much from the rectal 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 under the microscope. 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

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 (**A**merican **J**oint **C**ommittee on **C**ancer) TNM (**t**umor, **n**ode, **m**etastasis) system is used to stage rectal 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 tumor has grown through the rectal wall
- **N:** Whether any lymph nodes have cancer
- **M:** Whether the cancer has spread to areas far from the rectum (metastasized)

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

Stage 0

These cancers are also called *carcinoma in situ* of the rectum. The cancer is noninvasive. This means it has not grown beyond the first layer of the rectal 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 rectal wall. There is no cancer in nearby lymph nodes or in areas far from the rectum.

Stage II

The cancer has grown all the way through the rectal wall. It may have attached or grown into other nearby structures or organs. There is no cancer in nearby lymph nodes or in areas far from the rectum.

Stage III

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

Stage IV

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

Review

- The rectum is the last part of the large intestine. Stool is held in the rectum until it leaves the body through the anus.
- The rectal wall is made of layers of tissue. Cancer starts on the inside 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 rectal cancers start in polyps.
- The cancer stage is a rating of how much cancer there is in your body.

2

Treatment planning

- 14 Health history
- 15 Physical exam
- 15 Biopsy
- 16 Colonoscopy
- 17 Blood tests
- 18 Imaging tests
- 20 Tumor marker testing
- 21 Review



Your doctors will make a treatment plan just for you. First, they will 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.

Health history

Your medical history includes any health events and medicines you've taken in your life. Rectal 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

Rectal cancer often occurs for unknown reasons. Some people, however, are more likely to get rectal 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 rectal cancer. This is called an *inherited cancer syndrome*.

There are two main inherited cancer syndromes for rectal cancer—Lynch syndrome and FAP (**f**amilial **a**denomatous **p**olyposis). Lynch syndrome is more common than FAP.

Lynch syndrome is also called HNPCC (**h**ereditary **n**on-**p**olyposis **c**olorectal **c**ancer). It's the most common type of inherited syndrome to cause rectal cancer. It also increases the risk for other types of

cancer. Only 3 to 5 out of every 100 people with rectal cancer have Lynch syndrome.

FAP is a rare inherited syndrome that often leads to rectal cancer. However, only 1 out of 100 people with rectal 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 rectal 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.



Remember **YOU** are the leader of your treatment team. Educate yourself about your cancer and treatment options. It's your body, and you have the final say about any treatment decisions.

– Peg, 38

2-year survivor, Stage IV rectal cancer

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

Rectal biopsy

First, your doctor will perform a *digital rectal exam*. Your doctor will put a glove on his or her hand. Lubricant will be applied to his or her index finger. Next, your doctor will insert this finger into your rectum. He or she will be able to feel your rectum and nearby tissue.

Before the biopsy, your rectum may be numbed to prevent pain. For samples near your anus, an *anoscope* may be used. This is a round, hollow tool that has a light. It will be inserted a few inches into your rectum. For distant samples, a *sigmoidoscope* will be used. This tool is shaped like a tube. It has a light, camera, and cutting device.

Needle biopsy

Samples of tissue or fluid can sometimes be removed from the body with a needle. This procedure is called a *needle biopsy*. The methods of obtaining samples with a needle differ based on the body site. If your doctor suspects metastases, a needle



SNAPSHOT

Lynch syndrome

- ✓ Also called HNPCC (**h**ereditary **n**onpolyposis **c**olorectal **c**ancer)
- ✓ About 5 out of 100 people with colorectal cancer will also have Lynch syndrome
- ✓ People born with this syndrome are at high risk of getting colorectal cancer and some other cancers
- ✓ Caused by inherited mutations of the genes that fix damaged DNA, called MMR (**m**ismatch **r**epair) genes
- ✓ NCCN experts recommend testing all people with rectal cancer for problems with the MMR genes. This helps determine who should be tested for Lynch syndrome.

biopsy may be done. The samples will be sent to a pathologist for cancer testing.

Pathology report

A report will be written each time tissue is removed from your body and tested for cancer. The report is



SNAPSHOT

FAP (familial adenomatous polyposis)

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

called a *pathology report*. Pathology reports are very important to 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 under a microscope. 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.

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

Colonoscopy

A colonoscopy is a procedure that allows your doctor to examine your colon and rectum 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 rectum and the rest of the 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 rectum 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 (**complete blood count**) 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 rectal 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 outside the rectum.

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.

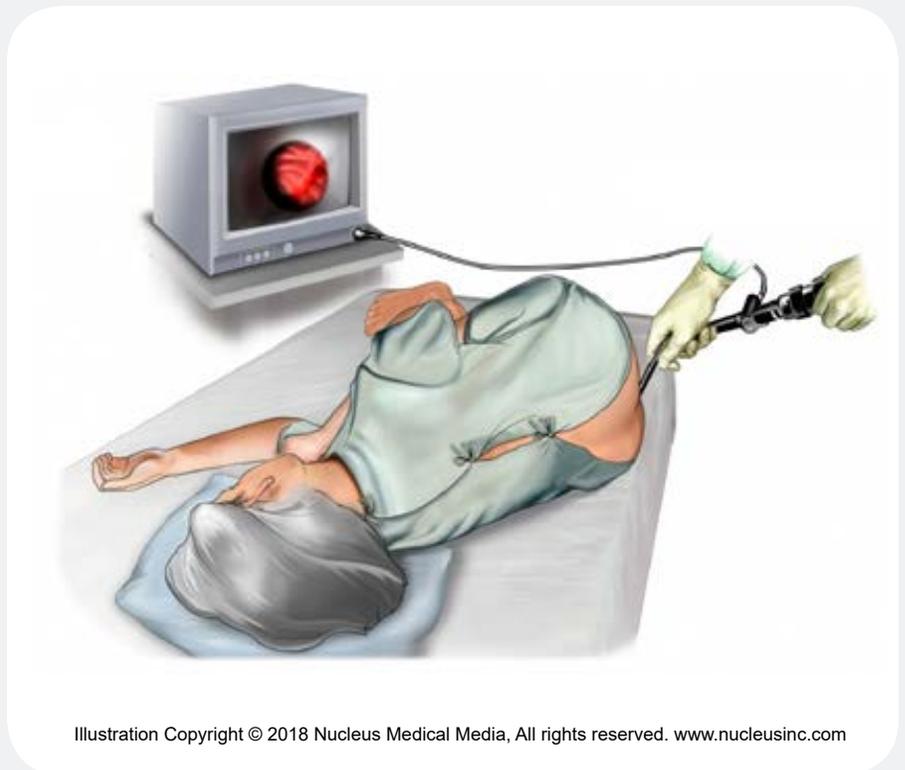


Illustration Copyright © 2018 Nucleus Medical Media, All rights reserved. www.nucleusinc.com

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 will help your doctor decide what the next steps of care should be.

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 rectum wall, CT scans of your chest and abdomen are recommended. The radiologist will look for cancer in nearby and distant sites.



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

Sometimes CT is combined with PET (positron emission tomography). When used together, it is called a PET/CT scan. PET/CT scan is not often used to plan treatment for rectal 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
- If you can't receive contrast dye for CT or MRI

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.

MRI

MRI (magnetic resonance imaging) uses a magnetic field and radio waves to make pictures. There are three reasons why you may receive an MRI. Your doctor may order an MRI if the CT scan was unclear. Contrast should be used. Second, MRI and chest CT without contrast may be done if you can't receive CT contrast. Third, you may receive a pelvic MRI to assess the extent of the cancer in your pelvis. The scan can show the tumor depth and if cancer is in lymph nodes.

Getting MRI is much like getting 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 be used to help you stay in place. MRI may cause your body to feel a bit warm. **See Figure 8.**

Endorectal ultrasound

Instead of pelvic MRI, you may receive an endorectal ultrasound. This test can also show the extent of

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.



cancer in your pelvis. A small probe will be inserted into your rectum. The probe will emit sound waves that will bounce off of tissue and make echoes. The echoes will make a picture that will be seen by your doctor on a screen.

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, either the primary tumor removed during surgery or a tumor in a distant site (a metastasis) will be 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

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.



you have this genetic defect the result will either be MSI-H (**m**icro**s**atellite **i**nstability **h**igh) or dMMR (**m**ismatch **r**epair **d**eficient). Both results mean the same thing.

NCCN experts recommend testing for this tumor marker in all people with rectal cancer for two 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 rectal cancer. Genes work as instruction manuals for making important proteins. Some people with rectal 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 rectal cancer do not work if the *RAS* genes are abnormal. For this reason, NCCN experts recommend testing for *KRAS* and *NRAS* mutations if your rectal cancer has spread to other parts of your body (metastasized).

BRAF mutation

About 5 to 9 out of every 100 people with rectal 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 rectal 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.

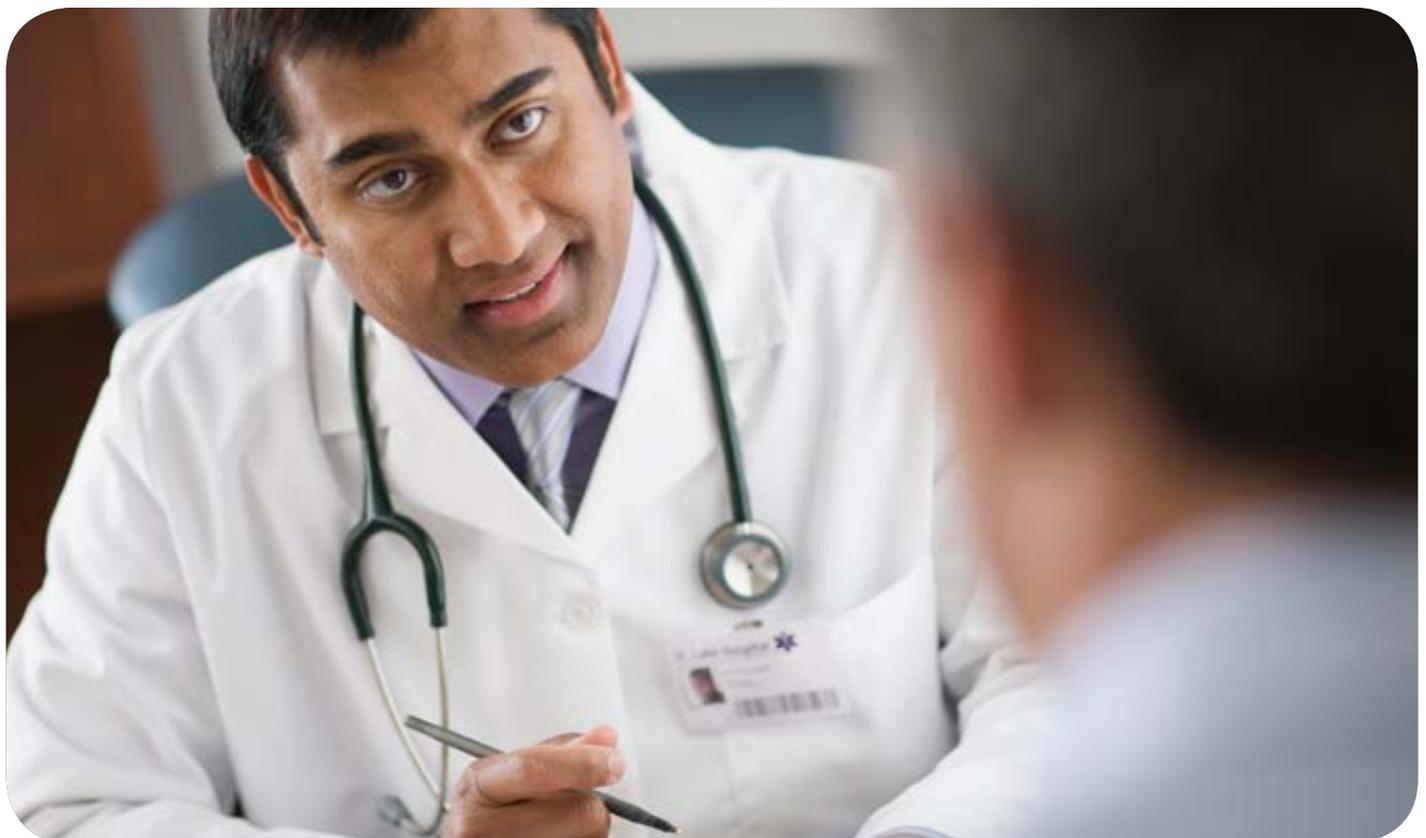
Review

- ▶ 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 rectal 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 rectal cancers. Testing for mutated *KRAS*, *NRAS*, and *BRAF* genes is recommended for rectal cancer that has spread to other parts of the body.

3

Overview of cancer treatments

23	Surgery
25	Chemotherapy
27	Targeted therapy
28	Immunotherapy
29	Radiation therapy
30	Ablation
30	Embolization
31	Clinical trials
32	Review



This chapter describes the ways rectal cancer is usually treated. Knowing what a treatment is will help you understand your treatment options listed in Parts 4 through 6. Not every person will receive every treatment described in this chapter.

Surgery

Some rectal cancers grow beyond the polyp and into the rectum wall. In many of these cases, surgery is a key part of treatment. This section describes the types of surgery used for rectal 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 rectum for surgery. Right before surgery, you will be given general anesthesia.

Transanal surgery

Some small (T1) tumors are treated with transanal surgery. This type of surgery will not cut through your skin. Instead, the tumor will be removed through your anus.

Your surgeon will remove the entire rectal wall and some fat underneath the tumor. Some normal-looking tissue around the tumor will also be removed. This is called the surgical margin. It is done to hopefully remove all the cancer. Likewise, the tumor should be removed in one piece to avoid leaving cancer cells behind.

An advantage of this approach is that your anal muscle will not be removed. A drawback is that you

will be watched very closely for the cancer returning. More details on transanal surgeries are given next.

Transanal local excision

This surgery removes small tumors near the anus. Pain during surgery is often prevented by numbing the treatment site. Otherwise, your entire pelvis may be numbed. Another option is that you will be put in a deep sleep-like state with general anesthesia. Before surgery, the tumor location will be confirmed with a rectal exam.

Your position during surgery depends on the tumor site. You may lie face down on a table that can be raised in the middle like a drawbridge. When raised, your buttocks will be higher than your head and feet. Otherwise, you may lie on your back with your legs raised in stirrups. This position is like sitting in a tipped-over chair.

A few tools will be used to assess the tumor. Your buttocks will be taped apart. Your anus will be spread open with a retractor. Another retractor will be used to expand your rectum. Surgery starts with marking the surgical margin. Your surgeon will make a dotted line around the tumor with a heated wire. Stitches may be used to bring the tumor more into view. The tumor will then be removed as described above. The surgical cut may be closed with stitches. At the end, your surgeon will perform a proctoscopic exam. This is to make sure your rectum wasn't closed or narrowed.

Transanal endoscopic microsurgery

This surgery removes tumors in the middle or upper rectum. It is different from a transanal local excision in a few ways. General anesthesia with a nerve block will be used. On the surgery table, you will be positioned with a bean bag and taped down. Tape is used since you will be turned during surgery. Based on the tumor location, you may lie on your stomach, back, or side.

A scope will be inserted into your rectum. The scope will have a light, camera, air ports, and an open channel. Air will be pumped into your rectum to expand it. The light and camera will allow your surgeon to see the tumor. The tumor will be removed with small tools inserted through the open channel.

Transabdominal surgery

A transabdominal surgery involves cutting into the abdomen to reach and remove the cancerous tissue. This surgery requires general anesthesia. There are two methods for accessing the insides of your pelvis. An open surgery makes one cut into your abdominal wall and maybe one cut between your legs. Minimally invasive surgery makes a few smaller cuts in your abdominal wall. There may be one cut made between your legs. Thin tools are inserted into the cuts that allow your surgeon to see and remove tissue.

NCCN experts advise a minimally invasive surgery only under certain conditions. Your surgeon should have experience with this method. Your abdomen should be thoroughly examined. Also, this surgery should only be done on tumors that aren't likely to return after treatment.

There is more than one type of transabdominal surgery. They differ in part by how much tissue is removed. For all surgeries, at least 12 lymph nodes should be removed. Some types of transabdominal surgery are described next.

Total mesorectal excision

TME (total mesorectal excision) is a standard surgery for rectal cancer. It removes your rectum with nearby fat, lymph nodes, and the membrane in one piece. Nerves are not removed.

Low anterior resection

LAR (low anterior resection) is used for tumors in the mid to upper rectum. It includes a TME. In addition, part of or your whole sigmoid colon is removed.

Abdominoperineal resection

APR (abdominoperineal resection) is used for tumors in the lower rectum. These tumors may have grown into the anus or nearby muscle (levator ani). Some can't be removed with a cancer-free surgical margin. APR requires a second cut into your skin between your anus and genitals. This area is called the perineum. A standard APR includes a TME and removes the sigmoid colon and anus. An extended APR may also remove the levator muscles. Sometimes, less tissue is removed. The outer ring of muscle in the anus may be spared. A permanent colostomy, described next, is needed.

Anastomosis and colostomy

An anastomosis is a type of surgery that connects two parts of your bowel. It follows transabdominal surgery. If your anus is fine, your colon may be attached to it for near-normal bowel movements. This is called a *coloanal anastomosis*.

A colostomy connects a part of the colon to the outside of the abdomen. This creates an opening in your abdomen. Stool can pass through the opening. This surgery may be done to allow your rectum to heal before an anastomosis. Other people need a colostomy because their anus was removed. In this case, a colostomy is permanent.

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.

Rectal surgery may cause certain side effects. Your urine stream may be delayed during healing. If nerves or other structures are cut, bladder and sexual functioning may be impaired. Scar tissue may block stool from passing through. Food may leak out where the bowel was connected.

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 rectal 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.

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®)

- There are other chemotherapy drugs and regimens not shown in [Guide 1](#) 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 for two days in a row, followed by 12 days of rest. The cycle would then restart.

While most chemo drugs for rectal cancer travel in the bloodstream through your whole body, chemo can also be given using HAI (**h**epatic **a**rterial **i**nfusion). This method is sometimes used for rectal cancer that has spread only 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 HAI should only be done at treatment centers with a lot of 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 9.**



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 9 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 rectal tumors. Without the blood they need to grow, cancer cells “starve” and die. A second type of targeted therapy for rectal 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 rectal cancer are listed in [Guide 2](#). Ask your treatment team for a full list of common and rare side effects. Not everyone with rectal cancer will benefit from treatment with a targeted therapy. In Parts 4 through 6, information on who should receive these drugs is provided.



SNAPSHOT

Targeted therapy

- ✓ Used to treat some rectal cancers that have spread to other parts of the body and/or can't be removed with surgery.
- ✓ Not everyone with rectal 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 rectal cancer are given by infusion. This means they are put directly into your bloodstream using an IV.

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

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 rectal 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 cells protein. This means that the T cells will do their job and attack the cancer cells.

Checkpoint inhibitors used for rectal cancer are shown in [Guide 3](#). Not everyone with rectal cancer will benefit from treatment with immunotherapy. **In Parts 4 through 6, 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



Radiation side effects can differ from patient to patient and male to female. If you're a female patient, please talk to your doctor about intercourse after radiation treatment. How to prevent pain during intercourse after radiation may be an uncomfortable topic to discuss but it will be worth it in the end.

– Marisa

Survivor, Stage III rectal 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.

External beam radiation

Most often, EBRT (external beam radiation therapy) is the method used to treat rectal cancer. This method delivers radiation from outside your body using a large machine. **See Figure 10.** 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.

During treatment, you will lie on a table as you did for simulation. Devices may be used to keep you from

moving. This will help to target the tumor. Radiation beams will be 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.

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 is a one-time treatment that is given while you are still asleep. It 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 10 External beam radiation therapy

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





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.

Ablation

Ablation destroys small tumors with little harm to nearby tissue. It is done by either an interventional radiologist or a surgeon. It isn't used often for rectal cancer.

Doctors sometimes consider ablation for metastases. Most often it is considered for rectal cancer that has spread to the liver or lungs. Ablation is only an option if all the first sites of cancer can be treated with this method, with or without surgery or radiation.

There are different types of ablation:

- *Cryoablation* kills cancer cells by freezing them with liquid nitrogen.
- *Radiofrequency* and *microwave ablation* kill cancer cells with high-energy radio waves. A probe placed into the tumor emits the waves. The probe is guided into place with help from an imaging test and is removed when treatment is done.

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

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

Joining a clinical trial can have both upsides and downsides. **See Figure 11** 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 7, *Making treatment decisions*.

Figure 11
Pros and cons of joining a clinical trial



Review

- ▶ A type of surgery called a transanal local excision can be used to remove small (T1) tumors near the anus.
- ▶ TME is a type of transabdominal surgery used for many rectal cancers. It removes the rectum and other tissue through a cut made in your abdomen.
- ▶ Radiation therapy most often uses high-energy x-rays to treat rectal cancer. The rays kill the cancer cells or stop new cells from being made.
- ▶ 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 rectal tumors. Without blood, cancer cells starve and die. A second type of targeted therapy for rectal cancer stops the cancer cells from receiving certain growth signals.
- ▶ Immunotherapy uses the body's immune system to attack cancer cells that have specific mutations.
- ▶ Clinical trials give people access to new tests and treatments that may become the next standard of care.

4

Treatment guide: Nonmetastatic cancer

34 Stage I

40 Stage II and III

42 Follow-up care

46 If cancer comes back

46 Review



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

Stage I

If the cancer has grown into the second or third layer of the rectal wall, but has not spread to nearby lymph nodes, it is stage I rectal cancer. Using the TNM scale, this is a T1 or T2, N0, M0 tumor.

Rectal cancer often forms in polyps found on the inside of the rectum. It can also take the form of lesions on the inside of the rectum.

Polyps with cancer

If not found and removed early enough, a cancerous polyp can grow into the rectum wall. If a polyp with cancer grows through the first layer and into the second layer of the rectum wall, it is considered invasive cancer and has a T score of T1. Whether or not a polyp with invasive cancer will need more treatment after the polyp is removed during a polypectomy depends on two things. The first is the shape of the polyp (whether it's pedunculated or sessile). The other is whether your doctor thinks there is a high risk of the cancer returning after the polyp is removed.

High-risk polyps

Both pedunculated and sessile polyps can have high-risk features. If these features are present, it can mean that the cancer is more likely to return. Below are the high-risk features your doctor will use to help decide the best treatment for you.

- The polyp 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 rectum. This is called *positive surgical margin*.
- The cancer 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 rectum. This is called *tumor budding*.

If you have a polyp (sessile or pedunculated) with high-risk features, surgery is recommended. If the tumor is small (T1) and located near your anus, a transanal local excision may be an option. This type of surgery removes the tumor through the anus. Otherwise, a transabdominal resection should be done. This type of surgery requires cutting into the abdomen to reach and remove the cancer. [See Guide 4.](#)

Guide 4. Stage I rectal cancer

T score	Type of polyp		Treatment options		What's next?
T1	Low-risk pedunculated polyp	→	Watch-and-wait	→	Start follow-up care
	Low-risk sessile polyp	┌→ ├→ └→	Watch-and-wait	→	Start follow-up care
			Transanal local excision	→	See Guide 5
			Transabdominal resection	→	See Guide 6
	Any high-risk polyp	┌→ └→	Transanal local excision	→	See Guide 5
Transabdominal resection			→	See Guide 6	
T2	Any	→	Transabdominal resection	→	See Guide 6

Low-risk polyps

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. **Sessile polyps**, on the other hand, may need more treatment. Even low-risk sessile polyps tend to be more dangerous if left untreated. So, while observation is an option, having surgery for a low-risk sessile polyp may be a good idea. If the tumor is small (T1) and located near your anus, a transanal local excision may be an option. This type of surgery removes the tumor through the anus. Otherwise, a transabdominal resection should be done. This type of surgery requires cutting into the abdomen to reach and remove the cancer. [See Guide 5.](#)

After transanal local excision

If you had a transanal local excision, the removed tissue is sent to a pathologist. The pathologist will assess how far the cancer has grown within the rectal wall. It is possible that the cancer has grown farther through the wall than first thought. If the cancer is confirmed to be T1 (it hasn't grown farther than the second layer of the colon wall) and has no high-risk features, no further treatment is needed. If the cancer is T1 with high-risk features, or if the cancer is T2, then more treatment is needed. There are two treatment paths. One begins with surgery, while the other begins with chemotherapy and radiation. The paths are explained below and shown in [Guide 5.](#)

Chemoradiation pathway

This option starts with chemotherapy and radiation (chemoradiation). There are options for treatment after chemoradiation is complete.

- Watch-and-wait (no treatment). This should only be considered if the chemotherapy and radiation removed all signs of cancer.

- Surgery (transabdominal resection). With this option, you may also have chemotherapy after surgery to kill any remaining cancer cells.
- Chemotherapy alone.

Surgery pathway

This option starts with another surgery (transabdominal resection). This option is preferred for T2 rectal cancers, which have grown into the third layer of the colon wall. See the next section, *After transabdominal resection*, for next steps if this pathway is taken.



When you are deciding on your treatment options remember that even though some decisions need to be made fast, don't rush. Think through your options and get second, or even third opinions. Have people you can trust to talk through your options so you feel comfortable in your decision.

– Cari, 37

3-year survivor, Stage IV rectal cancer

Guide 5. Treatment after transanal local excision and staging update
 Cancer is T1 (in second layer of rectal wall) and does NOT have high-risk features

Treatment options		What's next?
Watch-and-wait (no treatment)	→	Begin follow-up care

Cancer is T1 and HAS high-risk features, or the cancer is T2 (in third layer of rectal wall)

First treatment options	Next treatment options	What's next?
OPTION 1 Surgery (transabdominal resection)	→	→ See Guide 6
OPTION 2 Radiation AND chemotherapy with: <ul style="list-style-type: none"> • Capecitabine (preferred) • Infusional 5-FU (preferred) • Bolus 5-FU/leucovorin 	→ Watch-and-wait (if no signs of cancer)	→ Begin follow-up care
	→ Surgery (transabdominal resection)	→ You may have chemotherapy with: <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine
	→ Chemotherapy with: <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine 	→ Begin follow-up care

After transabdominal resection

This type of surgery removes the tumor and nearby lymph nodes through cuts made in your abdomen. It is an option for many T1 tumors and is recommended for T2 tumors. The tissue removed during surgery will be tested to either confirm or update the cancer stage. If the cancer is still stage I, you don't need more treatment. If it turns out that the cancer is actually more advanced than previously thought, the stage will change. This is called *upstaging*. If the cancer is upstaged, more treatment is usually needed. The options for treatment after this type of surgery are explained below and shown in [Guide 6](#).

If the cancer is upstaged to stage IIA, there are two treatment options:

- Watch-and-wait (no treatment). This will only be an option for some low-risk patients with no cancer in lymph nodes.
- Chemotherapy and radiation together, followed by chemotherapy alone.

If the cancer is upstaged to stage IIB, IIC, or III, there are two treatment options:

- Chemotherapy alone, followed by chemotherapy and radiation together, then more chemotherapy alone.
- Chemotherapy and radiation together, followed by chemotherapy alone.

Guide 6. Treatment after abdominal resection and staging update

Cancer is still stage I

Treatment options		Next treatment
Watch-and-wait (no treatment)	→	Begin follow-up care

Cancer stage was changed to IIA

Treatment options		Next treatment
<p>OPTION 1</p> <p>Radiation AND chemotherapy with:</p> <ul style="list-style-type: none"> • Infusional 5-FU (preferred) • Capecitabine (preferred) • Bolus 5-FU/leucovorin 	→	<p>Chemotherapy with:</p> <ul style="list-style-type: none"> • Infusional 5-FU/leucovorin (preferred) • Bolus 5-FU/leucovorin • Capecitabine
<p>OPTION 2</p> <p>Watch-and-wait (no treatment). This will only be an option for some low-risk patients.</p>	→	Begin follow-up care

Cancer stage was changed to IIB, IIC, or III

First treatment options		Next treatment		Next treatment
<p>OPTION 1</p> <p>Chemotherapy with one of these regimens:</p> <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine 	→	<p>Radiation AND chemotherapy with one of these regimens:</p> <ul style="list-style-type: none"> • Infusional 5-FU (preferred) • Capecitabine (preferred) • Bolus 5-FU/leucovorin 	→	<p>Chemotherapy with one of these regimens:</p> <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine
<p>OPTION 2</p> <p>Radiation AND chemotherapy with one of these regimens:</p> <ul style="list-style-type: none"> • Infusional 5-FU (preferred) • Capecitabine (preferred) • Bolus 5-FU/leucovorin 	→	<p>Chemotherapy with one of these regimens:</p> <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine 	---	---

Stage II and III

Treatment of stage II and stage III rectal cancer is broken down into two groups, according to how far the cancer has spread and whether the *circumferential margin* around the tumor is clear or involved. The circumferential margin is a measure of how far rectal cancer has invaded into the surrounding tissues. Circumferential margin is generally measured by pelvic MRI. A positive or involved circumferential margin means that the tumor has invaded farther into the surrounding tissues, making it more likely that some of the tumor will be missed during surgery. Therefore, more extensive post-surgical treatment may be necessary.

On the other hand, a clear circumferential margin means that the tumor has not invaded as far into the surrounding tissue, making it less likely that tumor will be left following surgery. Therefore, less extensive post-surgical treatment may be needed.

Less advanced invasive cancer

The treatment options discussed next apply to either of the below situations.

- ▶ The cancer has entered either the second layer (T1) or the third layer (T2) of the rectum wall AND there is cancer in nearby lymph nodes (stage III).
- ▶ The cancer has grown through the third layer of the rectum wall and into tissue surrounding the colon and rectum (T3) AND the circumferential margin is clear. There may or may not be cancer in lymph nodes.

If either of the descriptions above applies to your cancer, there are three possible treatment paths. They are explained next and shown in [Guide 7](#).

Treatment path 1

This path starts with chemotherapy and long-course radiation. Capecitabine and infusional 5-FU are preferred for chemotherapy, but bolus 5-FU/leucovorin is also an option. After this treatment, your doctor may want to do imaging tests to see if your cancer stage has changed. Depending on how well the chemo and long-course radiation worked, surgery (transabdominal resection) may now be an option. After surgery, you will have chemotherapy to kill any remaining cancer cells. The specific chemotherapy drugs you will receive will depend on the original size of your tumor (before chemotherapy and radiation) and whether any lymph nodes have cancer.

If surgery is not an option, you would begin systemic therapy as outlined in Part 6, *Treatment guide: Systemic therapy*.

Treatment path 2

This path starts with short-course radiation. Depending on how well short-course radiation worked, surgery (transabdominal resection) may now be an option. After surgery, you will have chemotherapy to kill any remaining cancer cells. The specific chemotherapy drugs you will receive will depend on the original size of your tumor (before chemotherapy and radiation) and whether any lymph nodes have cancer.

If surgery is not an option, you would begin systemic therapy as outlined in Part 6, *Treatment guide: Systemic therapy*.

Treatment path 3

This path starts with chemotherapy. FOLFOX and CAPEOX are preferred regimens, but 5-FU/LV and capecitabine are also options. After chemotherapy, there are two options for next treatment. One is chemoradiation (chemotherapy and radiation). The other is a short course of radiation. Next, your doctor will likely do imaging tests to see if your cancer stage has changed. If the treatments worked well enough,

Guide 7. Less advanced stage II and III rectal cancer

Option 1

First treatment		Next treatment		Next treatment		What's next?
Long-course radiation AND chemotherapy with: <ul style="list-style-type: none"> • Capecitabine (preferred) • Infusional 5-FU (preferred) • Bolus 5-FU/leucovorin 		Surgery (if possible)	→	Chemotherapy	→	Begin follow-up care
		Surgery not possible			→	Systemic therapy in Part 6

Option 2

First treatment		Next treatment		Next treatment		What's next?
Short-course radiation		Surgery (if possible)	→	Chemotherapy	→	Begin follow-up care
		Surgery not possible			→	Systemic therapy in Part 6

Option 3

First treatment		Next treatment		Next treatment		What's next?		
Chemotherapy with: <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine 		Radiation AND chemotherapy with: <ul style="list-style-type: none"> • Capecitabine (preferred) • Infusional 5-FU (preferred) • Bolus 5-FU/leucovorin 		Surgery (if possible)	→	Begin follow-up care		
				Surgery not possible	→	Systemic therapy in Part 6		
		Short-course radiation				Surgery (if possible)	→	Begin follow-up care
						Surgery not possible	→	Systemic therapy in Part 6

surgery may be an option. After surgery, no further treatment is needed. You can begin monitoring for the return of cancer.

If surgery isn't an option, you would begin systemic therapy as outlined in Part 6, *Treatment guide: Systemic therapy*.

More advanced invasive cancer

The treatment options discussed next apply to any of the below situations.

- ▶ The cancer has grown through the third layer of the rectum wall and into tissue surrounding the colon and rectum (T3) and the circumferential margin is involved. There may or may not be cancer in lymph nodes.
- ▶ The cancer has grown through the rectum wall and has entered or attached to nearby organs or structures (T4).
- ▶ The cancer can't be removed with surgery.

If any of the descriptions above applies to your cancer, there are three possible treatment paths.

Treatment path 1

This path starts with chemotherapy and long-course radiation. Your doctor may want to do imaging tests 6 weeks after you've finished the radiation to see if your cancer stage has changed, and to see if surgery is an option. If the circumferential margin is now clear, surgery is an option. After surgery, you would then have chemotherapy to remove any remaining cancer cells. If the circumferential margin is clear but surgery is still not an option for other reasons, you would begin systemic therapy as outlined in Part 6, *Treatment guide: Systemic therapy*.

If the imaging tests done 6 weeks after radiation show that the circumferential margin is not clear, the next treatment is 12 to 16 weeks of chemotherapy. The FOLFOX or CAPEOX regimens are preferred, but 5-FU/leucovorin and capecitabine are also options. After chemotherapy, your doctor will do more imaging tests to see if the cancer stage has changed. If surgery is now an option, you would have surgery followed by more chemotherapy to kill any remaining cancer cells. If surgery still isn't an option,

you would begin systemic therapy as outlined in Part 6, *Treatment guide: Systemic therapy*.

Treatment path 2

This path starts with 12 to 16 weeks of chemotherapy. FOLFOX and CAPEOX are preferred regimens, but FU/LV and capecitabine are also options. After chemotherapy, you would then have chemoradiation (chemotherapy and radiation). Next, your doctor will likely do imaging tests to see if your cancer stage has changed. If the treatments worked well enough, surgery may be an option. After surgery, no further treatment is needed. You can begin monitoring for the return of cancer.

If surgery isn't an option, you would begin systemic therapy as outlined in Part 6, *Treatment guide: Systemic therapy*.

Follow-up care

Follow-up care starts when there are no signs of cancer after treatment. It is also called *survivorship care*. An important part of follow-up care is 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. 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.

Stage I

If you had local surgery only (a transanal local excision), you should have regular proctoscopies and colonoscopies. If you had a transabdominal resection with full surgical staging, you should have regular colonoscopies. [See Guide 8.](#)

Guide 8. Follow-up cancer care for stage I rectal cancer

You had	Follow-up cancer care
Transanal local excision only	<ul style="list-style-type: none"> • Proctoscopy (with EUS or MRI with contrast) every 3–6 months for the first 2 years, then every 6 months for another 3 years • Colonoscopy in 1 year <ul style="list-style-type: none"> ◦ If advanced adenoma is found, repeat in 1 year ◦ If no advanced adenoma is found, repeat in 3 years, then every 5 years
Transabdominal resection with full surgical staging	<p>Colonoscopy in 1 year</p> <ul style="list-style-type: none"> ◦ If advanced adenoma is found, repeat in 1 year ◦ If no advanced adenoma is found, repeat in 3 years, then every 5 years

Stage II, III, and IV

The tests recommended by NCCN experts to monitor for the return of stage II, III, or IV rectal cancer are described below and shown in [Guide 9](#).

- **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. Stage II and III patients should have them every 6 to 12 months for 5 years. Stage IV patients should have them every 3 to 6 months for the first 2 years, then every 6 to 12 months for another 3 years. CT should be done with both IV and oral contrast. In cases where CT images are unclear or CT is not possible, 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 an 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:

Guide 9. Follow-up cancer care for stage II, III, and IV rectal cancer

Type of care	How often is this care needed?
Medical history & physical exam	Every 3–6 months for first 2 years, then every 6 months for 3 more years
CEA blood test	Every 3–6 months for first 2 years, then every 6 months for 3 more years
CT of chest, abdomen, pelvis	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	If no prior total colonoscopy, 3–6 months after treatment If prior total colonoscopy, 1 year after treatment <ul style="list-style-type: none"> • If no advanced adenoma, repeat in 3 years. If results are normal, then repeat every 5 years • If advanced adenoma, repeat in 1 year

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

Help with side effects

Rectal cancer and its treatment can cause long-term side effects. Some side effects you may experience are listed below.

- **Bowel changes.** 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

- **Nerve damage.** 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 duloxetine is not controlling your pain, your doctor may refer you to a specialist in pain management.

- **Ostomy.** 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.

- **Increased risk of fractures.** Radiation to the pelvis can mean you are at increased risk of pelvic fractures because your bones

Figure 12

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



Figure 13

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.



are not as dense as they were before. Your doctor may want to start monitoring the density of your bones.

- **Sexual side effects.** Some people may experience sexual side effects after treatment to the rectum. For men, this could mean difficulty getting an erection. For women, this could mean that sex is painful. It could also mean vaginal dryness.

Living healthy

There are a few steps you can take that will make a big difference in your overall health (**See Figure 12**).

- **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).
 - Taking 325 mg of aspirin every day. This may lower the odds of the cancer returning.
- **Maintain a healthy body weight. The best ways to do this are:**
 - Exercise 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.
 - Eat a healthy diet with lots of plant-based foods.

- Drink 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.

If cancer comes back

Guide 10 lists the treatment options for cancer that returns to the rectum, or close to where the rectum was. This is called a *local recurrence*. Options are grouped by whether you can have surgery or not. If the cancer is small enough, your first treatment may be surgery. Chemotherapy and radiation (chemoradiation) should follow. Alternatively, you may have chemoradiation first followed by surgery. IORT may be added.

If surgery isn't an option, chemotherapy with or without radiation may be received. For chemoradiation, capecitabine or infusional 5-FU is preferred. The side effects of these regimens may be too much for you. In this case, bolus 5-FU/LV may be received.

If cancer returns to areas far from the rectum, it is called a *distant recurrence*. Distant recurrences are addressed in Part 5, *Treatment guide: Metastatic cancer*.

Review

- Stage I rectal cancer has grown into the second layer of the rectal 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

Guide 10. Local recurrence

		Treatment		Next treatment
You may be able to have surgery		Surgery		Chemotherapy and radiation
		Chemotherapy and radiation		Surgery. Radiation may be given to the cancer site during surgery (IORT)
You probably won't be able to have surgery		Chemotherapy. Radiation may also be given.		

with surgery. Chemotherapy, chemoradiation, or both may follow.

- A sequence of treatments is used for stages II and III. Radiation therapy with or without chemotherapy is used to shrink cancer. Next, the remaining cancer is removed by surgery. If surgery isn't an option, more chemotherapy is often given. After surgery, chemotherapy is often given to prevent the cancer from returning.
- The cancer may return to the rectum or near to where the rectum was. Surgery may be an option. Chemoradiation may precede or follow surgery. When surgery isn't an option, you may receive chemotherapy with or without radiation therapy.
- Follow-up care is started when there are no signs of cancer after surgery. It includes tests to look for any new cancer and help for side effects. It also includes help to prevent or detect other diseases.
- Monitoring for the return of stage II, III, and IV rectal 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 should address both your physical and emotional well-being.
- 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 (eg, screening for other cancers and getting recommended immunizations).

5

Treatment guide: Metastatic cancer

49 Metastases at diagnosis

51 Distant recurrence

56 Review



Rectal 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 rectal cancer. Or, after successful treatment and a cancer-free period, cancer may return and spread to areas far from the rectum. This chapter discusses both of these scenarios.

Metastases at diagnosis

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

Treatment of metastatic rectal 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.

Cancer is in the liver or lungs

Nonsurgical treatment

The main treatment for stage IV rectal cancer that has spread to the liver or lungs and 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 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 or if surgery is otherwise not an option, the next treatment will depend on whether the primary tumor got bigger. If it did, you may have a short course of radiation therapy to the primary tumor. Chemoradiation (chemotherapy combined with radiation) is also an option if the primary tumor got bigger. After that, 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 6, Treatment guide: Systemic therapy*.

If chemotherapy worked well enough and the cancer can now be removed with surgery, your doctor may want to do a short course of radiation therapy next. Chemoradiation is also an option. After that, you will have surgery to remove the rectal tumor and the tumors in the liver and/or lungs. If a short course of radiation was used, surgery should be done within 1 week or delayed 6 to 8 weeks. Liver and lung metastases can be treated with local therapies, but surgery is preferred. 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 age 65. Bevacizumab can be restarted 6 to 8 weeks after surgery. Otherwise, it can slow healing.

Surgical treatment options

There are two treatment pathways that include surgery to treat rectal cancer that had spread to the liver or lungs at diagnosis (stage IV). The options depend on whether the circumferential margin is clear, as shown by MRI (see page 40 for an

explanation of circumferential margin). The pathways are described next and shown in [Guide 11](#). Surgery to remove the cancer in the rectum and in the liver and/or lungs can be done at the same time, or later in separate surgeries. Instead of removing the metastases with surgery, another option is to treat them using local therapy (image-guided ablation or SBRT [stereotactic body radiation therapy]). While surgery is preferred by NCCN experts to remove the metastases, local therapy may be appropriate for patients with many small metastases.

Guide 11. Surgical options for rectal cancer that has spread to the liver or lungs

		First treatment options		Next treatment	What's next?	
MRI shows that the circumferential margin is clear	→	Chemotherapy with: <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine 	→	Option 1: Short-course radiation therapy	Surgery to remove cancer in rectum and metastases	
				Option 2: Chemoradiation (chemo and radiation to pelvis)		
MRI shows that the circumferential margin is involved	→	Chemotherapy with: <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine 	→	Chemoradiation (chemo and radiation to pelvis)	Surgery to remove cancer in rectum and metastases	
				Short-course radiation therapy	Chemotherapy with: <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine 	Surgery to remove cancer in rectum and metastases
				Chemoradiation (chemo and radiation to pelvis)	Chemotherapy with: <ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • 5-FU/leucovorin • Capecitabine 	Surgery to remove cancer in rectum and metastases

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 6, *Treatment guide: Systemic therapy*. If the cancer is blocking the bowel (or will be soon), 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.

Follow-up care

Follow-up care for stage IV rectal cancer is similar to stage II and III rectal cancer. See Part 4, *Treatment guide: Nonmetastatic cancer* on page 33.

Distant recurrence

Cancer may return during the course of follow-up care. Your doctor may find cancer far from the rectum during a follow-up imaging test. Or, if your CEA blood test levels are getting higher each time your blood is tested, it may mean that cancer has come back. 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.

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

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

Rectal cancer that returned and spread far from the rectum, and that cannot be removed with surgery, is treated with systemic therapy. Systemic therapy may include chemotherapy, targeted therapy, immunotherapy, or a combination of the three. If you've had chemotherapy with FOLFOX or CAPEOX within the past 12 months, there are several possible systemic therapy options. These are described next and shown in [Guide 12](#). Systemic therapy options for everyone else are discussed in Part 6, *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 or if surgery is otherwise not an option, you can continue systemic therapy. The systemic therapy regimens that may be used are found in Part 6, *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). 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 age 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 received 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.



Being diagnosed with Stage IV rectal cancer at age 36 was overwhelming. Fortunately, there are many fantastic online resources and support groups. It helped me to talk to other patients and know that I'm never alone.

– Peg, 38

2-year survivor, Stage IV rectal cancer

Guide 12. Nonsurgical treatment options

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

Treatment options	May be given with	Notes
Chemotherapy with FOLFIRI regimen	<ul style="list-style-type: none"> • Bevacizumab (preferred) • Ziv-aflibercept • Ramucirumab 	---
Chemotherapy with irinotecan	<ul style="list-style-type: none"> • Bevacizumab (preferred) • Ziv-aflibercept • Ramucirumab 	---
Chemotherapy with FOLFIRI regimen	<ul style="list-style-type: none"> • Cetuximab • Panitumumab 	For normal <i>KRAS/NRAS</i> genes only
Chemotherapy with irinotecan	<ul style="list-style-type: none"> • Cetuximab • Panitumumab 	For normal <i>KRAS/NRAS</i> genes only
Nivolumab	Ipilimumab	For dMMR/MSI-H tumors only
Pembrolizumab	---	For dMMR/MSI-H tumors only
Irinotecan + cetuximab + vemurafenib	---	<i>BRAF</i> V600E mutation positive
Irinotecan + panitumumab + vemurafenib	---	<i>BRAF</i> V600E mutation positive

Surgical treatment options

There are two options that include surgery to treat rectal 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 13](#).

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 6, *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 6, *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 13. Surgical options for metastases at recurrence

Option 1

First treatment options	Next treatment options
<ul style="list-style-type: none"> • Metastasectomy, with or without local treatment (preferred) • Local treatment only 	<p style="text-align: center;">→</p> <p>If you haven't had any chemotherapy:</p> <ul style="list-style-type: none"> ◦ FOLFOX (preferred) ◦ CAPEOX (preferred) ◦ Capecitabine ◦ 5-FU/LV <p>If you've had chemotherapy:</p> <ul style="list-style-type: none"> ◦ Observation ◦ Systemic therapy in Part 6

Option 2

First treatment options	Next treatment options	Chemotherapy
<ul style="list-style-type: none"> • FOLFOX (preferred) • CAPEOX (preferred) • Capecitabine • 5-FU/LV 	<p style="text-align: center;">→</p> <ul style="list-style-type: none"> • Metastasectomy, with or without local treatment (preferred) • Local treatment only 	<p style="text-align: center;">→</p> <p>If chemotherapy worked:</p> <ul style="list-style-type: none"> ◦ Restart same chemotherapy regimen ◦ FOLFOX regimen ◦ Observation <p>If chemotherapy didn't work:</p> <ul style="list-style-type: none"> ◦ Systemic therapy in Part 6 ◦ Observation

Review

- Cancer that has spread to areas far from where it started is called a metastasis. Rectal cancer most often spreads to the liver, and sometimes the lungs.
- Metastases may already be present when you first learn that you have rectal cancer. This is stage IV rectal cancer. Metastases may also occur if the cancer reappears during follow-up care.
- Some rectal 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 rectal cancers with metastases cannot be treated with surgery. In most cases, chemotherapy is advised. Targeted therapy may be added.



My diagnosis experience caught me and my entire family by complete surprise. It was a very difficult diagnosis to accept and understand, but we managed to work around the difficult situations. The treatments on many occasions were painful. Some of my side effects are permanent and the medications sometimes don't help to alleviate the pain. I may have won the war on cancer but the battle with the side effects still continues.

– Victor, 52

4-year survivor, Stage III rectal cancer

6

Treatment guide: Systemic therapy

58	Oxaliplatin
60	Irinotecan
62	FOLFOXIRI
64	5-FU and capecitabine
66	Least toxic regimens
67	Review



This chapter presents the systemic therapy pathways used to treat advanced rectal 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.

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 second-line 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	Only for normal <i>KRAS/NRAS</i> genes
	• Panitumumab	Only for normal <i>KRAS/NRAS</i> genes
CAPEOX ±	Bevacizumab	---
Second-line regimens		Notes
FOLFIRI ±	• Bevacizumab	---
	• Ziv-aflibercept	---
	• Ramucirumab	---
	• Cetuximab	Only for normal <i>KRAS/NRAS</i> genes
	• Panitumumab	Only for normal <i>KRAS/NRAS</i> genes
Irinotecan ±	• Bevacizumab	---
	• Ziv-aflibercept	---
	• Ramucirumab	---
	• Cetuximab	Only for normal <i>KRAS/NRAS</i> genes
	• Panitumumab	Only for normal <i>KRAS/NRAS</i> genes
	• Cetuximab and vemurafenib	For people with the <i>BRAF</i> V600E mutation
	• Panitumumab and vemurafenib	For people with the <i>BRAF</i> 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.

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.

Targeted therapy with bevacizumab, cetuximab, or panitumumab may be given with the FOLFIRI chemotherapy regimen. Cetuximab and panitumumab should only be given for people with normal *KRAS/NRAS* genes.

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 second-line 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	Only for normal <i>KRAS/NRAS</i> genes
	• Panitumumab	Only for normal <i>KRAS/NRAS</i> genes
Second-line regimens		Notes
FOLFOX ±	Bevacizumab	---
CAPEOX +	Bevacizumab	---
Irinotecan +	• Cetuximab	Only for normal <i>KRAS/NRAS</i> genes
	• Panitumumab	Only for normal <i>KRAS/NRAS</i> genes
	• Cetuximab and vemurafenib	For people with the <i>BRAF</i> V600E mutation
	• Panitumumab and vemurafenib	For people with the <i>BRAF</i> 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. In 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. Either may be given 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 second-line 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
Irinotecan +	• Cetuximab	Only for normal <i>KRAS/NRAS</i> genes
	• Panitumumab	Only for normal <i>KRAS/NRAS</i> genes
	• Cetuximab and vemurafenib	For people with the <i>BRAF</i> V600E mutation
	• Panitumumab and vemurafenib	For people with the <i>BRAF</i> 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		• Best supportive care
• Join a clinical trial		

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
5FU/leucovorin ±	Bevacizumab	---
Capecitabine ±	Bevacizumab	---
Second-line options		Notes
FOLFOX ±	Bevacizumab	---
CAPEOX ±	Bevacizumab	---
FOLFIRI ±	• Bevacizumab	---
	• Ziv-aflibercept	---
	• Ramucirumab	---
Irinotecan ±	• Bevacizumab	---
	• 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
Irinotecan ±	• Cetuximab and vemurafenib	For people with the <i>BRAF</i> V600E mutation
	• Panitumumab and vemurafenib	For people with the <i>BRAF</i> V600E mutation
	• Cetuximab	Only for normal <i>KRAS/NRAS</i> genes
	• Panitumumab	Only for normal <i>KRAS/NRAS</i> 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 for tumors with normal *KRAS/NRAS* genes. Neither drug is likely to work if you have a *BRAF* V600E mutation. 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.

Guide 18. Least toxic systemic therapy options

Treatment options	Regimens that may be used	Notes
Chemotherapy	<ul style="list-style-type: none"> 5-FU + leucovorin Capecitabine 	---
Chemotherapy + targeted therapy	<ul style="list-style-type: none"> 5-FU + leucovorin + bevacizumab Capecitabine + bevacizumab 	---
Targeted therapy	<ul style="list-style-type: none"> Cetuximab Panitumumab 	Only for normal <i>KRAS/NRAS</i> genes
Immunotherapy	<ul style="list-style-type: none"> Nivolumab Pembrolizumab Nivolumab + ipilimumab 	Only for dMMR/MSI-H tumors

Review

- ▶ There are five pathways used to treat advanced rectal 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.

7

Making treatment decisions

- 69 It's your choice
- 69 Questions to ask your doctors
- 74 Weighing your options
- 75 Websites
- 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 6 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 are included on the following pages.

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

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

Colorectal Cancer Alliance

ccalliance.org

U.S. National Library of Medicine Clinical Trials Database

clinicaltrials.gov

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

Dictionary

abdomen

The belly area between the chest and pelvis.

ablation

A treatment that destroys very small tumors with heat, cold, lasers, or chemicals. Also called ablative therapy.

adenoma

The most common growth from the inner wall of the digestive tract. Also called adenomatous polyp.

adjuvant treatment

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

adventitia

The outer layer, in some places, of the digestive tract.

angiolymphatic invasion

The spread of cancer into the lymph vessels or bloodstream.

anus

The opening at the end of the intestines between the legs through which stool passes out of the body.

bilirubin

A yellow-brown substance that is part of a digestive fluid called bile.

biopsy

A procedure that removes fluid or tissue samples to be tested for a disease.

bolus

A fast injection of a drug.

boost

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

cancer grade

A rating of how much the cancer cells look like normal cells under a microscope.

cancer stage

A rating of the outlook of a cancer based on its growth and spread.

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.

circumferential margin

A measure of how far a rectal cancer has invaded into the surrounding tissues.

clinical stage

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

clinical trial

A type of research that assesses how well health tests or treatments work in people.

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 device that is guided through the anus to work inside the colon.

colonoscopy

A procedure to look inside the colon with a device that is guided through the anus.

colostomy

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

complete blood count (CBC)

A lab test that measures the number of red blood cells, white blood cells, and platelets.

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 rectal 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 rectal cancer.

gene

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

general anesthesia

A drug-induced, sleep-like state for pain relief.

hereditary non-polyposis colorectal cancer (HNPCC)

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

hyperplastic polyp

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

imaging test

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

inflammatory polyp

A polyp that often grows after the intestine swells.

infusion

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

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 rectal wall.

lamina propria

Connective tissue within the mucosa of the rectal 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 made in small, repeated DNA parts during the copy process because of an abnormal repair system.

microsatellite instability-high (MSI-H)

The presence of 2 or more abnormal DNA parts called microsatellites.

mismatch repair deficiency (dMMR)

An abnormal repair system for DNA errors that are made during the copy process.

mucosa

The first, inner layer of the rectal wall.

mucus

A sticky, thick liquid that moisturizes or lubricates.

muscularis propria

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

muscularis mucosae

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

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.

noninvasive cancer

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

observation

A period of testing for cancer growth.

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.

peritoneum

The tissue that lines the stomach and covers most of the organs in the stomach area of the body.

physical exam

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

polyp

An growth from the inner wall of the digestive tract.

portal vein embolization

A treatment that blocks the blood vessel to the liver tumor.

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 likely course and outcome of a disease based on tests.

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 wall layer, in some places, of the digestive tract. Also called the visceral peritoneum.

sessile polyp

A flat growth from the inner wall of the digestive tract.

side effect

An unhealthy or unpleasant 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 rectal wall made mostly of connective tissue.

subserosa

A thin layer of connective tissue that makes fluid.

supportive care

Health care that includes symptom relief but not cancer treatment. Also called palliative care.

surgical margin

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

targeted therapy

A treatment that may target and attack specific types of cancer cells.

total colonoscopy

Insertion of a thin tool into the rectum 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 in the fat around the rectum.

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

AJCC

American Joint Committee on Cancer

APR

abdominoperineal resection

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 colorectal cancer

IORT

intraoperative radiation therapy

LAR

low anterior resection

MMR

mismatch repair

MRI

magnetic resonance imaging

MSI

microsatellite instability

NCCN®

National Comprehensive Cancer Network®

PET

positron emission tomography

PET/CT

positron emission tomography/computed tomography

SBRT

stereotactic body radiation therapy

TME

total mesorectal excision

TNM

tumor, node, metastasis

NCCN Panel Members for Rectal Cancer

Al B. Benson, III, MD/Chair
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Alan P. Venook, MD/Vice-Chair
UCSF Helen Diller Family Comprehensive Cancer Center

Mahmoud M. Al-Hawary, MD
University of Michigan Rogel Cancer Center

Mustafa A. Arain, MD
UCSF Hellen Diller Family Comprehensive Cancer Center

Yi-Jen Chen, MD, PhD
City of Hope National Medical Center

Kristen K. Ciombor, MD
Vanderbilt-Ingram Cancer Center

* Stacey Cohen, MD
Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

Harry S. Cooper, MD
Fox Chase Cancer Center

Dustin Deming, MD
University of Wisconsin Carbone Cancer Center

Paul F. Engstrom, MD
Fox Chase Cancer Center

Ignacio Garrido-Laguna, MD, PhD
Huntsman Cancer Institute at the University of Utah

Jean L. Grem, MD
Fred & Pamela Buffett Cancer Center

Sarah Hoffe, MD
Moffitt Cancer Center

Joleen Hubbard, MD
Mayo Clinic Cancer Center

Steven Hunt, MD
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Ahmed Kamel, MD
University of Alabama at Birmingham Comprehensive Cancer Center

Natalie Kirilcuk, MD
Stanford Cancer Institute

Smitha Krishnamurthi, MD
Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

* Wells A. Messersmith, MD
University of Colorado Cancer Center

Jeffrey Meyerhardt, MD
MPH Dana-Farber Cancer Institute

Eric D. Miller, MD, PhD
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Mary F. Mulcahy, MD
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

James D. Murphy, MD, MS
UC San Diego Moores Cancer Center

Steven Nurkin, MD, MS
Roswell Park Cancer Institute

Michael J. Overman, MD
The University of Texas MD Anderson Cancer Center

Katrina Pedersen, MD, MS
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Leonard Saltz, MD
Memorial Sloan Kettering Cancer Center

David Shibata, MD
The University of Tennessee Health Science Center

John M. Skibber, MD
The University of Texas MD Anderson Cancer Center

Constantinos T. Sofocleous, MD, PhD
Memorial Sloan Kettering Cancer Center

Elena M. Stoffel, MD, MPH
University of Michigan Rogel Cancer Center

Eden Stotsky-Himelfarb, BSN, RN
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

* Christopher G. Willett, MD
Duke Cancer Institute

NCCN Staff

Kristina M. Gregory, RN, MSN, OCN
Vice President/Clinical Information Operations

Lisa Gurski, PhD
Oncology Scientist/Senior Medical Writer

* Reviewed the clinical content of this book.

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

NCCN Member Institutions

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

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
800.999.5465
nebraskamed.com/cancer

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.org/seidman
866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/services/cancer
216.844.8797 • Case CCC
case.edu/cancer

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
dfbwc.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

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
877.585.0303
huntsmancancer.org

Fred Hutchinson Cancer
Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.288.7222 • seattlecca.org
206.667.5000 • fredhutch.org

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
hopkinskimmellcancercenter.org

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

The Ohio State University
Comprehensive Cancer Center -
James Cancer Hospital and
Solove Research Institute
Columbus, Ohio
800.293.5066
cancer.osu.edu

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

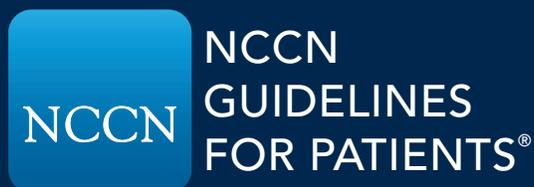
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
800.811.8480
vicc.org

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

Index

- 2nd opinion** 74
- ablation** 30, 50, 54
- BRAF* mutation** 21
- cancer staging** 12
- carcinoembryonic antigen (CEA)** 17, 21, 43–44, 47, 51
- carcinoma in situ** 12
- chemotherapy** 21, 25–27, 30–32, 36–56, 58, 60, 62, 64, 66
- clinical trial** 31–32, 58–65, 71
- colonoscopy** 11, 16–17, 43–44, 51
- complete blood count (CBC)** 17, 21
- computed tomography (CT)** 18–19, 43–44, 47, 51, 54
- digestive tract** 8–9
- embolization** 22, 30, 54
- familial adenomatous polyposis (FAP)** 14, 16, 21
- hereditary non-polyposis colorectal cancer (HNPCC)** 14, 15
- KRAS/NRAS* genes** 52–53, 58–66
- Lynch syndrome** 14–15, 21
- medical history** 14–15, 21, 43–44
- metastasectomy** 24, 55
- microsatellite instability (MSI)** 20–21, 52–53, 58–66
- mismatch repair (MMR)** 15, 20–21, 52–53, 58–66
- NCCN Member Institutions** 83
- NCCN Panel Members** 82
- polypectomy** 11–12, 34, 36, 46
- polyp** 11–12, 14–16, 23, 36, 43, 46
- radiation therapy** 29, 32, 46, 50
- shared decision-making** 69, 75
- supportive care** 58–66
- targeted therapy** 21, 27, 32, 49, 52, 56, 58, 60, 62, 64–66





Rectal Cancer

2018

NCCN Foundation® gratefully acknowledges Fight Colorectal Cancer for their support in making available these NCCN Guidelines for Patients®. NCCN independently develops and distributes the NCCN Guidelines for Patients. Our industry supporters do not participate in the development of the NCCN Guidelines for Patients and are not responsible for the content and recommendations contained therein.



National Comprehensive
Cancer Network®

3025 Chemical Road, Suite 100
Plymouth Meeting, PA 19462
215.690.0300

NCCN.org/patients – For Patients | NCCN.org – For Clinicians