LEARNING that you have cancer can be overwhelming.

The goal of this book is to help you get the best care. It presents 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 27 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. Key points of the book are summarized in the NCCN Quick Guide™. NCCN also offers patient books on colon cancer, ovarian cancer, stomach cancer, sarcoma, lymphomas, and other cancer types. Visit NCCN.org/patients for the full library of patient books, summaries, and other resources.
These patient guidelines for cancer care are produced by the National Comprehensive Cancer Network® (NCCN®).

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

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

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

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

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


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Rectal Cancer, Version 1.2017
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**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.

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**Colon Cancer Alliance**
The Colon Cancer Alliance is pleased to endorse the NCCN Guidelines for Rectal Cancer as a resourceful tool to help knock colon cancer out of the top three cancer killers. ccalliance.org.
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Who should read this book?

This book is about treatment for adenocarcinoma of the rectum. It does not discuss 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 cancer stages.

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.

Help! What do the words mean?

In this book, many medical words are included. These are words that your treatment team may say to you. Most of these words may be new to you. It may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Ask your treatment team to explain a word or phrase that you do not 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. Acronyms are short words formed from the first letters of several words. One example is DNA for deoxyribonucleic acid.

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.
# Rectal cancer basics

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You’ve learned that you have rectal cancer. It’s common to feel shocked and confused. Part 1 reviews some basics that may help you learn about rectal cancer.

The rectum

Before learning about rectal cancer, it is helpful to know about the rectum. The rectum is part of the digestive system. This system breaks down food for the body to use.

Digestive tract

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.

In the stomach, food is turned into a liquid. From the stomach, food enters the small intestine. In the small intestine, food is broken down into very small parts. This allows nutrients to be absorbed into the bloodstream.

From the small intestine, food moves into the large intestine. The large intestine changes unused food from a liquid into a solid by absorbing water. This solid, unused food is called feces or stool. The large intestine also expels stool from the body through the anus.

The rectum is part of the large intestine. It holds stool until the stool is expelled from the body. The rectum also triggers nerves that make you feel the urge to have a bowel movement.

The rectum is almost 5 inches long. It is in the back of your pelvis in front of your spine. It often contains three folds that are shaped like a half moon. See Figure 2.

Rectal wall

Layers of tissue make up the rectal wall. The inner layer that has contact with stool is called the mucosa. The mucosa consists of three sublayers. They are the epithelium, lamina propria, and muscularis mucosae.

The epithelium makes mucus to help move stool along. The lamina propria is a thin layer of support (connective) tissue. The muscularis mucosae is a thin strip of muscle.

The second layer of the rectal wall is called the submucosa. It consists of connective tissue, blood and lymph vessels, and nerve cells. Lymph is a clear fluid that gives cells water and nutrients. It also has white blood cells that fight germs. Blood and lymph drain from rectal tissue into vessels that are in the submucosa and then travel to other sites.

The third layer of the rectal wall is called the muscularis propria. It is mostly made of muscle fibers. These muscles help move stool through the rectum.

The last layer is a thin layer of connective tissue. It has a single row of cells that make fluid. This fluid allows the rectum to move smoothly against other organs. This layer is called either subserosa or adventia.

The upper part and front of the mid rectal wall is covered in serosa. The serosa, also called the visceral peritoneum, is a membrane. It also covers the front part of 1) the left and right sides of the colon and 2) the kidneys.

Most of the rectum that isn’t covered in serosa is covered in fat. The fat is thick in the middle of the rectum. It thins out the closer it gets to the anus. This fat is covered by connective tissue called the fascia propria.
Figure 1
The digestive tract

The digestive tract consists of 4 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 within the small intestine. The large intestine absorbs liquid from and pushes unused food out of the body.

Figure 2
The rectum

The rectum is part of the large intestine. The rectum is almost 5 inches long. It often contains three folds. Its wall has four main layers—the mucosa, submucosa, muscularis propria, and subserosa or adventia. The wall is either covered in serosa or fat.
A disease of cells

Your body is made of trillions of cells. Cancer is a disease of cells. Each type of cancer is named after the cell from which it derived. Rectal cancer is a cancer of rectal cells.

Almost all rectal cancers are adenocarcinomas. Adenocarcinomas are cancers of cells that line glands and, in the case of rectal cancer, make mucus. Adenocarcinomas of the rectum are the focus of this book.

Cells have a control center called the nucleus. The nucleus contains chromosomes, which are long strands of DNA (deoxyribonucleic acid) tightly wrapped around proteins. See Figure 3. Within DNA are coded instructions for building new cells and controlling how cells behave. These instructions are called genes.

There can be abnormal changes in genes called mutations. Some types of mutations that are linked to cancer are present in all cells. Other mutations are present only in cancer cells. Mutations cause cancer cells to not behave like normal cells and, sometimes, to look very different from normal cells.

Cancer’s threat

Cancer cells don’t behave like normal cells in three key ways. First, cancer cells grow more quickly and live longer than normal cells. Normal cells grow and then divide to form new cells when needed. They also die when old or damaged as shown in Figure 4. In contrast, cancer cells make new cells that aren’t needed and don’t die quickly when old or damaged. Over time, cancer cells form a mass called the primary tumor.

The second way cancer cells differ from normal cells is that they can grow into surrounding tissues. If not treated, the primary tumor can grow through the rectal wall. Cancer cells can even grow into nearby structures. Rectal cancers that haven’t grown into the second layer of the rectal wall are called “noninvasive cancers.” Rectal cancers that have grown into the second layer are called “invasive cancers.”

Third, unlike normal cells, cancer cells can leave the rectum. This process is called metastasis. In this process, cancer cells break away from the tumor and merge with blood or lymph. Then, the cancer cells travel in blood or lymph through vessels to other sites. Once in other sites, cancer cells may form secondary tumors and cause major health problems.
Figure 3
Genetic material in cells

Most human cells contain the “blueprint of life”—the plan by which our bodies are made and work. The plan is found inside of chromosomes, which are long strands of DNA that are tightly wrapped around proteins. Genes are small pieces of DNA that contain instructions for building new cells and controlling how cells behave. Humans have an estimated 20,000 to 25,000 genes.

Figure 4
Normal cell growth vs. cancer cell growth

Normal cells increase in number when they are needed and die when old or damaged. In contrast, cancer cells quickly make new cells and live longer because of abnormal changes in genes.
Polyps

Rectal cancer often starts in a polyp. A polyp is an overgrowth of cells that line the inner rectal wall. See Figure 5. Polyps need to be removed and tested for cancer. An endoscopic polypectomy is a minor surgery that removes polyps.

Not all polyps are the same. They differ in size, shape, and how their cells look. There are three types of rectal polyps.

- **Adenomatous polyps**, or **adenomas**, have cells that don’t look like normal rectal cells. They are the most common type of polyp. Most do not become cancer, but most polyps with cancer started as adenomas.

- **Hyperplastic polyps** have cells that grow fast. They are often found in the last part of the colon and in the rectum. They rarely become cancer.

- **Inflammatory polyps** often grow after a flare-up of an inflammatory bowel disease. They can have any shape. The chance of them becoming cancer is low.

Sessile polyps are flat polyps that grow flush along the rectal wall and do not have a stalk. Sometimes, they can be hard to spot. Pedunculated polyps are shaped like mushrooms. They have a stalk and round top. Serrated is a term for any polyp that has a saw-tooth pattern. Sessile serrated adenomas are rare but have been linked to cancer.

---

Figure 5
Polyp

A rectal polyp is an overgrowth of cells that line the inner surface of the rectal wall. Rectal cancer often starts in a polyp. However, most polyps do not become cancer.

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We are all very busy with our lives. However, CRC screening is quick and easy. If completed in a timely manner, it can mean the difference between life and death. Think of it this way. If you are clear, you only need a colonoscopy at age 50, 60, and 70. That is only three times in your entire life. No big deal.

—Evan
Survivor, Stage I
Cancer stage

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

In the AJCC system, the letters T, N, and M describe the areas of cancer growth. The T score describes the growth of the primary tumor. It also describes the level of invasion into nearby tissue. The N score describes nearby cancer growth within nearby lymph nodes. The M score tells if the cancer has spread to distant sites.

Five stages
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), or IV (4). The stages are defined as:

Stage 0
These cancers are also called carcinoma in situ of the rectum. The cancer has not grown beyond the first layer of the rectal wall. It is a noninvasive cancer. More treatment may not be needed if all the cancer was removed during an endoscopic polypectomy.

Stage I
The cancer has grown into either the second or third layer of the rectal wall. There is no cancer in nearby or distant sites.

Stage II
The cancer has grown outside the rectal wall. It may have attached or grown into other structures or organs. There is no cancer in nearby or distant sites.

Stage III
The cancer has spread from the rectum to nearby lymph nodes or there are tumor deposits. Nearby nodes include the presacral, perirectal, and internal iliac nodes. Tumor deposits are small secondary tumors within the rectal wall.

Stage IV
The rectal cancer has spread to distant organs. Common distant sites include your liver and lungs.

Clinical vs. pathologic stage
Rating of the cancer stage is often done twice. The first rating is based on tests before treatment. It is called the clinical stage. Tests include a physical exam and imaging described in Part 2.

The pathologic stage is a rating done after surgery. The pathologic stage may be the same or differ from the clinical stage. Sometimes the full extent of the cancer isn’t known until after surgery.

Review

- The rectum stores stool until it is expelled from the body.
- Layers of tissue make up the rectal wall.
- Rectal cancer is a cancer of cells that line the inner rectal wall and make mucus.
- Cancer cells form a tumor since they don’t grow and die as normal cells do.
- Cancer cells sometimes spread from the rectum to other sites through lymph or blood.
- Most rectal cancers start in polyps.
- The cancer stage is a rating by doctors of the extent of cancer.
## 2 Treatment planning

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Not all rectal cancers are the same. Your cancer doctor will want to learn all about the cancer you have. Part 2 describes the tests used to learn about rectal cancer. Based on the results, your treatment can be tailored to you. This is called personalized medicine.

Medical history

Your medical history includes any health events and medicines you’ve taken in your life. It helps your doctors decide if you can have surgery. It also helps doctors assess if chemotherapy will do you more good than harm.

Rectal cancer and other health conditions can run in families. Thus, 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.

Rectal cancer often occurs for unknown reasons. However, some people have syndromes that increase their chance of getting rectal cancer. A syndrome is a group of signs or symptoms that occur together and suggest the presence of or risk for a disease. Some syndromes that increase the risk for rectal cancer are passed down from parents to child (inherited).

Lynch syndrome is an inherited syndrome. It’s also called HNPCC (hereditary non-polyposis colorectal cancer). It’s the most common type of inherited syndrome to cause rectal cancer. It also increases the risk for other types of cancer. Even so, only 3 to 5 out of every 100 people with rectal cancer have Lynch syndrome.

FAP (familial adenomatous polyposis) is a rare inherited syndrome that often leads to rectal cancer. However, only 1 out of 100 people with rectal cancer have FAP. FAP starts with hundreds of polyps forming in the colon and rectum. You are likely to have cancer by age 50 if you have classic FAP. In attenuated FAP, the disease starts later in life and fewer than 100 polyps occur.

If you may have an inherited syndrome, you may be referred to a genetic counselor. A genetic counselor can talk with you about getting tested for syndromes related to rectal cancer.

“Remind yourself that you don’t have cancer, cancer has you! Take control of the fight and decide to win one day at a time. Embrace the process and find your source of faith.

–Tony
Survivor, Stage II
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.

A medical history is needed for treatment planning. See Guide 1 for a complete list of care that is advised prior to treatment. Some tests are for anyone with rectal cancer while others are for a select group.

**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 health conditions can cause organs to become enlarged and hard.

### Guide 1. Health care before cancer treatment

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<tr>
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<td>Some stage II, III, and IV if CT unclear or contrast isn’t an option. Sometimes used for metastases.</td>
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Total colonoscopy

A colonoscopy is a procedure that allows your doctor to examine your colon. A total colonoscopy is a study of your entire large intestine. Your doctor will look for polyps and other diseases.

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.

A colonoscopy is the device used for the test. Part of it looks like a thin tube. It has a light and camera.

This part will be inserted into your anus and gently guided through your large intestine.

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

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

Figure 6
Total colonoscopy

Your entire colon should be examined if you have rectal cancer. A total colonoscopy is a procedure that allows your doctor to look for and remove any tissue that looks abnormal. It involves inserting a thin device into your body that has a light, camera, and cutting tool.
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

Another blood test is a chemistry profile. 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 far.

Imaging tests

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

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

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.

Most imaging for rectal cancer is done with a large machine. Figure 7 shows one type. You will likely be lying down during testing. At least part of your body will be in the machine.

Figure 7

CT machine

Pictures of the insides of your body can be made with an imaging test. During the scan, you will lie on a table that will move into the tunnel of the imaging machine. The pictures will be viewed by a doctor who will look for signs of cancer.
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.

CT is advised to see if the cancer has spread. Get scans of your chest, abdomen, and pelvis. Contrast should be used. The radiologist will look for cancer in nearby and distant sites.

During the scan, you will need to lie face up on a table. The table will move through the machine. As the machine takes pictures, you may hear buzzing, clicking, or whirring sounds.

You will be alone in the room during the test. In a nearby room, the technician will operate the machine. He or she will be able to see, hear, and speak with you at all times. One scan is completed in about 30 seconds. You will likely be able to resume your activities right away unless you took a sedative.

**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 lie on top of and wear a coil device. The latter coil will cover your body from below your chest to the top of your legs. Coils will send and receive radio waves. Straps may be used to help you stay in place. MRI may cause your body to feel a bit warm.

**Endorectal ultrasound**

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

**PET/CT**

Sometimes CT is combined with PET (positron emission tomography). When used together, they are 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. PET/CT can show how big a tumor is if you have metastases. PET/CT can also find metastases other than in the liver that would exclude surgery. Last, PET/CT may be received if the CT scan is unclear or you can’t receive contrast.

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 will be detected with a special camera during the scan. Cancer cells will appear brighter than normal cells because they use sugar more quickly. PET can show even small amounts of cancer.
Biopsy

The only way to know if you have cancer is to test tissue. A biopsy is a procedure that removes samples of fluid or tissue for testing. A biopsy is advised before receiving treatment.

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

Cancer cell tests

Tissue removed from your body will be sent to a pathologist. This may be tissue from a biopsy or surgery. The pathologist will examine the samples using a microscope.

Pathology report
The pathologist will study the parts of the cells to classify any disease. This is called histologic typing. When cancer is found, he or she will do other tests to learn more about the cancer.

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

All lab results are recorded in a pathology report. A report will be written each time tissue is removed from your body and tested for cancer. These reports are vital to planning treatment.

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

Molecular testing
Not all rectal cancer cells are alike. Cancer cells can differ by which genes have mutations. Some gene mutations are known to have an effect on cancer treatment. Molecular testing includes tests of genes or their products (proteins). Molecular testing that is advised for rectal cancer is described next.

RAS mutation
RAS is a family of proteins found in cells. Some rectal cancers have abnormal genes that control the RAS proteins. As a result, the RAS proteins are overactive and promote cancer cell growth. Some
treatments for metastatic rectal cancer do not work if the RAS genes are abnormal. Thus, testing for mutations in KRAS and NRAS genes is advised for metastatic disease.

**BRAF mutation**
The BRAF V600E mutation is also known to affect some treatments. About 5 to 9 out of every 100 rectal cancers have a mutated BRAF gene. Testing for the BRAF V600E mutation is advised for metastatic disease.

**MMR and MSI**
Normal MMR (mismatch repair) proteins correct DNA errors that occur when copies of DNA are being made. In some rectal cancers, MMR mutations cause one or more MMR proteins to be absent. As a result, DNA errors aren’t corrected and the number of gene mutations increases. Doctors call this dMMR (defective mismatch repair).

The DNA errors caused by dMMR often occur in microsatellites. Microsatellites are a tiny part of the DNA code that is repeated many times in a row. See Figure 8. Due to dMMR, microsatellites may be shorter or longer than normal. This is called MSI (microsatellite instability).

Loss of MMR proteins and MSI are features of Lynch syndrome. One or both features is present in over 90 of every 100 Lynch syndrome-related cancers (>90%). However, these features can still occur in the

---

**Figure 8**
**MMR system**

A. The four types of MMR proteins are present to correct DNA errors when copies of DNA are being made. An error has been made in the C-G pair. G has been replaced by T.

B. The MMR system is deficient. Some MMR proteins are missing. A DNA microsatellite has been shortened in the bottom DNA copy.
absence of Lynch syndrome. They are found in about 15 out of every 100 rectal cancers (15%) without Lynch syndrome.

Testing for loss of MMR proteins or MSI is advised for all people with colon or rectal cancer. These features may affect your treatment plan. There are two tests that can be done.

PCR (polymerase chain reaction) is a test that can assess for MSI. The test consists of a process in which millions of copies of a DNA part are made. The copies will be examined for 5 MSI markers. Tumors can be rated as MSS (microsatellite-stable), MSI-L (microsatellite instability-low), and MSI-H (microsatellite instability-high). MSI-H is defined as the presence of 2 or more MSI markers. MSI-H suggests dMMR but more testing is needed to confirm.

An IHC (immunohistochemistry) panel is used to assess MMR proteins. It involves applying a chemical marker to cells then looking at them with a microscope. There are four types of MMR proteins. They are MLH1, MSH2, MSH6, and PMS2. If all are present, it is unlikely that any MMR gene is mutated.

If the MLH1 protein is missing, more testing should follow. The cancer may be tested for a BRAF V600E mutation or a modified MLH1 gene. If a BRAF mutation or modified gene is present, you don’t have Lynch syndrome. If not present or the other MMR proteins are missing, the cancer will be tested for MMR mutations to confirm Lynch syndrome.

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 may be done to look for signs of cancer spread to distant sites.

- Imaging tests allow your doctor to see how far the cancer has spread without cutting into your body.

- A biopsy is advised when surgery is an option. A needle biopsy may be done to test for cancer in distant sites.

- Molecular testing for MSI or missing MMR proteins is advised for all rectal cancers. Testing for mutated KRAS, NRAS, and BRAF genes is advised for metastatic cancer.
3
Overview of cancer treatments

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In Part 3, the main treatment types for rectal cancer are briefly described. Knowing what a treatment is will help you understand your treatment options listed in Parts 4 through 6. There is more than one treatment for rectal cancer. Not every person will receive every treatment described in this chapter.

**Surgery**

Some rectal cancers grow beyond the polyp and into the rectal wall. In many of these cases, surgery is a key part of treatment. Your surgery may consist of more than one type. This section describes the types of surgery used for rectal cancer.

Before surgery, the cancer site may be marked with a tattoo. An gastroenterologist may do the tattoo. The tattoo allows your surgeon to find the cancer site after the polyp has been removed. Marking isn’t always needed. For example, marking isn’t done if the cancer site can be easily found.

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.

**Transanal surgery**

Some stage I cancers 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 excision**

This surgery removes 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 be then 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’s not like a transanal 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 has a light, camera, air ports, and an open channel. Air will be pumped into your rectum to expand it. The light and camera 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 removes tissue through cuts made through your skin. This surgery requires general anesthesia. Most people lie on their back during the entire surgery. Some people are turned over to lie face down.

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 in 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 spared.

“

For me, the hardest time during my treatments was waking up in my hospital room after having gone through the surgery to remove the tumor from my rectum, and discovering I had a colostomy bag attached to my body. To learn how to live with a colostomy, while at the same time going through cancer treatments, was overwhelming to say the least. I am proof, though, that you can adjust to anything. We are all so much stronger than we think we are.

–Donna
Survivor, Stage III
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. See Figure 9.

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 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. An enterostomal therapist may mark you at the best spot for the colostomy.

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.

Figure 9
Low anterior resection with coloanal anastomosis
Surgery for most rectal cancers removes the whole rectum. Low anterior resection also removes part of your colon. Your remaining colon may be connected to your anus for bowel movements. This is called a coloanal anastomosis.
3 Overview of cancer treatments

Side effects
Side effects are unplanned physical or emotional reactions to treatment. 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. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better.

Radiation therapy
Radiation therapy most often uses high-energy x-rays to treat rectal cancer. The x-rays damage DNA in cancer cells. This either kills the cancer cells or stops new cancer cells from being made.

Radiation therapy is most often used to treat the primary rectal site. It is often given to the tumor before surgery. If done after surgery, it is given to the tumor bed and nearby lymph nodes.

The internal iliac, perirectal, and presacral nodes should also be treated. See Figure 10. For some T4 tumors, the external iliac nodes should also be included.

A radiation oncologist will oversee your radiation treatment. A radiation oncologist is a doctor who’s an expert in treating cancer with radiation. He or she will tailor treatment to you.

Figure 10
Radiation sites

Radiation therapy is most often used to treat the primary rectal site. It is often given to the tumor before surgery. If done after surgery, it is given to the tumor bed and nearby lymph nodes.
External radiation
For rectal cancer, the most common radiation method is EBRT (external beam radiation therapy). A large machine makes high energy x-rays used for treatment. This machine is called a LINAC (linear accelerator). See Figure 11.

The beams of high-energy x-rays are a type of photon radiation. They will move through your body at the speed of light. There is no ongoing radiation inside of you after the treatment session. You will not have to avoid people.

It takes a team of people to perform the radiation therapy. The radiation team consists of doctors, medical physicists, dosimetrists, nurses, and radiation therapists. Your team will work together to design your treatment plan and provide treatment.

Planning session
A planning session is needed to map out your treatment. The planning process is called simulation. It involves obtaining a CT scan of your body in the position that is needed for treatment. The scan is only used for treatment planning.

You will not have to do much to prepare. Don’t eat a heavy meal for 4 hours beforehand. Think about wearing easy-to-remove clothes since you’ll undress from the waist down. You’ll wear a gown during the session. The planning session takes about one hour.

In the CT room, a mold may be created and fitted to your body. The mold will help you stay in place during treatment. Often, people lie face down on the mold that is on top of the CT table. Your arms may be raised above your head. Colored laser lights will be used to help position you.

You may be given a contrast dye. It will make your rectum and lymph nodes easier to see on the scans. Contrast may be given with a rubber catheter inserted into your rectum. Air may also be pumped in or removed. Next, a CT scan will be done. The medical physicist or dosimetrist may take more measurements for treatment planning.

The CT images will be transferred to a treatment planning computer. Your rectum and other organs will be seen on the scan. This information will show your radiation oncologist where to direct the radiation.

After the treatment sites are set, your skin will be marked for treatment sessions. Your skin will be marked with a felt pen. Sometimes, set-up marks are made with tiny permanent tattoos. Photos of your set up are taken. The marks and photos will be used to position you for daily treatment sessions.

Figure 11
External beam radiation therapy
Radiation therapy is often delivered from a large machine called a linear accelerator. The rays pass through skin and travel to the tumor. Healthy tissue is protected using modern types of treatment.
After simulation, your radiation team will further plan your treatment. Plans will be made by viewing your CT scans on the treatment planning computer. Your radiation oncologist will work closely with a dosimetrist. They will plan the best dose, number and shape of radiation beams, and number of treatments. Your plan will be designed to treat the cancer while sparing normal tissue.

**Set-up session**

Once your treatment plan is made, a set-up session is needed. This session is sometimes called “port film” day or dress rehearsal. The set-up session occurs in the treatment room.

The radiation therapists will help place you in position on the treatment table. The set-up marks will be used for positioning. X-rays of the treatment fields will be taken and viewed by your doctor. These x-rays (or port films) are not for treatment. Your doctor will approve treatment when your set-up is correct.

**Treatment sessions**

Treatment is given once a day on Monday through Friday. Short-course radiation is finished in 5 visits. Long-course radiation takes about 28 visits. Each session can last between 10 to 30 minutes. In general, treatment is received at the same time each day.

Before treatment, you will be placed into position. If a mold was made, you will lie on it on top of the treatment table. You must be in the same position that was approved at the set-up session. X-rays of your pelvis are used to assure this.

Conformal techniques are used for treating rectal cancer. These techniques shape the radiation dose to the cancer site to spare healthy tissue. 3D-CRT (three-dimensional conformal radiation therapy) delivers, from different angles, a photon beam that matches the shape of the target.

Other types of conformal techniques are less often used. IMRT (intensity-modulated radiation therapy) is a form of 3D-CRT. It further modifies the beam’s intensity during treatment. IMRT is used in certain cases.

SBRT (stereotactic body radiation therapy) treats cancer with very precise, high-dose photon beams. Treatment is finished in 5 visits. At this time, SBRT is only used to treat some people with rectal cancer in the spine, liver, or lungs.

During treatment, you will be alone in the room. A therapist 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. The machine will move around you to different treatment angles. You will not see, hear, or feel the radiation.

**Intraoperative radiation**

IORT (intraoperative radiation therapy) delivers radiation inside your body during 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 is used to deliver extra radiation if cancer cells may remain after surgery. This extra radiation is called a boost. IORT uses radiation made of electrons or lower energy x-rays. Electrons do not travel far and are less likely to harm the tissue deep to the treatment site.

**Brachytherapy**

Some cancer centers do not have an IORT machine. In this case, a boost of radiation can be given with EBRT, brachytherapy, or both. Brachytherapy delivers radiation through radioactive objects that are placed where the tumor was. The objects remain in
your body for a short period of time following surgery. This type of treatment is not commonly used for rectal cancer.

**Side effects**
Side effects from radiation therapy differ among people. Factors like radiation dose and length of treatment play a role. Side effects are cumulative. This means they build up slowly and are worse at the end of treatment. Your doctor will check on you every week during treatment. He or she will review skin care, medicines, and other options to help you feel better.

**Acute effects**
Acute effects are those that happen during treatment or shortly after the last session. Acute effects will generally improve after treatment. Fatigue is an acute effect. Skin changes and hair loss at the treatment site are expected.

Often, people describe skin changes as like a sunburn. Unlike a sunburn, skin changes build up slowly during treatment. Your skin may become red, irritated, and dry. It may also itch, darken, peel, and sometimes crack open. Skin in regions of friction or rubbing is prone to cracking open.

Radiation can affect the wall of your gut. Thus, another common acute effect is watery stools (diarrhea). You may also feel nauseated.

Radiation may irritate your urine system. You may have discomfort when peeing. You may have trouble starting and maintaining a urine stream.

**Late effects**
Late effects are those that happen after treatment. Some do not go away. Rarely, chronic diarrhea or bloody stools occur. Strong bowel urges or loss of bowel control also uncommonly occur. There is a rare risk for weakening of pelvic bones. At worst, they may fracture. Rarely, scar tissue blocks the gut.

You may have sexual problems. Men may not be able to get normal erections. Women's vaginal canal may not stretch as normal causing dryness and pain during sex. Vaginal dilators from your doctor may prevent or reduce this late effect. Women’s sex drive may also drop due to damage to ovaries.

You may not be able to have children naturally after treatment. The cells in men that make sperm may not work well. Likewise, eggs in women may be damaged.

Tell your doctor if you want to talk with a fertility specialist before treatment. A fertility specialist is an expert in helping people have babies. You and the fertility specialist can discuss your options for how to have a baby after treatment.

Not all the side effects of radiation have been listed here. Please ask your treatment team for a complete list of side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better.
Chemotherapy

Chemotherapy, or “chemo,” includes drugs that disrupt the life cycle of cancer cells. The types of chemotherapy differ in the way they work. Some kill cancer cells by damaging their DNA or by disrupting the making of DNA. Others interfere with cell parts that are needed for making new cells. Thus, no new cells are made to replace dying cells. Chemotherapy can affect both cancer and normal cells.

Some chemotherapy drugs work when cells are in an active growth phase. See Figure 12. During the active growth phase, cells grow and divide to form a new cell. Chemotherapy that disrupts the growth phase works well for cancer cells that are growing and dividing quickly. Other chemotherapy drugs work in any growth or resting phase.

“

I was in shock until my ignorance began to be replaced by information, then hope began to reappear.

–Tom
Survivor, Stage III

Figure 12
Chemotherapy and the cell cycle

A cell goes through many changes to divide into two cells. Science has grouped these changes into 7 main phases. There may be another phase of rest, too. Some chemotherapy drugs work in any phase. Other chemotherapy drugs work in one or two growth phases. In growth phases, DNA is copied and two full sets of chromosomes are made. A full set of chromosomes is pulled into each end of the cell. The cell then divides into two cells each with their own set of chromosomes.

Chemotherapy may work in some or all phases of cell division.
What to expect
Chemotherapy regimens used for rectal cancer are listed in Guide 2. Sometimes, only one drug is used. Other times, more than one drug is used because drugs differ in the way they work. A combination regimen is the use of two or more chemotherapy drugs.

Most chemotherapy drugs for rectal cancer are liquids that are injected into your body. They are almost always injected into a vein. A slow injection is called an infusion. Bolus injections are fast. Only capecitabine and trifluridine/tipiracil are in pill form.

Chemotherapy will enter your bloodstream. Once in the bloodstream, it can travel throughout your body to treat cancer. Doctors use the term “systemic”

Guide 2. Chemotherapy types

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*Levoleucovorin can be used instead of leucovorin
when talking about a cancer treatment for the whole body.

Chemotherapy received by HAI (hepatic arterial infusion) differs. It is given through a port or pump within your artery supplying blood to your liver. If a pump is used, it is placed within the artery during surgery. HAI may be a treatment option for rectal cancer in the liver. NCCN experts advise that HAI should only be done at treatment centers with much experience in this method.

Chemotherapy is given in cycles of treatment days followed by days of rest. The cycles vary in length depending on which drugs are used. Common cycles are 14 or 21 days long. Giving chemotherapy in cycles gives your body a chance to recover after receiving chemotherapy. If you will have chemotherapy, ask your doctor how many cycles will be given. Also ask how many days of treatment there are within a cycle.

**Side effects**

Side effects differ among people. Some people have many side effects. Other people have few. Some side effects can be very serious. Others can be unpleasant but not serious. Most side effects appear shortly after treatment starts and will stop after treatment. However, other side effects are long-term or may appear years later.

Side effects of chemotherapy depend on multiple factors. These factors include the drug type, amount taken, length of treatment, and the person. In general, side effects are caused by the death of fast-growing cells. These cells are found in the hair follicles, gut, mouth, and blood. Thus, common side effects of chemotherapy include low blood cell counts, not feeling hungry, nausea, vomiting, diarrhea, hair loss, and mouth sores.

Oxaliplatin causes a very unique side effect. It can cause a short-lived and sometimes painful sensitivity in areas exposed to cold. Examples of these areas are your mouth when drinking cold liquids and your fingers when holding a cold object. If more oxaliplatin is used over time, loss of sensation and tingling in fingers and toes can occur. It can take months or years for these symptoms to resolve. After long-term treatment, you may have a permanent loss of sensation in your feet or fingers (sensory neuropathy).

Not all side effects of chemotherapy are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

**Supportive care**

Supportive care doesn’t aim to treat cancer but aims to improve quality of life. It is also called palliative care. It can address many needs. One example is treatment for physical and emotional symptoms.

Supportive care can also help with treatment decisions as you may have more than one option. It can also help with coordination of care between health providers. Talk with your treatment team to plan the best supportive care for you.
Targeted therapy

Targeted therapy is a class of drugs that stops the action of molecules that help cancer cells grow. It is less likely to harm normal cells than chemotherapy. Targeted therapy for rectal cancer targets either the VEGF (vascular endothelial growth factor) or EGFR (epidermal growth factor receptor) pathway. Targeted therapy used for rectal cancer is listed in Guide 3.

Targeted therapies are briefly described next. Some side effects are listed. Ask your treatment team for a full list of common and rare side effects. In Parts 4 through 6, information on who should receive these drugs is provided.

VEGF pathway
Cancer cells need the food and oxygen in blood to grow. Cancer cells get blood from blood vessels that have grown into the tumor. VEGF is one of the molecules that triggers the growth of these blood vessels.

VEGF is made by cancer cells. It travels from cancer cells to endothelial cells. Endothelial cells form blood vessels.

Guide 3. Targeted therapy

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Surface receptors are proteins within cell membranes that extend from the inside to the outside of cells. VEGF attaches to surface receptors on the outside of endothelial cells. Attachment of VEGF to receptors triggers growth signals. There are four medicines used to stop the growth signals caused by VEGF.

**Bevacizumab**
Bevacizumab attaches to VEGF before it attaches to receptors on endothelial cells. See Figure 13. As a result, VEGF can’t attach to receptors. No growth signals caused by VEGF are started.

Bevacizumab is given by infusion. It takes about 90 minutes to get the first dose and 30 minutes for later doses. Bevacizumab is always given with chemotherapy. It is given every two or three weeks depending on the chemotherapy.

Common side effects of bevacizumab are high blood pressure, nosebleeds, and headache. You might also have a runny nose, protein in the urine, and rectal bleeding. Rare but serious side effects include stroke, heart attack, blood clots, kidney damage, holes in the gut, abnormal passage between body parts, and bleeding. Very rarely, brain damage occurs.
3 Overview of cancer treatments

Targeted therapy

**Ramucirumab**
Ramucirumab attaches to VEGF receptors on the outside of endothelial cells. This blocks VEGF from attaching. No growth signals caused by VEGF are started.

Ramucirumab is given by infusion. It takes 60 minutes to receive the full dose. Ramucirumab is always given with chemotherapy. It is given every two weeks on the first day of chemotherapy.

Common side effects of ramucirumab are high blood pressure and diarrhea. Serious side effects include bleeding, blood clots, holes in the gut, abnormal passage between body parts, and slow wound healing. Very rarely, brain damage occurs.

**Regorafenib**
Regorafenib attaches to VEGF receptors on the inside of endothelial cells. This blocks growth signals from the receptor. Regorafenib may also attach to surface receptors within cancer cells and stop growth signals.

Regorafenib is made as a pill that is taken once a day. However, it is taken in cycles consisting of treatment days followed by a period of no treatment. The cycle for regorafenib consists of 3 weeks of treatment then 1 week of no treatment. The cycle is then repeated.

While on regorafenib, you may feel tired or weak. You may also feel pain including stomach (abdominal) pain. Other common side effects are diarrhea, nausea, decreased appetite, and weight loss.

**Figure 13**
VEGF targeted therapy

Cancer cells need blood to grow. They send VEGF to endothelial cells to start the growth of blood vessels. Regorafenib stops growth signals within endothelial cells. Ramucirumab blocks VEGF from attaching to receptors. Ziv-aflibercept traps VEGF by being a receptor decoy. Bevacizumab disables VEGF from attaching to receptors.
You may develop an infection, fever, change in voice, mouth sores, and high blood pressure.

Your hands and feet may become red and have pain. This is called hand-foot skin reaction. It is important to remove calluses on hands and feet before starting regorafenib.

Rare but serious side effects of regorafenib include heart attack, holes in the gut, abnormal passage between body parts, and severe bleeding. Liver damage may be severe. Very rarely, brain damage occurs.

Ziv-aflibercept
Ziv-aflibercept works by acting as a decoy. VEGF thinks ziv-aflibercept is a surface receptor and attaches to it. Thus, ziv-aflibercept traps VEGF so it is unable to bind to the real receptor. Hence its other name is VEGF-trap. By trapping VEGF, growth signals caused by VEGF within endothelial cells won’t be started.

Ziv-aflibercept is given by infusion. You’ll receive it over the course of about 1 hour every two weeks. It is given with chemotherapy.

While taking ziv-aflibercept, you may have diarrhea, mouth sores, voice changes, and nose bleeds. You may have headaches and stomach pain. You may feel tired. Loss of appetite and weight loss are common. Tests may show low blood cell counts, protein in urine, liver inflammation, increased blood pressure, or kidney damage.

Rare but serious side effects include blood clots, holes in the gut, abnormal passage between body parts, and severe bleeding. Infections may be serious. Very rarely, brain damage occurs.

**EGFR pathway**
Cell growth is started by growth signals. EGFR is one of the surface receptors in rectal cancer cells that can trigger growth signals. When EGF (epidermal growth factor) attaches to EGFR, the chemical pathway that sends growth signals is turned on.

Some people with rectal cancer have abnormal changes in their gene that controls EGFRs. These changes cause the cancer cells to have too many EGFRs. For a small group of people, the EGFRs may be overactive.

With too many or overactive EGFRs, new cancer cells form quickly. There are two medicines used to block the growth signals from EGFRs. See Figure 14. These medicines don’t work if the cancer cells have mutations in KRAS or NRAS genes.

**Cetuximab**
Cetuximab treats rectal cancer by attaching to the ends of EGFRs that are outside of the cell. Thus, EGF is blocked from attaching and triggering growth signals. Cetuximab also attracts immune cells that help to kill the cancer cells.

Cetuximab is given by infusion, usually once a week or every other week. It may take 2 hours to receive the first dose. Later doses will take only 1 hour. Cetuximab may be given with or without chemotherapy.

Common side effects of cetuximab are skin problems. These problems include acne-like rash, dry skin, eye inflammation, and skin infections. Other common side effects are diarrhea and loss of appetite. Blood magnesium levels may drop. Rare but serious side effects include a severe reaction to the infusion and lung damage.
Panitumumab
Panitumumab is the same type of drug as cetuximab. However, it does somewhat differ from cetuximab in its structure. It works much like cetuximab by attaching to EGFRs and attracting immune cells.

Panitumumab is given by IV infusion over 1 hour every other week. It may be given with or without chemotherapy.

Panitumumab rarely causes infusional reactions. Common side effects are skin rash and swelling around the nails. You may get diarrhea, nausea, and feel tired. Blood magnesium levels may drop. Rare but serious side effects include lung and eye damage.

Immunotherapy
The immune system is your body's natural defense against infection and disease. The immune system includes many chemicals and proteins. These chemicals and proteins are made naturally in your body. Immunotherapy increases the activity of your immune system. By doing so, it improves your body’s ability to find and destroy cancer cells.

PD-1 inhibitors
T-cells are part of your immune system. One job of T-cells is to attack cancer cells. PD-L1 is a molecule that can stop T-cells from doing their job.

Rectal cancers that have dMMR or MSI-H also have PD-L1 on the cells’ surface. PD-L1 attaches to PD-1 on T-cells. This stops T-cells from attacking cancer cells.

Figure 14
EGFR targeted therapy
Some rectal cancers consist of cells with too many or overactive EGFRs. EGFRs trigger growth signals with cancer cells. Cetuximab and panitumumab block EGF from attaching to EGFR and turning it on.
PD-1 inhibitors are a type of medicine that stops the action of PD-L1. They attach to PD-1 on T-cells. This blocks PD-L1 on cancer cells from attaching. See Figure 15. Thus, T-cells are able to attack cancer cells.

There are two types of PD-1 inhibitors used for rectal cancer. Their structures differ from each other. As a result, each one attaches to PD-1 in a different way. They are described next.

**Nivolumab**
Nivolumab is sold as Opdivo®. It is given by infusion every two weeks. It takes about 60 minutes to receive the full dose.

One common side effect of nivolumab is feeling tired. Other common side effects are diarrhea, nausea, constipation, and not feeling hungry. A rash may appear on your skin or your skin may itch. You may get a cough, have trouble breathing, or get an airway infection. Muscle, bone, and joint pain and fever are also common. Severe problems with your lungs, gut, liver, kidney, skin, and hormones may occur.

**Pembrolizumab**
Pembrolizumab is sold as Keytruda®. Pembrolizumab is given by infusion. It is given every three weeks. It takes about 30 minutes to receive the full dose.

Side effects are much like those for nivolumab. You may feel tired. You may also have problems with your gut, skin, airways, and muscles. Severe problems with your lungs, gut, liver, kidney, skin, and hormones may occur.

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**Figure 15 Immunotherapy**

Some rectal cancers consist of cells that have PD-L1 on their surface. PD-L1 attaches to PD-1 on T-cells. This stops T-cells from attacking cancer cells. PD-1 inhibitors attach to PD-1 and block PD-L1. As a result, T-cells are able to attack cancer cells.
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 lung. 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 is more than one way to “ablate” a tumor. Cryoablation kills cancer cells by freezing them with liquid nitrogen. Radiofrequency and microwave ablation kills 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. It is done by an interventional radiologist. He or she often teams up with a surgeon or radiation oncologist.

A catheter will be inserted into an artery in your leg. It will then be guided to the blood vessels that feed the tumor. Once in place, the beads will be inserted into the blood vessels.

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 or Y-90. Embolization is an option for some people with liver metastases.

Clinical trials

One of your treatment choices may be to join a clinical trial. Joining a clinical trial is strongly supported. NCCN believes that you will receive the best management in a clinical trial.

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 a test or treatment in people.

Clinical trials study how safe and helpful tests and treatments are for people. When found to be safe and helpful, they may become tomorrow’s standard treatment. Because of clinical trials, the tests and treatments in this book are now widely used to help people with rectal cancer. Future tests and treatments that may have better results than today’s treatments will depend on clinical trials.

New tests and treatments go through a series of clinical trials. These trials aim to ensure they’re safe and work. Without clinical trials, there is no way to know if a test or treatment is safe or helpful. Clinical trials have four phases. Some examples of the four phases for treatment are:

- **Phase I trials** aim to find the safest and best dose of a new drug. Another aim is to find the best way to give the drug with the fewest side effects. These trials often involve about 20 people.

- **Phase II trials** assess if a drug works for a specific type of cancer. These trials often involve 20 to 100 people.
3 Overview of cancer treatments

Phase III trials compare a new drug to a standard treatment head-to-head. These trials often involve hundreds or thousands of people.

Phase IV trials test drugs approved by the U.S. FDA (Food and Drug Administration) to learn more about side effects with long-term use.

Joining a clinical trial has benefits. First, you’ll have access to the most current cancer care. However, please note that it is unknown how well new treatments will work if at all. Second, you will receive the best management of care. Third, the results of your treatment—both good and bad—will be carefully tracked. Fourth, you may help other people who will have cancer in the future.

Clinical trials have risks, too. Like any test or treatment, there may be side effects. Also, new tests or treatments may or may not improve your health. In fact, your health may worsen during a trial. Other downsides may include more hospital trips, paperwork, and extra costs 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. Thus, if patients improve, it’s because of the treatment and not because of differences between them.

Complementary and alternative medicine

CAM (complementary and alternative medicine) is a group of treatments that aren’t often given by doctors. There is much interest today in CAM for cancer. Many CAMs are being studied to see if they are truly helpful.

Complementary medicines are treatments given along with usual medical treatments. While CAMs aren’t known to kill cancer cells, they may improve your comfort and well-being. Two examples are acupuncture for pain management and yoga for relaxation.

Alternative medicine is used in place of usual medicine. Some alternative medicines are sold as cures even though they haven’t been proven to work in clinical trials. If there was good proof that CAMs or other treatments cured cancer, they would be included in this book.

It is important to tell your treatment team if you are using any CAMs. They can tell you which CAMs may be helpful and which CAMs may limit how well medical treatments work.
To join, you’ll need to review and sign 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.

Review

- TME is a standard surgery used for many rectal cancers. It removes the rectum and other tissue through a cut made in your abdomen. Some small rectal cancers may be removed with thin tools inserted into your anus.

- Radiation therapy most often uses high-energy x-rays to treat rectal cancer. A large machine precisely delivers the x-rays to the tumor. 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 enables T-cells to start attacking rectal cancer cells with dMMR or MSI-H.

- Ablation destroys small tumors by freezing or burning them. It isn’t often used for rectal cancer.

- Embolization treats cancer by blocking blood flow to the tumor and damaging cancer cells with chemotherapy or radiation. It is used for a very select group of people.

- Clinical trials give people access to new tests and treatments that otherwise can’t usually be received. These new tests and treatments may, in time, be approved by the FDA.
4
Treatment guide: Nonmetastatic cancer

43 Stage I
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53 Review
Part 4 is a treatment guide for rectal cancer that hasn’t spread to distant sites. The cancer is confined within the rectum, has grown to nearby structures, or has spread to nearby lymph nodes. Treatment options are partly based on cancer stage.

Stage I

Stage I consists of either T1 or T2 tumors. T1 tumors haven’t grown beyond the second layer of the rectal wall. They are sometimes called “polyps with cancer” because the cancer hasn’t grown far. T2 tumors haven’t grown beyond the third layer. Stage I cancers have not spread to lymph nodes or distant sites.

T1 tumors

Not all people with T1 tumors will need treatment. Treatment is based on the polyp shape and if there’s still cancer in your body. Shapes of polyps are shown in Figure 16. Cancer is more likely present if these high-risk features are present:

- **Fragmented specimen** is a tumor that was removed in pieces.
- **Positive surgical margin** is cancer within the normal-looking tissue around the tumor.
- **Unknown surgical margin** is unclear results of the normal-looking tissue around the tumor.
- **Cancer grade 3 or 4** means cancer cells don’t look much like normal cells.
- **Angiolymphatic invasion** is cancer spread into the tumor’s lymph and blood vessels.
- **Tumor budding** is a group of 5 or fewer cancer cells separate from the main tumor.

Figure 16

Shapes of polyps

Treatment for stage I, T1 tumors is partly based on the shape of the polyp. A pedunculated polyp has a stalk and round top. A sessile polyp doesn’t have a stalk.
Guide 4 lists the options for initial treatment. Options are partly based on T score. If you have surgery, a pathologist will test the removed tissue.

**Follow-up care**
For T1 tumors not at high risk, you may start follow-up care. A polypectomy likely removed all the cancer. However, sessile polyps have worse outcomes than other polyps. Thus, surgery is also an option for sessile polyps.

**Transanal excision**
This surgery removes the tumor through the anus. Lymph nodes aren’t removed. It should only be done under conditions that’ll likely result in a cure. These conditions include a small T1 tumor near your anus. There should be no signs of cancer in your lymph nodes. Ask your doctor if this surgery is an option for you.

**Transabdominal resection**
This surgery removes the tumor through cuts made in your abdomen. Lymph nodes are removed, too. It is an option for many T1 tumors and T2 tumors.

**Pathology**
A pathologist will assess how far the cancer has grown within the rectal wall. If removed, lymph nodes will be tested for cancer. Test results may show that you need more treatment.

Guide 5 lists options for additional treatment after surgery. Options are grouped by type of initial surgery. Not all cancers need more treatment.

Additional treatment often includes chemotherapy, chemoradiation, or both. FOLFOX or CAPEOX is preferred for chemotherapy. Otherwise, you may receive 5-FU/LV or capecitabine. However, there’s no proof that FOLFOX is better than 5-FU/LV for people 70 years of age and older.

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.

Your doctor will assess treatment results. CT scans of your chest, abdomen, and pelvis are advised. Contrast should be used.

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Guide 4. Initial treatment

<table>
<thead>
<tr>
<th>T score</th>
<th>Polyp type</th>
<th>Risk level</th>
<th>What are the options?</th>
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<td>Not high</td>
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</tr>
<tr>
<td></td>
<td>Sessile polyp</td>
<td>Not high</td>
<td>• Start follow-up testing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Transanal excision</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Transabdominal resection</td>
</tr>
<tr>
<td>Any</td>
<td></td>
<td>High</td>
<td>• Transanal excision</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Transabdominal resection</td>
</tr>
<tr>
<td>T2</td>
<td>Any</td>
<td>Any</td>
<td>• Transabdominal resection</td>
</tr>
</tbody>
</table>
Guide 5. Additional treatment

After transanal excision

Option 1 for high-risk T1 and all T2 tumors

<table>
<thead>
<tr>
<th>Primary treatment</th>
<th>Pathologic stage</th>
<th>What are the options after surgery?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transabdominal resection</td>
<td>Stage I</td>
<td>• Start follow-up care</td>
</tr>
<tr>
<td></td>
<td>Upstage to stage II or III</td>
<td>Sandwich approach</td>
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<tr>
<td></td>
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<td>First treatment</td>
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<td>• FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 5-FU/LV or capecitabine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Second treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Capecitabine or infusional 5-FU + radiation therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bolus 5-FU/LV + radiation therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Third treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 5-FU/LV or capecitabine</td>
</tr>
</tbody>
</table>

After transanal excision

Treatment options after transanal excision are based on cancer stage and features. Follow-up care may be started for T1 tumors that have likely been fully removed. More treatment is advised for high-risk T1 tumors and all T2 tumors.

T1 tumors may have one or more high-risk features. High-risk features include cancer in the surgical margins, lymph vessels, or lower-third of the rectum. Another high-risk feature is cancer cells that don’t look much like normal cells.

Option 1

Option 1 starts with a transabdominal resection. The removed tissue will be tested. A pathologic stage will be assigned. CT scans are advised.

If still stage I, you don’t need more treatment. The cancer was likely fully removed. Thus, with option 1, you may avoid chemotherapy and radiation.

The cancer may be upstaged to stage II or III. Chemotherapy and chemoradiation are advised. Treatment should start as soon as possible for best results. Six months of chemotherapy for both treatments is preferred.

A “sandwich” treatment approach is often used. This approach consists of receiving chemotherapy before and after chemoradiation. The other approach is chemoradiation followed by chemotherapy.
Guide 5. Additional treatment continued

After transanal excision

Option 2 for high-risk T1 and all T2 tumors

<table>
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<tr>
<th>Primary treatment</th>
<th>What are the options after chemoradiation?</th>
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<tr>
<td>• Capcitabine or infusional 5-FU + radiation therapy</td>
<td>• Consider starting follow-up care if no signs of cancer</td>
</tr>
<tr>
<td>• Bolus 5-FU/LV + radiation therapy</td>
<td>• Transabdominal resection</td>
</tr>
<tr>
<td></td>
<td>• Consider FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td>• Consider 5-FU/LV or capcitabine</td>
</tr>
</tbody>
</table>

After transabdominal resection

<table>
<thead>
<tr>
<th>Pathologic stage</th>
<th>What are the options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>• Start follow-up care</td>
</tr>
<tr>
<td>Upstaged to stage II</td>
<td>• Start follow-up care</td>
</tr>
<tr>
<td></td>
<td>• FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td>• 5-FU/LV or capcitabine</td>
</tr>
<tr>
<td></td>
<td>• FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td>• 5-FU/LV or capcitabine</td>
</tr>
<tr>
<td></td>
<td>• None</td>
</tr>
<tr>
<td></td>
<td>• Capcitabine or infusional 5-FU + radiation therapy</td>
</tr>
<tr>
<td></td>
<td>• Bolus 5-FU/LV + radiation therapy</td>
</tr>
<tr>
<td></td>
<td>• FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td>• 5-FU/LV or capcitabine</td>
</tr>
</tbody>
</table>

After transanal excision continued

Option 2

Option 2 starts with chemoradiation. Afterward, CT scans are advised. You may start follow-up care if there are no signs of cancer. Thus, with option 2, there is a chance of avoiding surgery.

Signs or no signs of cancer, you may receive a transabdominal resection next. Afterward, CT scans are advised. A benefit of surgery is removing lymph nodes that may have cancer. Also, cancer staging is more likely to be correct. Chemotherapy may follow surgery.

A third option after chemoradiation is chemotherapy. It may further treat any cancer that may be in your body. Surgery is avoided.
After transabdominal resection
After the initial resection, you should receive CT scans. A pathologic stage will be assigned. If still stage I, no more treatment is needed. Start follow-up care.

Some cancers are upstaged to stage II or III. For stage II, you may have three options. One option is to start follow-up care. More treatment can be received if follow-up tests detect cancer. The second option is chemotherapy. A third option is a “sandwich” of chemotherapy before and after chemoradiation. The “sandwich” approach is advised for upstaged III cancers.

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

A transanal excision may have been your only treatment. In this case, a proctoscopy with EUS or MRI is advised. This test is done to assess for cancer at the surgical site.

For all stage I cancers, routine colonoscopies are advised. Get tested 1 year after treatment has ended. If results are normal, the next test should be received in 3 years and then every 5 years.

An advanced adenoma may be found during a colonoscopy. Get your next colonoscopy within 1 year. 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 precancerous cells (high-grade dysplasia).

“

When I was first diagnosed with Stage 1 Rectal Cancer I was absolutely terrified. The stress on me and my family was overwhelming because there was a period of having a diagnosis but not knowing the stage and disease prognosis.

—Evan
Survivor, Stage I
Stages II and III

Guide 7 presents the three treatment options for stage II and III cancers. More than one type of treatment is used. These treatments are given in a sequence to achieve the best outcomes. Treatment may include radiation with or without chemotherapy, surgery, and chemotherapy by itself. Across all treatment, six months of chemotherapy is preferred.

Neoadjuvant treatment
Treatment given before surgery improves results. This treatment is called neoadjuvant treatment. Its aim is to reduce the extent of the cancer.

For a long time, the standard of care was chemoradiation. However, newer research suggests that short-course radiation may be used in some cases. Current research is testing the best approach for neoadjuvant treatment.

Radiation received before surgery has benefits. It may work better on tissue that hasn't been exposed to surgery. Side effects are less as the small intestine is more easily avoided. Also, the bowel parts to be re-attached are more likely to be healthy.

Option 1
Option 1 starts with chemoradiation. A long course of radiation is advised. Chemotherapy helps radiation to work better. Capecitabine or infusional 5-FU is preferred. Side effects of these regimens may be too much for you. If so, bolus 5-FU/LV may be received.

Option 2
Option 2 starts with chemotherapy. This is called induction chemotherapy. FOLFOX or CAPEOX is preferred for chemotherapy. Otherwise, you may receive 5-FU/LV or capecitabine. Chemoradiation, as described for Option 1, should follow.

There may be benefits to option 2. Outcomes may be better. Side effects may be less severe.

Option 3
Option 3 starts with short-course radiation. Chemotherapy isn't received at this time. This option is only for T1, T2, or T3 tumors.

Some results of a short radiation course are equal to a long course. It works well in treating rectal cancer within and near the rectum. It also extends life as much as a long course.

Your treatment team should discuss if this is an option for you. One factor to discuss is the extent of cancer. Some cancers do not shrink enough for surgery during a short course. Another factor is the side effects of short-course radiation.

Imaging
After neoadjuvant treatment, the cancer will be re-staged. Staging helps to plan the best surgical method. Many cancers are down-staged.

Imaging tests will be used for staging. The most commonly used tests are MRI, CT, and EUS. There may be a clinical trial of imaging that you may join.

Primary treatment
Primary treatment is the main method used to rid your body of cancer. The goal is to have surgery for primary treatment. However, some tumors may be too large for surgery.

Transabdominal resection
A transabdominal resection is advised. The tumor and lymph nodes should be removed. Surgery should occur 5 to 12 weeks after chemoradiation. After short-course radiation, surgery can occur within 1 to 2 weeks.

Radiation therapy
Radiation during surgery (IORT) may be an option. It is sometimes used if cancer is in the surgical margin. It is also used as a boost for T4 and recurrent cancers.
Guide 7. Treatment options

Option 1

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
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</thead>
<tbody>
<tr>
<td><em>Chemoradiation</em></td>
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<td></td>
</tr>
<tr>
<td>- Capecitabine or infusional 5-FU + long-course radiation</td>
<td>• Transabdominal resection</td>
<td>• FOLFOX or CAPEOX 5-FU/LV or capecitabine</td>
</tr>
<tr>
<td>- Bolus 5-FU/LV + long-course radiation</td>
<td>• Systemic treatment in Part 6 if surgery isn’t an option</td>
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Option 2

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
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</thead>
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<tr>
<td><em>Induction chemotherapy</em></td>
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</tr>
<tr>
<td>- FOLFOX or CAPEOX 5-FU/LV or capecitabine</td>
<td>• Transabdominal resection</td>
</tr>
<tr>
<td>- Chemoradiation</td>
<td>• Systemic treatment in Part 6 if surgery isn’t an option</td>
</tr>
<tr>
<td>- • Capecitabine or infusional 5-FU + long-course radiation</td>
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</tr>
<tr>
<td>- • Bolus 5-FU/LV + long-course radiation</td>
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Option 3 for T1–T3 tumors

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
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</thead>
<tbody>
<tr>
<td><em>Radiation therapy</em></td>
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<tr>
<td>- Short-course radiation</td>
<td>• Transabdominal resection</td>
<td>• FOLFOX or CAPEOX 5-FU/LV or capecitabine</td>
</tr>
<tr>
<td></td>
<td>• Systemic treatment in Part 6 if surgery isn’t an option</td>
<td></td>
</tr>
</tbody>
</table>

Not all treatment centers provide IORT. Instead, you may receive external radiation, brachytherapy, or both. These treatments can be started soon after surgery.

Pathology and imaging
A pathologist will test the tissue removed during surgery. He or she will assess the current extent of the cancer in removed tissue. Based on test results, a pathologic stage will be assigned.

Before adjuvant treatment, imaging is needed. Imaging can show how well treatment worked.

CT scans of your chest, abdomen, and pelvis are advised.

Systemic treatment
It is very rare but you may be unable to have surgery. Surgery may not be possible because of where the cancer is. Some health issues also exclude surgery. Instead of surgery, you may receive treatment listed in Part 6 excluding FOLFOXIRI.

Adjuvant treatment
After primary treatment, you may receive adjuvant treatment. It is advised unless you had induction.
chemotherapy. It is given to prevent the cancer from returning, especially in distant sites. Start adjuvant treatment as soon as you can for the best results.

Adjuvant treatment consists of chemotherapy. FOLFOX or CAPEOX is preferred. Otherwise, you may receive 5-FU/LV or capecitabine. 5-FU/LV or capecitabine may be a good choice if they worked well for neoadjuvant treatment.

**Guide 8** lists important follow-up care. Follow-up care starts when there are no signs of cancer after surgery. It is also called survivorship care. This care should address your whole health and well-being.

Your cancer doctor and primary doctor should work together to help you. Each doctor can have a role in survivorship. Talk with your doctors about the care you want and need so you get the best plan.

**Cancer tests**
A medical history and physical exam are advised. Get this care every 3 to 6 months for 2 years. If results are normal for 2 years, repeat care 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. Thus, scans of your chest, abdomen, and pelvis are advised. Get these scans every 6 to 12 months for a total of 5 years. CT should be done with both IV and oral contrast.

CT images may be unclear or not possible. In this case, MRI of the abdomen and pelvis with non-contrast CT of the chest is an option. PET/CT is not advised. It may only be considered if CEA rises across more than one test.

Ongoing colonoscopies are also part of follow-up care. You may never have had a total colonoscopy if your rectum 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).

**Side effect care**
You may still have some side effects when follow-up care is started. Ask your cancer doctor how long they may last. Some side effects may appear months or years after treatment has ended. Ask your doctor what’s your chance that you’ll get these late effects.

There may be ways to help relieve side effects. There are medicines and other methods to decrease diarrhea. A medicine called duloxetine may help painful neuropathy. Fatigue may be helped with exercise or methods to conserve energy. It may help to get bone density tests to check for weakened pelvic bones.

Treatment of rectal cancer may cause sexual problems. You may also have problems with passing urine. Your cancer doctor may refer you to a gynecologist or urologist as needed.

**Other care**
It’s important to take care of other health issues besides rectal cancer. Take steps to prevent or detect other diseases early. Such steps can include getting
immunizations like the flu shot. Taking low-dose aspirin may be helpful.

Cancer screening is also important. Get a skin cancer exam. Ladies—learn how to do a breast self-exam. A mammogram may also be needed. Men—it may be time to get screened for prostate cancer.

Start or keep a healthy lifestyle. Limit your alcohol use. Quit smoking. Protect yourself from the sun. Be at a healthy weight. Eat healthfully. Healthy eating includes eating a balanced diet, eating the right amount of food, and drinking enough fluids.

Many people benefit from some exercise. Exercise tones muscles, lowers stress, and improves health. Exercise programs differ between people based on their needs. Talk with your treatment team about which exercises would be best for you.

"After treatment ends, don't fall back into old habits, you've been given a second chance, make up a survivors plan and follow it. Overcome the fear of recurrence by advocating for your health and others.

—Tom
Survivor, Stage III"
Guide 9 lists the treatment options for local recurrences. Local recurrence may occur in the rectum or close to where the rectum was. Options are grouped by whether you can have surgery or not.

If the cancer is small enough, your first treatment may be surgery. Chemoradiation should follow. If the cancer is large, 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.

I had surgery, radiation, chemotherapy, and more surgeries. Obviously, it was not a walk in the park. I met a woman my age who had the same cancer, same treatments and doctors I had, only she was diagnosed 6 months prior to me. Talking with her was extremely beneficial for the both of us.

—Donna
Survivor, Stage III
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 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.

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.

The cancer may return in 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.
5

Treatment guide: Metastatic disease

56 Metastases at diagnosis
63 Metastases at recurrence
65 Review
### Metastatic disease

Part 5 is a treatment guide for rectal cancer that has spread to the liver or lungs but not elsewhere. Treatment options are partly based on whether the metastasis was found at diagnosis or recurrence. Treatment for other metastases is discussed in Part 6.

The spread of cancer to distant sites—metastatic disease—occurs in at least half of people with colorectal cancer. Colorectal cancer most often spreads to the liver. Among every 100 people with colorectal cancer, 20 to 34 people will have liver metastases at diagnosis. Most options for liver metastases also apply to lung metastases.
Metastases at diagnosis

This section explains treatment options for metastases found at diagnosis. These cancers are stage IV. Options for rectal cancer that can be treated with surgery are explained first. However, most people with metastases can’t have surgery. If you can’t have surgery, treatment options are explained on page 60.

Guide 10 presents surgical options for liver or lung metastases at diagnosis. Surgery is only an option if all tumors can be fully removed. In other words, it’s an option if a cure is possible.

Surgery is also only an option if your liver won’t be too small afterward. To enlarge your liver, you may receive portal vein embolization. Portal vein embolization is the blocking of the blood vessel to the liver tumor. This blockage causes the healthy part of the liver to grow larger. This procedure will be done before surgery.

The best treatment approach is unknown. Little research has been done. Thus, five options are given.

Neoadjuvant treatment

All options start with neoadjuvant treatment. This treatment is used to reduce the extent of the cancer. Two to three months of treatment are advised.

Option 1

The first option starts with chemotherapy. FOLFIRI, FOLFOX, or CAPEOX may be received. There are pros and cons to starting with chemotherapy. Some of these are:

Pros

➤ You may receive early treatment of possible cancer not yet found.

➤ Knowing your response to chemotherapy early can help with treatment planning.

➤ If the cancer grows while taking chemotherapy, you can avoid local treatment.

Cons

➤ Fat may build up in your liver and your liver may swell.

➤ You may become unable to have surgery if the cancer grows or shrinks too much.

➤ Injury to small blood vessels may occur in your liver.

Option 2

Option 2 starts with chemotherapy followed by chemoradiation. Chemotherapy is described in Option 1. For chemoradiation, radiation will be given within your pelvis. It may decrease the chance of cancer cells remaining in your pelvis after treatment.

Chemotherapy helps radiation to work better. Infusional 5-FU or capecitabine is preferred. The side effects of these regimens may be too much for you. In this case, bolus 5-FU/LV may be received.
## Guide 10. Surgical options

### Option 1

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOLFIRI, FOLFOX, CAPEOX</td>
<td>Transabdominal resection +</td>
<td>Consider chemoradiation:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infusional 5-FU + pelvic radiation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Capecitabine + pelvic radiation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bolus 5-FU/LV + pelvic radiation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-FU/LV or capecitabine</td>
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</table>

### Option 2

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOLFIRI, FOLFOX, CAPEOX</td>
<td>Infusional 5-FU + radiation</td>
<td>Same as neoadjuvant chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Capecitabine + radiation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bolus 5-FU/LV + radiation</td>
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</table>

### Option 3

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOLFIRI, FOLFOX, CAPEOX</td>
<td>Short-course pelvic radiation for T1–T3 tumors</td>
<td>Same as neoadjuvant chemotherapy</td>
</tr>
</tbody>
</table>

### Option 4

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusional 5-FU + pelvic radiation</td>
<td>Transabdominal resection +</td>
<td>FOLFOX or CAPEOX</td>
</tr>
<tr>
<td>Capecitabine + pelvic radiation</td>
<td>Metastasectomy ± local treatment or Local treatment</td>
<td>5-FU/LV or capecitabine</td>
</tr>
<tr>
<td>Bolus 5-FU/LV + pelvic radiation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Option 5

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-course pelvic radiation therapy for T1–T3 tumors</td>
<td>Transabdominal resection +</td>
<td>FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td>Metastasectomy ± local treatment or Local treatment</td>
<td>5-FU/LV or capecitabine</td>
</tr>
</tbody>
</table>
5 Metastatic disease

Option 3
Option 3 starts with chemotherapy followed by short-course radiation. This option is only for rectal cancers with T1, T2, or T3 tumors.

Some results of a short radiation course are equal to a long course. It works well in treating rectal cancer within and near the rectum. It also extends life as much as a long course.

Your treatment team should discuss if this is an option for you. One factor to discuss is the extent of cancer. Some cancers do not shrink enough for surgery during a short course. Another factor is the side effects of short-course radiation.

Option 4
Option 4 starts with chemoradiation. Chemotherapy by itself is not received at this time. Chemoradiation is described under Option 2.

Option 5
Option 5 starts with short-course radiation. Chemotherapy is not received at this time. Short-course radiation is described under Option 3.

Imaging
After neoadjuvant treatment, the extent of the cancer will be assessed. This assessment helps to plan the best surgical method. Imaging tests will be used. The most commonly used tests are MRI, CT, and EUS. There may be a clinical trial of other imaging tests that you may join.

Primary treatment
Primary treatment is the main method used to rid your body of cancer. Surgery is often used. Surgery should occur as soon as possible after chemotherapy. After short-course radiation, surgery can occur within 1 to 2 weeks.

Surgery
A transabdominal resection is advised. A metastasectomy may also be done to remove the distant cancer. Both surgeries can be done during one operation. They can also be done apart in two operations.

Local treatment
Local treatment to the liver or lung may be added to surgery. Another option is local treatment instead of metastasectomy. However, NCCN experts prefer metastasectomy over local treatment. Local treatment includes ablation and SBRT.

Radiation therapy
Radiation during surgery (IORT) within the pelvis may be an option. It is sometimes used if cancer is in the surgical margin. It is also used as a boost for T4 and recurrent cancers.

Not all treatment centers provide IORT. Instead, you may receive external radiation, brachytherapy, or both. These treatments can be started soon after surgery. Don’t start adjuvant treatment until radiation is finished.

Pathology and imaging
A pathologist will test the tissue removed during surgery. He or she will assess the current extent of the cancer in removed tissue. Based on test results, a pathologic stage will be assigned.

Before adjuvant treatment, imaging is needed. Imaging can show how well treatment worked. CT scans of your chest, abdomen, and pelvis are advised.
5 Metastatic disease

Adjuvant treatment
After primary treatment, you may receive adjuvant treatment. It is given to prevent the cancer from returning, especially in distant sites. Start adjuvant treatment as soon as you can for the best results.

Adjuvant treatment consists of chemotherapy. FOLFOX or CAPEOX is preferred. Otherwise, you may receive 5-FU/LV or capecitabine. 5-FU/LV and capecitabine may be a good choice if they worked well for neoadjuvant treatment.

Option 1
Option 1 may end with chemoradiation. Your doctor may advise this treatment based on your test results. Infusional 5-FU or capecitabine is preferred. However, bolus 5-FU/LV may be received instead.

Options 2 and 3
Options 2 and 3 end with chemotherapy. Adjuvant chemotherapy should consist of the same regimen as for neoadjuvant chemotherapy. This regimen is likely to work well if it did before.

Options 4 and 5
Options 4 and 5 also end with chemotherapy. FOLFOX or CAPEOX is preferred. Otherwise, you may receive 5-FU/LV or capecitabine.
Guide 11 lists nonsurgical options for liver or lung metastases present at diagnosis. Options are grouped by whether cancer symptoms are present or not.

Symptoms absent
Systemic treatment may be an option. The goal of treatment is to slow down the growth of the cancer. If treatment works, symptoms may be prevented or delayed. Part 6 contains lists of chemotherapy that may be received. Targeted therapy may be added.

For some people, chemotherapy may greatly shrink the cancer. If it shrinks enough, surgery to cure the cancer may be an option. Most people with metastatic rectal cancer won’t be able to have surgery. Surgery is unlikely if there is widespread cancer in your liver or lung. If surgery is possible, tests to assess the tumor size are advised every two months during chemotherapy.

If taking bevacizumab, it should be stopped 6 weeks before surgery. It increases your chance for a stroke, bleeding, and other arterial events. These events are even more likely if you are older than 65 years. Bevacizumab can be re-started 6 to 8 weeks after surgery. Otherwise, it can slow healing.

Surgery should occur as soon as possible after chemotherapy. After surgery, you may receive more chemotherapy. Chemotherapy received before and after surgery should not exceed 6 months. Targeted therapy may be added.

Symptoms present
There are treatments for a number of symptoms. Systemic treatment may improve symptoms within 1 to 2 weeks. Likewise, chemoradiation may relieve symptoms within the pelvis. Infusional 5-FU or capecitabine is preferred. The side effects of these regimens may be too much for you. In this case, bolus 5-FU/LV may be received.

The tumor may have grown so large that it blocks the flow of stool. Surgery to remove the part of the rectum with cancer may be an option. Surgery may also stop bleeding.

Other options to unblock the rectum are a diversion and stent. A diversion is a type of surgery. It attaches the colon to the surface of the abdomen, and a “bag” is needed. A stent is a wire mesh tube. It is placed in the rectum to allow stool to pass.

Short-course radiation may downsize the rectal cancer. This option is only for rectal cancers with T1, T2, or T3 tumors. Your treatment team should discuss if this is an option for you. Factors to discuss are the extent of cancer and side effects of short-course radiation.

After treatment for symptoms, systemic treatment is advised. Part 6 contains lists of chemotherapy that may be received. Targeted therapy may be added.

Guide 12 lists important follow-up care for stage IV cancer. Follow-up care starts when there are no signs of cancer after surgery. It is also called survivorship care. This care should address your whole health and well-being.

Your cancer doctor and primary doctor should work together to help you. Each doctor can have a role in survivorship. Talk with your doctors about the care you want and need so you get the best plan.

Cancer tests
A medical history and physical exam are advised. Get this care every 3 to 6 months for 2 years. If results are normal for 2 years, repeat care 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.
Guide 11. Nonsurgical treatment

<table>
<thead>
<tr>
<th>Symptom status</th>
<th>What are the options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>The cancer isn’t causing symptoms</td>
<td>• Systemic treatment listed in Part 6</td>
</tr>
<tr>
<td>The cancer is causing symptoms</td>
<td>• Systemic treatment listed in Part 6</td>
</tr>
<tr>
<td></td>
<td>• Infusional 5-FU + radiation</td>
</tr>
<tr>
<td></td>
<td>• Bolus 5-FU + radiation</td>
</tr>
<tr>
<td></td>
<td>• Capecitabine + radiation</td>
</tr>
<tr>
<td></td>
<td>• Rectal surgery</td>
</tr>
<tr>
<td></td>
<td>• Diverting ostomy</td>
</tr>
<tr>
<td></td>
<td>• Stent</td>
</tr>
<tr>
<td></td>
<td>• Short-course radiation for T1–T3 tumors</td>
</tr>
</tbody>
</table>

Guide 12. Follow-up care

<table>
<thead>
<tr>
<th>Type of care</th>
<th>How often is this care needed?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical history and physical exam</td>
<td>• Every 3–6 months for 2 years</td>
</tr>
<tr>
<td></td>
<td>▪ If normal, then repeat every 6 months for 3 years</td>
</tr>
<tr>
<td>CEA blood test</td>
<td>• Every 3–6 months for 2 years</td>
</tr>
<tr>
<td></td>
<td>▪ If normal, then repeat every 6 months for 3 years</td>
</tr>
<tr>
<td>CT of chest, abdomen, pelvis</td>
<td>• Every 3–6 months for 2 years</td>
</tr>
<tr>
<td></td>
<td>▪ If normal, then repeat every 6–12 months for 3 years</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>• If no prior total colonoscopy, 3–6 months after treatment</td>
</tr>
<tr>
<td></td>
<td>▪ If prior total colonoscopy, 1 year after treatment</td>
</tr>
<tr>
<td></td>
<td>▪ If no advanced adenoma, repeat in 3 years</td>
</tr>
<tr>
<td></td>
<td>▪ If results are normal, then repeat every 5 years</td>
</tr>
<tr>
<td></td>
<td>▪ If advanced adenoma, repeat in 1 year</td>
</tr>
<tr>
<td>Side effect care</td>
<td>• As needed</td>
</tr>
<tr>
<td>Prevent and screen for other diseases</td>
<td>• Follow guidelines</td>
</tr>
<tr>
<td>Help for healthy lifestyle</td>
<td>• As needed</td>
</tr>
</tbody>
</table>
CT scans may help find metastases. Thus, scans of your chest, abdomen, and pelvis are advised. Get these scans every 3 to 6 months for 2 years. If results are normal, then get a scan every 6 to 12 months for another 3 years. CT should be done with both IV and oral contrast.

CT images may be unclear or not possible. In this case, MRI of the abdomen and pelvis with non-contrast CT of the chest is an option. PET/CT is not advised. It may only be considered if CEA rises across more than one test.

Ongoing colonoscopies are also part of follow-up care. You may never have had a total colonoscopy if your rectum 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).

**Side effect care**
You may still have some side effects when follow-up care is started. Ask your cancer doctor how long they may last. Some side effects may appear months or years after treatment has ended. Ask your doctor what’s your chance that you’ll get these late effects.

There may be ways to help relieve side effects. There are medicines and other methods to decrease diarrhea. A medicine called duloxetine may help painful neuropathy. Fatigue may be helped with exercise or methods to conserve energy. It may help to get bone density tests to check for weakened pelvic bones.

Treatment of rectal cancer may cause sexual problems. You may also having problems with passing urine. Your cancer doctor may refer you to a gynecologist or urologist as needed.

**Other care**
It’s important to take care of other health issues besides rectal cancer. Take steps to prevent or detect other diseases early. Such steps can include getting immunizations like the flu shot. Taking low-dose aspirin may be helpful.

Cancer screening is also important. Get a skin cancer exam. Ladies—learn how to do a breast self-exam. A mammogram may also be needed. Men—it may be time to get screened for prostate cancer.

Start or keep a healthy lifestyle. Limit your alcohol use. Quit smoking. Protect yourself from the sun. Be at a healthy weight. Eat healthfully. Healthy eating includes eating a balanced diet, eating the right amount of food, and drinking enough fluids.

Many people benefit from some exercise. Exercise tones muscles, lowers stress, and improves health. Exercise programs differ between people based on their needs. Talk with your treatment team about which exercises would be best for you.
Metastases at recurrence

This section explains treatment options for rectal cancer that returns in the liver or lungs. Options for rectal cancer that can be treated with surgery are explained first. However, most people with metastases can’t have surgery. If you can’t have surgery, treatment options are explained on page 65.

Guide 13 presents surgical options for liver or lung metastases at recurrence. Surgery is only an option if all tumors can be fully removed. In other words, it’s an option if a cure is possible.

Surgery is also only an option if your liver won’t be too small afterward. To enlarge your liver, you may receive portal vein embolization. Portal vein embolization is the blocking of the blood vessel to the liver tumor. This blockage causes the healthy part of the liver to grow larger. This procedure will be done before surgery.

Surgery with chemotherapy is advised for metastases. The best order of chemotherapy and surgery is unknown. Thus, two options are given.

Option 1

Option 1 starts with primary treatment. It may consist of metastasectomy. Local treatment to the liver or lung may be added. Local treatment includes ablation and SBRT. Local treatment without surgery is also an option. However, NCCN experts prefer surgery over local treatment.

Results of primary treatment should be assessed with CT with contrast. Scans of your chest, abdomen,

Guide 13. Surgical options

Option 1

<table>
<thead>
<tr>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Metastasectomy ± local treatment</td>
<td>• No prior chemotherapy</td>
</tr>
<tr>
<td>• Local treatment</td>
<td>◦ FOLFOX or CAPEOX</td>
</tr>
<tr>
<td></td>
<td>◦ Capecitabine or 5-FU/LV</td>
</tr>
<tr>
<td></td>
<td>• Prior chemotherapy</td>
</tr>
<tr>
<td></td>
<td>◦ Observation</td>
</tr>
<tr>
<td></td>
<td>◦ Chemotherapy ± targeted therapy in Part 6</td>
</tr>
</tbody>
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Option 2

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FOLFOX or CAPEOX</td>
<td>• Metastasectomy</td>
<td>• If neoadjuvant worked:</td>
</tr>
<tr>
<td>• FLOX or capecitabine</td>
<td>± local treatment</td>
<td>◦ Re-start neoadjuvant regimen</td>
</tr>
<tr>
<td>or 5-FU/LV</td>
<td>• Local treatment</td>
<td>◦ FOLFOX</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Observation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If neoadjuvant didn’t work:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Chemotherapy ± targeted therapy in Part 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Observation</td>
</tr>
</tbody>
</table>
and pelvis are needed. Imaging should be done prior to adjuvant treatment.

Adjuvant treatment is based on whether you had chemotherapy before. If not, preferred options are FOLFOX and CAPEOX. Otherwise, you may receive FLOX, capecitabine, or 5-FU/LV. Six months of chemotherapy is preferred.

If you’ve had chemotherapy, observation is an option. Observation is a period of testing to assess for cancer growth. Another option is chemotherapy. Targeted therapy may be added but more research is needed. Regimens are listed in Part 6. Six months of chemotherapy is preferred.

**Option 2**

Option 2 starts with neoadjuvant chemotherapy. FOLFOX and CAPEOX are preferred regimens. FLOX, capecitabine, or 5-FU/LV are other options.

After 2 to 3 months of chemotherapy, you may receive primary treatment. One option is a metastasectomy. Local treatment may be added. It includes ablation and SBRT. Local treatment without surgery is another option. However, NCCN experts prefer surgery over local treatment alone.

Results of primary treatment should be assessed with CT with contrast. Scans of your chest, abdomen, and pelvis are needed. Imaging should be done prior to adjuvant treatment.

Adjuvant treatment is based on the success of neoadjuvant treatment. If neoadjuvant chemotherapy worked, you may re-start that treatment or take FOLFOX. Together, chemotherapy given before and after surgery should not exceed 6 months. A third option is observation.

If neoadjuvant treatment didn’t work, you may have two options. One option is chemotherapy. Targeted therapy may be added but more research is needed. Regimens are listed in Part 6. Six months of chemotherapy is preferred. The second option is observation.

**HAI ± 5-FU/LV**

Instead of systemic chemotherapy after surgery, HAI may be an option. Systemic 5-FU/LV may be added. NCCN experts advise that this option should only be received at treatment centers with much experience in this method. More research is needed to learn how well this treatment works.

**Guide 14** lists nonsurgical options for liver or lung metastases present at recurrence. Options are based on your history of chemotherapy. Options for people who had FOLFOX or CAPEOX in the past 12 months are explained below. Options for everyone else are listed in Part 6.

**FOLFOX or CAPEOX ≤12 months**

Two options are FOLFIRI and irinotecan. Targeted therapy may be added. Bevacizumab is preferred but other options are ziv-aflibercept or ramucirumab. If the tumor has normal RAS genes, other options are to add panitumumab or cetuximab to chemotherapy. However, these drugs won’t likely work if the tumor has a **BRAF V600E** mutation.

The cancer cells may have a dMMR system or MSI-H. The MMR system is explained in Part 2. In this case, nivolumab or pembrolizumab is an option.

**After chemotherapy**

Chemotherapy may greatly shrink the tumors. If they shrink enough, surgery to cure the cancer may be an option. However, this doesn't happen often. If surgery is possible, tests to assess the tumor size are advised every two months during chemotherapy.

Bevacizumab should be stopped 6 weeks before surgery. It will increase your chance for a stroke, bleeding, and other arterial events. These events are even more likely if you are older than 65 years.

<table>
<thead>
<tr>
<th>Chemotherapy history</th>
<th>What are the options?</th>
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</table>
| Adjuvant FOLFOX or CAPEOX ≤12 months ago | • FOLFIRI ± bevacizumab or ziv-aflibercept or ramucirumab  
• Irinotecan ± bevacizumab or ziv-aflibercept or ramucirumab  
• If normal KRAS/NRAS gene:  
  ◦ FOLFIRI + panitumumab or cetuximab  
  ◦ Irinotecan + panitumumab or cetuximab  
• If dMMR or MSI-H:  
  ◦ Nivolumab  
  ◦ Pembrolizumab |
| Adjuvant FOLFOX or CAPEOX >12 months ago | • Treatments listed in Part 6 |
| Prior 5-FU/LV or capecitabine            | • Treatments listed in Part 6 |
| Never had chemotherapy                  | • Treatments listed in Part 6 |

Bevacizumab can be re-started 6 to 8 weeks after surgery. Otherwise, it can slow healing.

After surgery, more chemotherapy is an option. Observation may be an option, too. Chemotherapy received before and after surgery should not exceed 6 months. Targeted therapy may be added but more research is needed. Read Part 6 for options.

**HAI ± 5-FU/LV**
Instead of systemic chemotherapy after surgery, HAI may be an option. Systemic 5-FU/LV may be added. NCCN experts advise that this option should only be received at treatment centers with much experience in this method. More research is needed to learn how well this treatment works.

**Review**

- Cancer in distant sites is called a metastasis. Rectal cancer most often spreads to the liver and sometimes the lungs.
- Metastases may be present when you first learn that you have rectal cancer. Metastases may also occur if the cancer re-appears during follow-up care.
- Some rectal cancers with metastases can be treated with surgery. Local treatment 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.
## 6 Chemotherapy

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Chemotherapy

Part 6 presents the chemotherapy pathways used to treat advanced rectal cancer. There are many options. If one option doesn’t work or stops working, another option is given.

Oxaliplatin

Guide 15 maps a treatment path that starts with oxaliplatin. After oxaliplatin, there are other options for second-line treatment and beyond. Some of these options depend on what treatment you’ve had before.

First-line options
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 RAS genes. However, neither is likely to work if a BRAF V600E mutation is present.

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
Oxaliplatin may not prevent the cancer from progressing. If this happens, you may start FOLFIRI or irinotecan. Bevacizumab, ziv-aflibercept, or ramucirumab may be added. Bevacizumab is preferred due to less harsh side effects and lower costs.

Cetuximab or panitumumab may be options for tumors with normal RAS genes. You must not have received either drug before. Either drug may be added to FOLFIRI or irinotecan. If you can’t take irinotecan, either drug can be used alone.

Guide 15. Oxaliplatin pathway

What are first-line options?
- FOLFOX ±
  - Bevacizumab
  - Cetuximab or panitumumab for tumors with normal KRAS/NRAS genes
- CAPEOX ± bevacizumab

What are second-line options?
- FOLFIRI or irinotecan ±
  - Bevacizumab or ziv-aflibercept or ramucirumab
  - Cetuximab or panitumumab 1) for tumors with normal KRAS/NRAS genes and 2) if neither drug was received before
- Cetuximab or panitumumab 1) for tumors with normal KRAS/NRAS genes and 2) if neither drug was received before
- Pembrolizumab or nivolumab if dMMR or MSI-H

What are third-line and beyond options?
- Some second-line regimens if not received before
- Regorafenib
- Trifluridine + tipiracil
- Clinical trial
- Best supportive care
Irinotecan

Guide 16 maps a treatment path that starts with FOLFIRI. After FOLFIRI, there are other options for second-line treatment and beyond. Some of these options depend on what treatment you’ve had before.

**First-line options**

Irinotecan is part of the FOLFIRI regimen. It should be used with caution and at a low dose if you have Gilbert’s disease. Gilbert’s disease is a health problem that people are born with. The disease impairs the liver from correctly processing bilirubin. Irinotecan should be used with caution and at a low dose if you have high bilirubin levels in your blood for any reason.

Targeted therapy may be added to FOLFIRI. Bevacizumab may help treat rectal cancer. Cetuximab or panitumumab may help treat tumors with normal RAS genes. However, neither is likely to work if a BRAF V600E mutation is present.

**Second-line options**

FOLFIRI may not prevent the cancer from progressing. If this happens, you may start to take an oxaliplatin regimen—FOLFOX or CAPEOX. Bevacizumab may be added.

Cetuximab or panitumumab may be options for tumors with normal RAS genes. You must not have received either drug before. Either drug may be added to irinotecan. If you can’t take irinotecan, either drug can be used alone.

The cancer cells may have a dMMR system or MSI-H. The MMR system is explained in Part 2. In this case, nivolumab or pembrolizumab may be an option. If these drugs don’t work, your next options include other second-line options listed above.

**Third-line and beyond**

If the cancer progresses again, one of the 4 second-line treatments may be an option. If not, your options may include regorafenib or trifluridine with tipiracil. There may also be a clinical trial that you could join. Supportive care may give you relief from symptoms.

**Guide 16. Irinotecan pathway**

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<tr>
<td>• FOLFIRI ±</td>
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<td>◦ Bevacizumab</td>
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<tr>
<td>◦ Cetuximab or panitumumab for tumors with normal KRAS/NRAS genes</td>
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<th>What are second-line options?</th>
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<td>• FOLFOX or CAPEOX ± bevacizumab</td>
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<tr>
<td>• Irinotecan + cetuximab or panitumumab 1) for tumors with normal KRAS/NRAS genes and 2) if neither drug was received before</td>
</tr>
<tr>
<td>• Cetuximab or panitumumab 1) for tumors with normal KRAS/NRAS genes and 2) if neither drug was received before</td>
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<tr>
<td>• Pembrolizumab or nivolumab if dMMR or MSI-H</td>
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<td>• Some second-line regimens if not received before</td>
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<td>• Regorafenib</td>
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<td>• Trifluridine + tipiracil</td>
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<td>• Clinical trial</td>
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<tr>
<td>• Best supportive care</td>
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FOLFOXIRI

Guide 17 maps a treatment path that starts with FOLFOXIRI. After FOLFOXIRI, there are other options for second-line treatment and beyond. Some of these options depend on what treatment you’ve had before.

First-line options
The FOLFOXIRI pathway starts with both oxaliplatin and irinotecan. It is an intense regimen and is not for everybody. It is not advised for stage II or III cancers. Bevacizumab may be added.

Second-line options
FOLFOXIRI may not prevent the cancer from progressing. In this happens, there are 5 second-line options. Some options do not apply to everyone.

Cetuximab or panitumumab may be options for tumors with normal RAS genes. However, neither are likely to work if a BRAF V600E mutation is present. Either drug may be received with irinotecan. If you’re unable to take irinotecan, either drug may be used alone.

The cancer cells may have a dMMR system or MSI-H. The MMR system is explained in Part 2. In this case, nivolumab or pembrolizumab may be an option. If these drugs don’t work, your next options include other second-line options.

There are two other options if the cancer has progressed on all other regimens. One option is to receive regorafenib. The other option is trifluridine with tipiracil.

Third-line and beyond
If the cancer progresses again, one of the second-line treatments may be an option. If not, there may be a clinical trial that you could join. Supportive care may give you relief from symptoms.

Guide 17. FOLFOXIRI pathway

What are first-line options?
- FOLFOXIRI ± bevacizumab

What are second-line options?
- Irinotecan + cetuximab or panitumumab for tumors with normal KRAS/NRAS genes
- Cetuximab or panitumumab for tumors with normal KRAS/NRAS genes
- Pembrolizumab or nivolumab if dMMR or MSI-H
- Regorafenib
- Trifluridine + tipiracil

What are third-line and beyond options?
- Some second-line regimens if not received before
- Clinical trial
- Best supportive care
5-FU and capecitabine

There are two other options if the cancer has progressed on all other regimens. One option is to receive regorafenib. The other option is trifluridine with tipiracil.

Joining a clinical trial may be an option. Ask your doctor if there is a trial that is right for you. If there are no other options, supportive care may give you relief from symptoms.

First-line options
There are two options for first-line treatment. One option is 5-FU/LV. Receiving 5-FU by infusion is preferred over bolus injection. The second option is capecitabine. Bevacizumab may be added to either option.

The side effects of these regimens aren’t usually as bad as those caused by oxaliplatin or irinotecan. Thus, 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, options include regimens with oxaliplatin, irinotecan, or both. Targeted therapy may be added. Bevacizumab is preferred over ziv-aflibercept and ramucirumab.

The cancer cells may have a dMMR system or MSI-H. The MMR system is explained in Part 2. In this case, nivolumab or pembrolizumab may be an option. If these drugs don’t work, your next options include other second-line options listed above.

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.

Cetuximab or panitumumab may be options for tumors with normal RAS genes. You must not have received either drug before. Either drug added to irinotecan may be an option. If you can’t take irinotecan, either drug can be used alone.

What are first-line options?
- 5-FU/LV ± bevacizumab
- Capecitabine ± bevacizumab

What are second-line options?
- FOLFOX or CAPEOX ± bevacizumab
- FOLFIRI or irinotecan ± bevacizumab or ziv-aflibercept or ramucirumab
- Irinotecan + oxaliplatin ± bevacizumab
- Pembrolizumab or nivolumab if dMMR or MSI-H

What are third-line and beyond options?
- Some second-line regimens if not received before
- Irinotecan + cetuximab or panitumumab for tumors with normal KRAS/NRAS genes
- Cetuximab or panitumumab for tumors with normal KRAS/NRAS genes
- Regorafenib
- Trifluridine + tipiracil
- Clinical trial
- Best supportive care
Least toxic regimens

Guide 19 lists regimens that are likely to be the least harmful to you. Infusional 5-FU/LV is an option. 5-FU has fewer severe side effects when given by infusion rather than bolus. Another option is to take capecitabine with or without bevacizumab.

Cetuximab or panitumumab may be an option. These drugs treat tumors with normal RAS genes. Neither drug is likely to work if a BRAF V600E mutation is present.

The cancer cells may have a dMMR system or MSI-H. The MMR system is explained in Part 2. In this case, nivolumab or pembrolizumab may be an option.

If first-line treatment works, you may find that you are able to do more activities. In this case, the regimens listed in the prior sections may be options. If first-line drugs don’t work, supportive care may give you relief from symptoms.

Guide 19. Least toxic pathway

What are first-line options?

- Infusional 5-FU/LV ± bevacizumab
- Capecitabine ± bevacizumab
- Cetuximab or panitumumab for tumors with normal KRAS/NRAS genes
- Pembrolizumab or nivolumab if dMMR or MSI-H

What are second-line options?

- More intense chemotherapy
- Supportive care

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.
Making treatment decisions

- 73 It’s your choice
- 73 Questions to ask your doctors
- 78 Deciding between options
- 79 Websites
- 79 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. Part 7 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 listed on the following pages.

"I did attend an ostomy support group during my treatments, which was helpful. These were people who knew exactly what I was going through since some of them were rectal cancer survivors."

—Donna
Survivor, Stage III
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?
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 rectal cancer. Find a support group at the websites listed on page 79.

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.

I was not ready for a permanent ostomy and my second opinion guaranteed me a reversal after resection of my very low lying rectal tumor. I will be forever grateful that I took the time to get a second opinion. Seek out those that point the compass in the direction that brings you peace and consolation.

–Marra
Survivor, Stage III
Websites

American Cancer Society
cancer.org/cancer/colonandrectumcancer/detailedguide/index

Cancer Support Community
cancersupportcommunity.org

Colon Cancer Alliance
calliance.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

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

81 Dictionary
85 Acronyms
abdomen
The belly area between the chest and pelvis.

abdominoperineal resection
An operation that removes your rectum, anus, and part of your colon.

ablation
Treatment using radiofrequency or cold to destroy cancer cells.

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

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

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

adventitia
The outer layer, in some places, of the rectal wall.

angiolymphatic invasion
Cancer has spread into the tumor’s lymph or blood vessels.

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

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

bolus
A fast injection of a drug.

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

brachytherapy
Treatment with radiation received from an object placed near or in the tumor.

cancer grade
How closely the cancer cells look like normal cells.

cancer stage
Rating of the growth and spread of tumors.

carcinoembryonic antigen (CEA)
A protein that gets released by some tumors and can be detected in blood as a tumor marker.

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

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

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

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

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

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

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

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

complete blood count (CBC)
A test of the number of blood cells.

computed tomography (CT)
A test that uses x-rays from many angles to make a picture of the inside of the body.

contrast
A dye put into your body to make clearer pictures during imaging tests.
defective mismatch repair (dMMR)
Abnormal changes in genes that contain instructions for making proteins that fix errors in DNA.

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.

epidermal growth factor receptor (EGFR)
A protein on the edge of a cell that sends signals for the cell to grow.

epithelium
Tissue that lines the colorectal 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 colorectal cancer.

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

general anesthesia
A controlled loss of wakefulness from drugs.

hereditary non-polyposis rectal cancer (HNPPC)
An inherited medical condition that increases the odds of colorectal cancer. Also called Lynch syndrome.

histologic typing
The study of cells to classify disease.

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

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

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

immunohistochemistry (IHC)
A lab test of cancer cells to find specific cell traits involved in abnormal cell growth.

inflammatory bowel disease
A medical condition that causes the intestine to swell.

inflammatory polyp
A polyp that often grows after the intestine swells.

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

intensity-modulated radiation therapy (IMRT)
Radiation therapy that uses small beams of different strengths based on the thickness of the tissue.

intraoperative radiation therapy (IORT)
Radiation therapy that is given inside the body at the end of an operation.

invasive cancer
Cancer cells have grown into the second layer of the 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.

low anterior resection
An operation that removes your rectum and part of your colon.
**lymph**
A clear fluid containing white blood cells.

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

**magnetic resonance imaging (MRI)**
A test that uses a magnetic field and radio waves to make pictures of the insides of the body.

**medical history**
All health events and medications taken to date.

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

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

**microsatellite instability (MSI)**
Errors in a small DNA part that happen when DNA is making a copy of itself.

**microsatellite instability-high (MSI-H)**
The presence of 2 or more MSI markers.

**mismatch repair (MMR) proteins**
Proteins that correct DNA errors that occur when copies of DNA are being made.

**mucosa**
The first, inner layer of the rectal wall.

**mucus**
a sticky, thick liquid that moisturizes or lubricates.

**muscularis mucosae**
A thin layer of muscle within the mucosa of the rectal wall.

**muscularis propria**
The third layer of the rectal wall made mostly of muscle.

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

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

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

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

**observation**
A period of testing for cancer growth.

**parietal peritoneum**
The outer layer of tissue lining around the abdomen.

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

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

**pedunculated polyp**
A polyp shaped like a mushroom with a stalk.

**pelvis**
The area between the hip bones.

**perineural invasion**
Spread of cancer into nearby nerves.

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

**polymerase chain reaction (PCR)**
A process in which copies of a DNA part are made.

**polyp**
An extra growth of tissue from the epithelium of the rectal wall.

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

**positron emission tomography (PET)**
Use of radioactive material to see the shape and function of body parts.

**positron emission tomography/computed tomography (PET/CT)**
A test that uses radioactive material and x-rays to view the shape and function of organs and tissues.
primary tumor
The first mass of cancer cells in the body.

prognosis
The pattern and outcome of a disease.

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

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

radiologist
A doctor who specializes in reading imaging tests.

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

recurrence
The return of cancer after a cancer-free period.

serosa
The outer covering, in some places, of the rectal wall; also called the visceral peritoneum.

sessile polyp
A polyp that is flat.

side effect
An unplanned physical or emotional response to treatment.

small intestine
The digestive organ that absorbs nutrients from eaten food.

stereotactic body radiation therapy (SBRT)
Radiation therapy that uses precise, high-dose beams.

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

submucosa
The second layer of the rectal wall made mostly of connective tissue.

subserosa
A thin layer of connective tissue that makes fluid.

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

surface receptor
A protein found in the membrane of cells.

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

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

three-dimensional conformal radiation therapy (3D-CRT)
Radiation therapy that uses beams that match the shape of the tumor.

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

total mesorectal excision
An operation that removes your rectum and nearby tissue in one piece.

transabdominal excision
An operation that removes tissue through cuts into the abdomen.

transanal excision
An operation that removes tissue through the anus.

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

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

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

vascular endothelial growth factor (VEGF)
A molecule that binds to cells that form blood vessels.

villous polyp
A polyp with a ruffled structure.
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D-CRT</td>
<td>three-dimensional conformal radiation therapy</td>
</tr>
<tr>
<td>AJCC</td>
<td>American Joint Committee on Cancer</td>
</tr>
<tr>
<td>APR</td>
<td>abdominoperineal resection</td>
</tr>
<tr>
<td>CAM</td>
<td>complementary and alternative medicine</td>
</tr>
<tr>
<td>CBC</td>
<td>complete blood count</td>
</tr>
<tr>
<td>CEA</td>
<td>carcinoembryonic antigen</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>dMMR</td>
<td>defective mismatch repair</td>
</tr>
<tr>
<td>DNA</td>
<td>deoxyribonucleic acid</td>
</tr>
<tr>
<td>EBRT</td>
<td>external beam radiation therapy</td>
</tr>
<tr>
<td>EGF</td>
<td>epidermal growth factor</td>
</tr>
<tr>
<td>EGFR</td>
<td>epidermal growth factor receptor</td>
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<tr>
<td>FAP</td>
<td>familial adenomatous polyposis</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>HAI</td>
<td>hepatic arterial infusion</td>
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<tr>
<td>HNPCC</td>
<td>hereditary non-polyposis colon cancer</td>
</tr>
<tr>
<td>IHC</td>
<td>immunohistochemistry</td>
</tr>
<tr>
<td>IMRT</td>
<td>intensity-modulated radiation therapy</td>
</tr>
<tr>
<td>IORT</td>
<td>intraoperative radiation therapy</td>
</tr>
<tr>
<td>LAR</td>
<td>low anterior resection</td>
</tr>
<tr>
<td>LINAC</td>
<td>linear accelerator</td>
</tr>
<tr>
<td>MMR</td>
<td>mismatch repair</td>
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<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
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<tr>
<td>MSI</td>
<td>microsatellite instability</td>
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<tr>
<td>MSI-H</td>
<td>microsatellite instability-high</td>
</tr>
<tr>
<td>MSI-L</td>
<td>microsatellite instability-low</td>
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<tr>
<td>MSS</td>
<td>microsatellite stable</td>
</tr>
<tr>
<td>NCCN</td>
<td>National Comprehensive Cancer Network</td>
</tr>
<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
</tr>
<tr>
<td>PET</td>
<td>positron emission tomography</td>
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<tr>
<td>PET/CT</td>
<td>positron emission tomography/computed tomography</td>
</tr>
<tr>
<td>SBRT</td>
<td>stereotactic body radiation therapy</td>
</tr>
<tr>
<td>TME</td>
<td>total mesorectal excision</td>
</tr>
<tr>
<td>VEGF</td>
<td>vascular endothelial growth factor</td>
</tr>
</tbody>
</table>
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case.edu/cancer

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206.667.5000 • fredhutch.org

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hopkinskimmelcancercenter.org

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

Mayo Clinic Cancer Center
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Jacksonville, Florida
Rochester, Minnesota
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904.953.0853 • Florida
507.538.3270 • Minnesota
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Moffitt Cancer Center
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moffitt.org

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

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Memphis, Tennessee
888.226.4343 • sjude.org
901.683.0055 • westclinic.com

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cancer.stanford.edu

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coloradothecancercenter.org

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mcanter.org

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mdanderson.org

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uwhealth.org/cancer

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