Colon Cancer
Colon Cancer

Learning that you have colon 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 colon cancer.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 26 of the world’s leading cancer centers. Experts from NCCN® have written treatment guidelines for doctors who treat colon cancer. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of colon cancer. NCCN also offers patient books on esophageal cancer, ovarian cancer, and many other cancer types. Visit NCCN.org/patients for the full library of patient books as well as other resources.
NCCN aims to improve the care given to patients with cancer. NCCN staff work with experts to create helpful programs and resources for many stakeholders. Stakeholders include health providers, patients, businesses, and others. One resource is the series of books for patients called the NCCN Patient Guidelines®. Each book presents the best practice for a type of cancer.

The patient books are based on clinical practice guidelines written for cancer doctors. These guidelines are called the NCCN Guidelines®. Clinical practice guidelines list the best health care options for groups of patients. Many doctors use them to help plan cancer treatment for their patients.

Panels of experts create the NCCN Guidelines. Most of the experts are from NCCN Member Institutions. Panelists may include pathologists, radiologists, gastroenterologists, surgeons, radiation oncologists, medical oncologists, and patient advocates. 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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The NCCN Foundation supports the mission of the National Comprehensive Cancer Network® (NCCN®) to improve the care of patients with cancer. One of its aims is to raise funds to create a library of books for patients. Learn more about the NCCN Foundation at NCCN.org/foundation.

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Who should read this book?

This book is about treatment for adenocarcinoma of the colon. It does not discuss rectal cancer. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with your doctors what care is best. As you read through this book, you may find it helpful to make a list of questions to ask your doctors.

Where should I start reading?

Starting with Part 1 may be helpful for many people. It explains what colon cancer is. Parts 2 and 3 cover cancer staging and tests that help doctors plan treatment. An overview of treatments used for colon cancer is presented in Part 4. Parts 5 through 7 are treatment guides. Part 5 presents treatment options for when you are first diagnosed with colon cancer. Part 6 presents options for if the cancer returns after prior treatment. Part 7 lists treatment pathways for colon cancers that can’t be treated with surgery. Part 8 offers some helpful tips on getting the best care.

Does the whole book apply to me?

There is important information in this book for many situations. Thus, you will likely not get every test and treatment listed. Your treatment team can point out what applies to you and give you more information.

The recommendations in this book include what NCCN experts feel is the most useful based on science and their experience. However, these recommendations may not be right for you. Your doctors may suggest other tests or treatments based on your health and other factors. If your treatment team suggests other tests or treatments, feel free to ask them why.

Making sense of medical terms

In this book, many medical words are included that describe cancer, tests, and treatments. These are words that you will likely hear from your treatment team. Most of the information may be new to you, and it may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Don’t be shy to 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. Words in the Dictionary are underlined when first used on a page.

Acronyms are also defined when first used and in the Glossary. Acronyms are words formed from the first letters of other words. One example is FAP for familial adenomatous polyposis.
Colon cancer basics
What is the colon?

**Large intestine**
The digestive system breaks down food for the body to use. After being swallowed, food moves through four organs known as the digestive tract as shown in Figure 1.1. First, food passes through the esophagus and into the stomach. The stomach turns solid food into a liquid. From the stomach, food enters the small intestine where food is broken down into very small parts and nutrients are absorbed into the bloodstream.

After the small intestine, food moves into the large intestine. The large intestine changes unused food from a liquid into a solid form by absorbing water. This solid, unused food is called feces or stool. The large intestine also expels stool from the body. The colon is part of the large intestine. It is almost 5 feet long. Its four parts are the ascending, transverse, descending, and sigmoid colon.

**Colon wall**
The wall of the colon has four main layers as shown in Figure 1.2. The inner layer that has contact with stool is called the mucosa. The mucosa is made of three sublayers—the epithelium, lamina propria, and
**Figure 1.1 The digestive tract**

The digestive tract breaks down food for the body to use.

![Diagram of the digestive tract](illustration)

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**Figure 1.2 The colon**

The colon wall has four main layers: the mucosa, submucosa, muscularis propria, and serosa or adventitia.

![Diagram of the colon wall layers](illustration)

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muscularis mucosae. The epithelium absorbs water from stool and makes mucus. Mucus helps move stool through the colon. The lamina propria is a thin layer of connective tissue. The muscularis mucosae is a thin strip of muscle.

The second layer of the colon 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 food. It also has white blood cells that fight germs. Blood and lymph drain from colon tissue into vessels that are in the submucosa and then travel to other sites.

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

The fourth layer is the outer most part of the colon wall. It consists either of adventitia or serosa. Adventitia is connective tissue that binds the colon to other structures. The serosa, also called the visceral peritoneum, is a membrane. It has a thin layer of connective tissue, called the subserosa, which is covered by a single row of cells that make lubricating fluid. This fluid allows the colon to move smoothly against other organs.

How colon cancer starts and spreads

Adenocarcinoma
Cancer is a disease of cells—the building blocks of tissue in the body. Almost all colon cancers are adenocarcinomas. Adenocarcinomas are cancers that start in cells that line glands and, in the case of colon cancer, make mucus. Adenocarcinomas of the colon are the focus of this book.

Inside of cells are coded instructions, called genes, for building new cells and controlling how cells behave. Changes in genes, called mutations, can cause normal colon cells to become cancer cells. It is not fully understood how genes change and cause cancer.

Polyps
Colon cancer often starts in a polyp. A polyp is an overgrowth of cells from the epithelium of the colon wall. Not all polyps are the same. They all grow from the mucosa, but they differ in size, shape, and how their cells look. The chance of cancer forming in polyps differs by the type of polyp. There are three types of colon polyps.

- Adenomatous polyps, or adenomas, have cells that don’t look like normal colon 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.
Doctors also assess the shape of a polyp. Flat polyps grow flush along the colon wall. They can be hard to spot during an exam. Sessile polyps are raised above the colon wall but don’t have a stalk. 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 adenomatous polyps are rare but have been linked to cancer.

**Metastasis**

Cancer cells don’t behave like normal cells in three key ways. First, the changes in genes cause normal colon cells to grow more quickly and live longer. Normal cells divide and multiply when new cells are needed, but otherwise live in a resting state. They also die when old or damaged. 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 (invade) nearby tissues. If not treated, the primary tumor will likely grow through the colon wall. Colon cancer that has grown into the colon wall is called invasive cancer.

Third, unlike normal cells, cancer cells don’t stay in place. They can spread to other parts of the body. This process is called metastasis. Colon cancer can spread through blood or lymph vessels that are in the submucosa. Metastases can occur in nearby or distant sites.

The uncontrolled growth and spread of cancer makes it dangerous. Cancer cells replace normal cells and can cause organs to stop working. Thus, doctors are searching for better ways to find and treat cancer. The cancer tests and treatments discussed in this book are the most current standards of practice.
Review

- The colon absorbs water from unused food.
- The wall of the colon has four layers.
- Colon cancer often starts in cells that line the inside wall and make mucus.
- Cancer cells form a tumor since they don’t grow and die as normal cells do.
- Cancer cells can spread to other body parts through lymph or blood.
Cancer staging is a rating by your doctors of how far the cancer has grown and spread. In Part 2, the scoring system used for cancer staging is explained. Your doctors will plan additional tests and treatment based on the extent of the cancer.

Pathologic review

If you had a polyp, it was likely removed with an endoscopic polypectomy. For this minor surgery, a colonoscope is used to see and remove the polyp. A colonoscope is a thin tube-shaped device that has a light, camera, and open channel for inserting cutting tools. The cutting tool used may be forceps or a snare as shown in Figure 2.1.

A removed polyp is sent to a pathologist for review. A pathologist is a doctor who studies parts of cells with a microscope to classify disease. This is called histologic typing. All test results are included in a pathology report. Your pathology report states what type of colon cancer you have. The pathology report also states how far the cancer has grown into the colon wall.
TNM scores

The AJCC (American Joint Committee on Cancer) staging system is used to stage colon cancer. In this system, the letters T, N, and M describe a different area of cancer growth. Using test results, including the pathologic review, your doctors will assign a score to each letter. These scores will be combined to assign the cancer a stage.

**T = Tumor**
The T score tells into which tissues the primary tumor has grown. The primary tumor first grows through the layers of the colon wall as shown in Figure 2.2. Outside of the wall, it will then grow into nearby organs and structures.

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**Figure 2.1**
**Polypectomy**
Polyps may be removed with a snare and then sent to a pathologist for review.

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**Figure 2.2**
**Primary tumor growth**
In the far left column, a tumor is shown in the mucosal layer of the colon wall. In the columns to the right, the tumor is shown to be growing though the colon wall and has spread into the lymph nodes.
T scores for colon cancer include:

- **Tis** tumors have not grown beyond the first layer of the colon wall (mucosa).
- **T1** tumors have grown into the second layer of the colon wall (submucosa).
- **T2** tumors have grown into the third layer of the colon wall (muscularis propria).
- **T3** tumors have grown into the fourth layer of the colon wall (serosa or adventitia).
- **T4a** tumors have grown through the serosa (also called visceral peritoneum).
- **T4b** tumors have grown next to or into nearby organs or structures.

**N = Nodes**
The N score reflects how far the cancer has spread within nearby lymph nodes. Nearby lymph nodes include nodes right outside the colon wall and nodes along the major arteries that supply blood to the colon. The N category also reflects the presence of tumor deposits. Tumor deposits are small secondary tumors near but separate from the primary tumor.

N scores for colon cancer include:

- **N0** means there is no cancer in nearby lymph nodes.
- **N1** means the cancer has spread to 1 to 3 nearby lymph nodes.
  - **N1a** means the cancer has spread to 1 nearby lymph node.
  - **N1b** means the cancer as spread to 2 to 3 nearby lymph nodes.
  - **N1c** means there is no cancer in the lymph nodes but there are tumor deposits within the fat that is inside or right outside the colon wall.
- **N2** means the cancer has spread to 4 or more nearby lymph nodes.
  - **N2a** means the cancer has spread to 4 to 6 nearby lymph nodes.
  - **N2b** means the cancer as spread to 7 or more nearby lymph nodes.

**M = Metastasis**
The M category tells you if the cancer has spread to distant sites. Distant sites include the liver, lungs, or distant lymph nodes. Colon cancer can also spread to the parietal peritoneum, which is a thin layer of tissue that covers the abdominal wall. M scores for colon cancer include:

- **M0** means the cancer hasn’t spread to distant sites.
- **M1** means the cancer has spread to distant sites.
  - **M1a** cancer has spread to one distant site.
  - **M1b** cancer has spread to two or more distant sites or to the parietal peritoneum.

**Colon cancer stages**

Chart 2.1 shows the staging groups labeled by Roman numerals 0 to IV. The stages are defined by the TNM scores. Dukes and MAC are two other definitions used for staging, but these definitions are not often used.

Cancer is often staged twice. The first rating is done before treatment and is called the clinical stage. The second rating is done after treatment, such as surgery, and is called the pathologic stage.

In general, earlier cancer stages have better outcomes. However, doctors define cancer stages with information from thousands of patients, so a cancer stage gives an average outcome. It may not tell the outcome for one person. Some people will do better than expected. Others will do worse. Other factors not used for staging cancer, such as your general health, are also very important.
# Chart 2.1 Colon cancer stages

## Anatomic stage/prognostic groups

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Dukes*</th>
<th>MAC*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
<td>A</td>
<td>B1</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>B</td>
<td>B2</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
<td>B</td>
<td>B2</td>
</tr>
<tr>
<td>Stage IIC</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
<td>B</td>
<td>B3</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1–T2</td>
<td>N1/N1c</td>
<td>M0</td>
<td>C</td>
<td>C1</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2a</td>
<td>M0</td>
<td>C</td>
<td>C1</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T3–T4a</td>
<td>N1/N1c</td>
<td>M0</td>
<td>C</td>
<td>C2</td>
</tr>
<tr>
<td></td>
<td>T2–T3</td>
<td>N2a</td>
<td>M0</td>
<td>C</td>
<td>C1/C2</td>
</tr>
<tr>
<td></td>
<td>T1–T2</td>
<td>N2b</td>
<td>M0</td>
<td>C</td>
<td>C1</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T4a</td>
<td>N2a</td>
<td>M0</td>
<td>C</td>
<td>C2</td>
</tr>
<tr>
<td></td>
<td>T3–T4a</td>
<td>N2b</td>
<td>M0</td>
<td>C</td>
<td>C2</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>N1–N2</td>
<td>M0</td>
<td>C</td>
<td>C3</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

* Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (Any T N1 M0 and Any T N2 M0). MAC is the modified Astler-Coller classification.

Carcinoma in situ

**Carcinoma in situ** is stage 0 colon cancer. The cancer has not grown beyond the first layer of the colon wall—the **mucosa**. There are no blood or lymph vessels in the mucosa. As such, the cancer can’t spread to other tissues in your body. If you have carcinoma in situ, you will likely not need any more tests. You will not need treatment since all the cancer was removed during the **endoscopic polypectomy**.

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**Review**

- Polyps are often removed by an endoscopic polypectomy.
- The removed polyp will be tested to assess how far the cancer has grown into the colon wall.
- Colon cancer is grouped into stages based on the growth and spread of the tumor.
- Cancer is often staged before and after the start of treatment.
- If you have stage 0 colon cancer, you will likely not need any more tests or treatment.
3
Treatment planning
Part 3 discusses tests that are needed to plan treatment. Some are used to confirm the clinical stage of the cancer. Others are used to know which treatments would work best.

### Medical and family history

To plan cancer treatment, your doctors will ask you about any health events and medications you’ve taken in your lifetime. This information is called a medical history. A medical history helps your doctors know if you can have surgery. It also helps doctors assess if chemotherapy will do you more good than harm.

Since some health problems run in families, your doctor will also 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 the diseases started. This information is called a family history.

Colon cancer often occurs for unknown reasons. But some people have syndromes that increase their chances of getting colon 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 colon cancer are inherited—passed down from parents to child.

**HNPCC** (hereditary non-polyposis colon cancer), also known as Lynch syndrome, is the most common type of inherited syndrome to cause colon cancer. It also increases the risk for other types of cancer. Even so, only 3 to 5 out of 100 people with colon cancer have Lynch syndrome.

**FAP** (familial adenomatous polyposis) is a rare inherited syndrome that often leads to colon cancer. However, only 1 out of 100 people with colon 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 start of the disease is later in life and fewer than 100 polyps develop.

If your doctors think you 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 colon cancer. To be tested, you must provide a sample of blood. Using the sample, a pathologist can test your genes for abnormal changes that cause these syndromes.

**Total colonoscopy**

A total colonoscopy allows your doctor to look for other polyps or diseases in all of your large intestine. To prepare for this test, your doctor may place you on a liquid diet for 1 to 3 days. You may also be given a laxative or an enema to clean out your intestine the night before the test. Right before the test, you may be given a sedative to lessen any pain. You will be asked to wear a hospital gown and lie on your side during the test as shown in Figure 3.1.

A colonoscope 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 during the test to help your doctor guide the colonoscope. The picture from the colonoscope will be viewed by your doctor on a screen. If a polyp is found, a cutting tool will be used 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 stools, or weakness, contact your doctor.

![Figure 3.1 Colonoscopy](Illustration Copyright © 2014 Nucleus Medical Media, All rights reserved. www.nucleusinc.com)
Imaging tests

Imaging tests allow your doctors to see inside your body. Pictures (images) are made with scanning machines. Scanning machines are large and have an opening in which pictures are taken.

CT scan

A CT (computed tomography) scan of the chest, abdomen, and pelvis is recommended for cancer that has spread beyond the second layer of the colon wall. Pictures from these areas will help inform your doctor if the cancer has spread to nearby or distant sites. Test results may change the clinical stage of the cancer.

Getting a CT scan is often easy. Before the test, you may need to stop taking some medicines, stop eating and drinking for a few hours, and remove metal objects from your body. A contrast dye should be used to make the pictures clearer. The dye will be injected into your vein and you will also need to drink barium. The contrast may cause you to feel flushed or get hives. Rarely, serious allergic reactions occur. Tell your doctor and the technicians if you have had bad reactions in the past.

During the scan, you will need to lie face up on a table that moves through the imaging machine. See Figure 3.2. A CT scan takes many pictures of a body part from different angles using x-rays. As the machine takes pictures, you may hear buzzing, clicking, or whirring sounds. You will be alone, but a technician will operate the machine in a nearby room. He or she will be able to see, hear, and speak with you at all times. One scan is completed in about 30 seconds. A computer combines all the x-rays to make detailed pictures.

You will likely be able to resume your activities right away unless you took a sedative. You may not learn of the results for a few days since a radiologist needs to see the pictures. A radiologist is a doctor who’s an expert in reading the images.

A PET/CT (positron emission tomography/computed tomography) scan is not recommended for most people. PET/CT should only be used to assess an unclear finding of a CT scan with contrast. You may also have a PET/CT scan if you shouldn’t receive contrast.

Figure 3.2 CT scan machine

A CT machine is large and has a tunnel in the middle. During the test, you will lie on a table that moves slowly through the tunnel.
Blood tests

Blood tests are used to look for signs of disease. A CBC (complete blood count) measures the number of white blood cells, red blood cells, and platelets. Your blood counts may be low because the cancer has spread into your bones, the cancer is causing bleeding, or because of another health problem.

Another blood test is a chemistry profile. When colon cancer spreads, it can cause high or low levels of chemicals in the blood. One example is a high CEA (carcinoembryonic antigen) level. CEA is normally low in healthy adults unless a woman is pregnant. If not pregnant or if you’re a man, high CEA levels suggest the cancer has spread far.

Molecular testing

Abnormal genes aren’t always passed down from parents to children. Instead, there can be non-inherited changes in genes. Molecular testing assesses for genes known to have an effect on cancer treatment. Molecular testing is done with tissue removed from the tumor. If you have stage IV colon cancer, molecular testing of the following genes is recommended.

**RAS mutation**
RAS is a family of proteins found in cells. Some colon cancers have abnormal genes that control the RAS proteins. As a result, the RAS proteins made by the abnormal genes are overactive and promote cancer cell growth. Some treatments for colon cancer do not work if the genes that control KRAS and NRAS—members of the RAS family—are abnormal.

**BRAF mutation**
If the RAS genes are normal, the BRAF gene may be tested next. The protein made by the BRAF gene is involved with signals within cells that trigger cell growth. About 5 to 9 out of 100 colon cancers have a mutated BRAF gene. BRAF testing is not used to decide use of targeted therapy, which is discussed in Part 4. Instead, it helps doctors decide prognosis. Prognosis is the pattern and outcome of a disease based on tests.
Review

- HNPCC (a.k.a. Lynch syndrome) and FAP are syndromes that are linked to colon cancer. You may be tested for these syndromes.
- You may receive imaging and blood tests to assess how far the cancer has spread.
- Treatment options for stage IV cancer are based on whether the tumor has abnormal changes in the RAS genes.
Overview of cancer treatments
Colon cancer is a serious disease that can be treated. The main types of treatment are briefly described in Part 4. This information may help you understand the treatment options presented in Parts 5 through 7.

Surgical treatment

Colectomy

Some colon cancers grow beyond the polyp and into the colon wall. In many of these cases, a colectomy is done to remove that part of the colon. After removing part of the colon, the two ends of the remaining colon are sewn or stapled back together.

For some people, the cancer site may be marked with a tattoo before surgery. 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.

There are a few steps to prepare for the surgery. You may need to stop taking some medications to reduce the risk of severe bleeding. Eating less, changing to a liquid diet, or using enemas or laxatives will empty your colon for surgery. Right before surgery, you will be given general anesthesia.

A colectomy may be done with either an open or a laparoscopic method. The open approach removes tissue through a large cut in your abdomen. The laparoscopic method involves making a few small...
Ablation

Ablation destroys small tumors with little harm to nearby tissue. It isn’t used often for colon cancer. Doctors sometimes consider its use for metastatic disease. Most often it is considered for colon cancer that has spread to the liver or lung. Ablation is done by an interventional radiologist or surgeon.

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 will be guided into place by ultrasound, CT, or other imaging equipment and will be removed when treatment is done.

Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy rays. The rays damage DNA (deoxyribonucleic acid). DNA is a chain of chemicals in cells that contains genes. This either kills the cancer cells or stops new cancer cells from being made.

Radiation therapy is not often used to treat colon cancer. External radiation therapy uses a machine outside the body to deliver radiation. Internal radiation therapy places a radioactive object near or inside the body.
Chemotherapy

Chemotherapy, or “chemo,” is a class of drugs that is used to kill cancer cells. Some chemotherapy drugs kill cancer cells by damaging their DNA or disrupting the making of DNA. Other drugs interfere with cell parts that are needed for making new cells.

Chemotherapy for colon cancer has been shown in clinical trials to work well and be safe. However, if the cancer is stage IV, chemotherapy isn’t expected to destroy all cancer cells. Instead, it may shrink or slow the growth of tumors and reduce pain. In some people, chemotherapy can prolong life. For many stage IV cancers, a regimen is used until it stops working and then a new regimen is started.

Chemotherapy drugs used for colon cancer are listed in Chart 4.1. 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. Single agents and combination regimens used for colon cancer are shown in Chart 4.2.

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 and days of treatment there are within a cycle.

---

**Chart 4.1 Cancer drugs for colon cancer**

<table>
<thead>
<tr>
<th>Generic (chemical) name</th>
<th>Brand name (sold as)</th>
<th>Type of drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab</td>
<td>Avastin®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>Xeloda®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>Erbitux®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Floxuridine</td>
<td>–</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Fluorouracil (5-FU)</td>
<td>–</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Irinotecan hydrochloride</td>
<td>Camptosar®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Leucovorin calcium</td>
<td>–</td>
<td>Improves 5-FU</td>
</tr>
<tr>
<td>Levoleucovorin</td>
<td>Fusilev®</td>
<td>Improves 5-FU</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>Eloxatin®</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Panitumumab</td>
<td>Vectibix®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Regorafenib</td>
<td>Stivarga®</td>
<td>Targeted therapy</td>
</tr>
<tr>
<td>Ziv-aflibercept</td>
<td>Zaltrap®</td>
<td>Targeted therapy</td>
</tr>
</tbody>
</table>
Overview of cancer treatments

Chemotherapy

Most chemotherapy drugs for colon cancer are liquids that are injected into your body. Only capecitabine is in pill form. A slow injection is called infusion. Bolus injections are fast.

The side effects of chemotherapy can differ between people. Some people have many side effects. Others have few. Some side effects can be very serious while others can be unpleasant but not serious. Side effects of chemotherapy depend on the drug type, amount taken, length of treatment, and the person.

In general, side effects are caused by the death of fast-growing normal cells. These cells are found in the gut, mouth, blood, and hair follicles. Thus, common side effects of chemotherapy include low blood cell counts, not feeling hungry, nausea, vomiting, diarrhea, hair loss, and mouth sores. Please ask your treatment team for a complete list of known common and rare side effects.

<table>
<thead>
<tr>
<th>Agent or regimen</th>
<th>Generic (chemical) name</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-FU/LV</td>
<td>5-FU = fluorouracil</td>
</tr>
<tr>
<td></td>
<td>LV = leucovorin</td>
</tr>
<tr>
<td>Capecitabine alone</td>
<td>Capecitabine</td>
</tr>
<tr>
<td>CapeOX</td>
<td>Cape = capecitabine</td>
</tr>
<tr>
<td></td>
<td>OX = oxaliplatin</td>
</tr>
<tr>
<td>FLOX</td>
<td>F = fluorouracil</td>
</tr>
<tr>
<td></td>
<td>L = leucovorin</td>
</tr>
<tr>
<td></td>
<td>OX = oxaliplatin</td>
</tr>
<tr>
<td>FOLFLOX</td>
<td>FOL = leucovorin</td>
</tr>
<tr>
<td></td>
<td>F = fluorouracil</td>
</tr>
<tr>
<td></td>
<td>OX = oxaliplatin</td>
</tr>
<tr>
<td>FOLFOXIRI</td>
<td>FOL = leucovorin</td>
</tr>
<tr>
<td></td>
<td>F = fluorouracil</td>
</tr>
<tr>
<td></td>
<td>OX = oxaliplatin</td>
</tr>
<tr>
<td></td>
<td>IRI = irinotecan</td>
</tr>
<tr>
<td>IROX</td>
<td>IR = irinotecan</td>
</tr>
<tr>
<td></td>
<td>OX = oxaliplatin</td>
</tr>
</tbody>
</table>
Targeted therapy

Targeted therapy is a class of cancer drugs that is newer than chemotherapy. It stops the action of molecules that aid the growth of cancer cells. Targeted therapy is less likely to harm normal cells than chemotherapy. There are five targeted therapy drugs used to treat colon cancer:

**Bevacizumab**
Cancer cells need the food and oxygen in blood to grow. Thus, cancer cells release VEGF (vascular endothelial growth factor). VEGF is a molecule that binds to cells that form blood vessels. The binding starts changes within the cells that cause blood vessels to form and to grow into tumors. Bevacizumab attaches to VEGF, which stops VEGF from binding to cells. Cancer cells then don’t receive the blood they need to live.

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, diarrhea, and feeling tired and weak. You might also have nosebleeds, shortness of breath, nausea, and vomiting. Rare but serious side effects include stroke, heart attack, kidney damage, holes in the intestine, and bleeding within the body.

**Cetuximab**
EGFR (epidermal growth factor receptor) is a surface receptor. A surface receptor is a protein in the outer membrane of cells. When molecules outside the cells attach to EGFRs, changes within the cell occur that start cell growth.

Some people with colon cancer have abnormal changes in their gene that controls EGFRs. These changes cause EGFRs to be overactive, which in turn causes new cancer cells to form quickly. Cetuximab treats colon cancer by binding to the ends of EGFRs that are outside of the cell—like a key into a lock—to stop cell growth. It also attracts immune cells that help to kill the cancer cells.

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

Some people have an infusion reaction to cetuximab. Symptoms of a reaction include chills and fever. If you have a reaction, you will be given cetuximab more slowly.

Besides a reaction, common side effects of cetuximab include an acne-like rash, infections, mouth sores, and feeling tired and weak. Other possible side effects are nausea, diarrhea, trouble sleeping, and swelling of feet. Rare but serious side effects include heart, lung, eye, or kidney damage.

**Panitumumab**
Panitumumab works much like cetuximab by targeting EGFRs and attracting immune cells. It 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 include skin rash, diarrhea, feeling tired, and constipation. Rare but serious side effects include lung and eye damage and blood clots in the lungs.

**Regorafenib**
Regorafenib attaches to surface receptors within cells that form blood vessels. This may stop new blood vessels from forming so that cancer cells don’t get the blood supply they need. 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.

Common side effects of regorafenib include feeling tired or week, fever, and diarrhea. Your hands and feet may become red and have pain. This is called hand-foot syndrome. Rare but serious side effects include severe liver damage, heart attack, and blindness.

**Ziv-aflibercept**

Like bevacizumab, ziv-aflibercept also targets VEGF. It works by acting as a decoy. VEGF thinks bevacizumab 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, VEGF-trap. By trapping VEGF, cancer cells will not receive the blood they need to live.

Ziv-aflibercept is always given with chemotherapy. It is given by infusion in about 1 hour every two weeks. Common side effects include diarrhea, mouth sores, high blood pressure, feeling tired, voice changes, and nose bleeds. You may also experience blood clots, urinary tract infection, and darkening of the skin. Rare but serious side effects include stroke, holes in the intestine, bleeding in the brain or lungs, and kidney damage.
Clinical trials

New tests and treatments aren’t offered to the public as soon as they’re made. They need to be studied. New uses of tests and treatments also need to be studied.

A clinical trial is a type of research that studies a test or treatment. Clinical trials study how safe and helpful tests and treatments are. Many patients with cancer are offered the option to join a clinical trial. Clinical trials are a standard of care.

Through clinical trials, some tests and treatments are found to be safe and helpful. These tests or treatments may become tomorrow’s standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help patients.

Tests and treatments go through a series of clinical trials to make sure 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. Examples of the four phases for treatment are:

- **Phase I** trials aim to find the best dose of a new drug with the fewest side effects.
- **Phase II** trials assess if a drug works for a specific type of cancer.
- **Phase III** trials compare a new drug to the standard treatment.
- **Phase IV** trials test new drugs approved by the FDA in many patients with different types of cancer.

Joining a clinical trial has benefits. First, you’ll have access to the most current cancer care. 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 patients with cancer.

Clinical trials have risks, too. Like any test or treatment, there may be side effects. Also, new tests or treatments may not work better than current treatments. Another downside may be that paperwork or more trips to the hospital may be needed.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to know that any progress is because of the treatment and not because of differences between patients. To join, you’ll need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you’re getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 8.
Complementary and alternative medicine

You may hear about other treatments from your family and friends. They may suggest using CAM (complementary and alternative medicine). CAM 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. 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 treatments work.
Review

- A colectomy is an operation that removes the part of the colon with cancer. A lymphadenectomy is the removal of lymph nodes and a metastasectomy is the removal of metastases.

- Ablation and radiation therapy are sometimes used to treat colon cancer.

- Chemotherapy is a class of drugs that stops cells from completing their growth cycle.

- Targeted therapy stops the action of molecules that aid the growth of cancer cells.

- Clinical trials give people access to new tests and treatments.
Treatment guide: First-time treatment
Part 5 is a treatment guide for when you are first diagnosed with colon cancer. Treatment options are organized by cancer stage.

In stage I (T1), the cancer has grown into the submucosa but not beyond. These tumors are sometimes called “polyps with cancer” because the cancer has not grown far.

In stages I (T2), II, and III, the cancer has spread beyond the submucosa. However, the cancer has not spread to distant sites.

Stage IV is metastatic disease. The cancer has spread to distant sites. This section focuses on treatment options for colon cancer that has spread to the liver, lungs, or both organs.
5.1 Stage I (T1) colon cancer

Chart 5.1.1 Surgical treatment

<table>
<thead>
<tr>
<th>Test results</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pendunculated polyp without high-risk features</td>
<td>Start follow-up testing</td>
</tr>
<tr>
<td>Sessile polyp without high-risk feature</td>
<td>Start follow-up testing, or Colectomy + lymphadenectomy</td>
</tr>
<tr>
<td>Any tumor with high-risk features</td>
<td>Colectomy + lymphadenectomy</td>
</tr>
</tbody>
</table>

Chart 5.1.1 addresses surgical treatment for polyps with cancer. It shows whether surgery is needed after a polypectomy for stage I, T1 tumors.

Surgery for T1 tumors is based on whether the cancer is likely to return. Cancer that is likely to return is called high risk. High-risk features include:

- Fragmented specimen – the tumor was removed in pieces,
- Grade 3 or 4 – the cancer cells don’t look like the normal cells in which the cancer started,
- Positive surgical margins – cancer was found in the normal-looking tissue around the tumor,
- Unknown surgical margins – the presence of cancer in the normal-looking tissue around the tumor can’t be confirmed,
- Angiolymphatic invasion – the cancer has spread into the lymph vessels or bloodstream.

The option for high-risk T1 tumors is colectomy with lymphadenectomy. The options for T1 tumors without high-risk features are based on whether the polyp is pedunculated or sessile as shown in Figure 5.1. A pedunculated polyp has a stalk and round top. A sessile polyp doesn’t have a stalk.

If you had a pedunculated polyp, it is likely that all the cancer was removed. No more treatment is recommended. You can start follow-up testing. If you had a sessile polyp, two options are listed. Your doctor will likely advise for follow-up testing if he or she is sure that all the cancer was removed. If unsure, a colectomy with lymphadenectomy or follow-up testing within a short timeframe will likely be recommended.

Figure 5.1 Shapes of polyps

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www.nucleusinc.com
Chart 5.1.2 Follow-up testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Schedule</th>
</tr>
</thead>
</table>
| Colonoscopy    | At 1 year after treatment  
|                | • If no advanced adenoma, repeat in 3 years  
|                | – If results are normal, then repeat every 5 years  
|                | • If advanced adenoma, repeat in 1 year |

Chart 5.1.2 addresses follow-up testing for polyps with cancer. Follow-up testing is started when there are no signs of cancer after treatment. It can be helpful for finding new cancer growth early. A colonoscopy is recommended 1 year after treatment has ended.

If results are normal, have your next colonoscopy in 3 years and then every 5 years. If the test finds an advanced adenoma, your next colonoscopy will be needed within 1 year. Advanced adenomas include a villous polyp, a polyp larger than the width of an AAA battery, or a polyp with pre-cancerous cells.
5.2 Stages I (T2), II, and III colon cancer

Chart 5.2.1 Primary treatment

<table>
<thead>
<tr>
<th>Test results</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tumor can be treated with surgery and isn’t blocking the gut</td>
<td>• Colectomy + lymphadenectomy</td>
</tr>
<tr>
<td>• Tumor can be treated with surgery and is blocking the gut</td>
<td>• Colectomy + lymphadenectomy,</td>
</tr>
<tr>
<td></td>
<td>• Colectomy + lymphadenectomy followed by diversion, or</td>
</tr>
<tr>
<td></td>
<td>• Diversion followed by colectomy + lymphadenectomy</td>
</tr>
<tr>
<td>• Tumor can’t be treated with surgery</td>
<td>• Treatments listed in Part 7</td>
</tr>
</tbody>
</table>

Chart 5.2.2 Adjuvant treatment

<table>
<thead>
<tr>
<th>Pathologic stage</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stage I (T2 tumor)</td>
<td>• Start follow-up testing</td>
</tr>
<tr>
<td>• Stage IIA without high-risk features</td>
<td>• Clinical trial,</td>
</tr>
<tr>
<td></td>
<td>• Start follow-up testing, or</td>
</tr>
<tr>
<td></td>
<td>• Consider capecitabine or 5-FU/LV</td>
</tr>
<tr>
<td>• Stage IIA with high-risk features</td>
<td>• Capecitabine or 5-FU/LV,</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>• FOLFOX, CapeOX, or FLOX,</td>
</tr>
<tr>
<td>Stage IIC</td>
<td>• Clinical trial, or</td>
</tr>
<tr>
<td></td>
<td>• Start follow-up testing</td>
</tr>
<tr>
<td>• Stage III</td>
<td>• FOLFOX or CapeOX,</td>
</tr>
<tr>
<td></td>
<td>• FLOX,</td>
</tr>
<tr>
<td></td>
<td>• Capecitabine, or</td>
</tr>
<tr>
<td></td>
<td>• 5-FU/LV</td>
</tr>
</tbody>
</table>

Chart 5.2.1 lists the options for primary treatment. Primary treatment is the main treatment used to rid your body of cancer. Surgery should be done if possible for stages I (T2), II, and III. Otherwise, you can receive the treatments listed in Part 7.

Surgery includes a colectomy with lymphadenectomy. In some cases, the tumor has grown so large that it blocks the flow of stool. There are three options when there is a blockage. First, your surgeon can do a colectomy that unblocks your gut. The second option is cancer surgery and a diversion to allow stool...
to pass. The third option involves a two-step process. The first surgery is a diversion to allow stool to pass, and the second surgery is to remove the cancer.

**Chart 5.2.2** lists the adjuvant treatment options after surgery. Adjuvant treatment is given when all visible cancer has been removed by surgery but unseen cancer cells may remain. The aim of this treatment is to kill the unseen cancer cells.

The pathologic stage of cancer is used to recommend which adjuvant treatment to receive. If adjuvant treatment is right for you, it should be received as soon as possible for the best results.

More treatment after surgery isn’t needed for stage I (T2). These tumors didn’t grow far into the colon wall. Thus, all of the cancer was likely removed.

Stage II colon cancer is more likely to return than stage I. More than one option is given. Talk with your doctors about the risks and benefits of each option. Options should be discussed in light of your overall health, personal wishes, and type of colon cancer.

It is important to know that chemotherapy may have little, if any, benefit for stage II colon cancer. If the tumor has high microsatellite instability, 5-FU chemotherapy will not help. Microsatellite instability is abnormal changes in DNA that happen when DNA is making a copy of itself.

For stage IIA, options are based on pathologic stage plus risk factors for recurrence. High-risk features include:

- High grade – A grade of 3 or 4 with low microsatellite instability,
- Positive margins – Cancer was found in the surgical margins,
- Unknown margins – The presence of cancer in margins can’t be confirmed,
- Angiolymphatic invasion – Cancer has spread into the lymph vessels or bloodstream,
- Bowel obstruction – The tumor has grown large enough to block the gut,
- Limited lymphadenectomy – Fewer than 12 lymph nodes were examined,
- Perineural invasion – Cancer has spread around or into the nerves, and
- Localized perforation – Holes have formed in the colon from the tumor.

There are three options for stage IIA colon cancer without high-risk features. First, you can enroll in a clinical trial that is testing new treatments. Second, you can start follow-up testing and wait to see if the cancer will return. Third, you can talk with your doctors about starting chemotherapy. Capecitabine alone or 5-FU/LV is the only reasonable chemotherapy for stage IIA without high-risk features.

High-risk stage IIA, stage IIB, and stage IIC cancers have four options. You may start chemotherapy. Capecitabine or 5-FU/LV is the first option. FOLFOX, CapeOX, or FLOX is the second option. For T4 tumors, consider radiation therapy with chemotherapy if the tumor has grown into a nearby organ or structure. The third option is to join a clinical trial testing new treatment. A third option is to start follow-up testing to wait and see if the cancer will return.

For stage III, chemotherapy is the only suggested option. The risk for recurrence is high. Recurrence is more likely for stage III than for stage I and II because cancer cells may have spread through lymph.

FOLFOX or CapeOX is often given for stage III. There is also good research supporting the use of FLOX. If oxaliplatin is not right for you, other options include capecitabine alone or 5-FU/LV.
Follow-up testing is for people who have no signs of cancer after treatment. It can be helpful for finding new cancer growth early. Tests differ based on whether the cancer is stage I versus stages II and III.

**Chart 5.2.3** lists the follow-up tests for stage I (T2 tumors) cancers. A **colonoscopy** is recommended 1 year after treatment has ended. If results are normal, have your next colonoscopy in 3 years and then every 5 years. If the test finds an advanced adenoma, your next colonoscopy will be needed within 1 year. Advanced adenomas include a **villous polyp**, a polyp larger than the width of an AAA battery, or a polyp with pre-cancerous cells.

**Chart 5.2.4** lists the follow-up tests for stage II and III cancers. You should receive a **medical history** and physical exam every 3 to 6 months for 2 years. If results are normal for 2 years, then get these tests every 6 months for 3 years.

### Chart 5.2.3 Follow-up testing for stage I (T2)

<table>
<thead>
<tr>
<th>Test</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colonoscopy</strong></td>
<td>In 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>
</tbody>
</table>

### Chart 5.2.4 Follow-up testing for stages II and III

<table>
<thead>
<tr>
<th>Test</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical history and physical exam</strong></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><strong>CEA blood test</strong></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><strong>CT of chest, abdomen, pelvis</strong></td>
<td>Every year for up to 5 years if stage II and high risk</td>
</tr>
<tr>
<td></td>
<td>Every year for up to 5 years if stage III</td>
</tr>
<tr>
<td><strong>Colonoscopy</strong></td>
<td>Within 1 year if colonoscopy before treatment or within 3–6 months if no colonoscopy before 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>
</tbody>
</table>
Ongoing tests of CEA levels are mainly used to find cancer recurrences. If your risk for recurrence is low, your doctor may not order this test. CEA blood tests should be done every 3 to 6 months for 2 years. If results are normal for 2 years, get this test every 6 months for a total of 3 years.

CT scans may help find metastases. For stage II, you should only receive a CT scan if you have a high risk of recurrence. Scans of your chest, abdomen, and pelvis are suggested each year for a maximum of 5 years if results are normal. CT should be done with both IV and oral contrast. MRI (magnetic resonance imaging) may be done if you can’t have CT. An MRI uses radio waves and powerful magnets to make pictures.

A colonoscopy is also needed since your risk for another tumor is high within 2 years after diagnosis. You may never have had a colonoscopy of your entire colon if your gut was blocked. If so, get your first colonoscopy within 3 to 6 months after treatment. If you had a colonoscopy before, get another test 1 year after treatment.

Your second colonoscopy after treatment is based on the initial results. However, colonoscopies may be needed more often if you are younger than 50 years old or have Lynch syndrome. If results are normal, have your next colonoscopy in 3 years and then every 5 years. If the test finds an advanced adenoma, your next colonoscopy will be needed within 1 year. Advanced adenomas include a villous polyp, a polyp larger than the width of an AAA battery, or a polyp with pre-cancerous cells.
### 5.3 Stage IV colon cancer

This section is for people with metastases in the liver, lungs, or both organs but not elsewhere. Colon cancer most often spreads to the liver. Among 100 people with colon cancer, 20 to 34 people will have liver metastases at diagnosis. Research on metastases other than in the liver is limited. As a result, the information below focuses on liver metastases but also applies to lung metastases. Treatment for other stage IV cancers found at diagnosis is discussed in Part 7.

#### Chart 5.3.1 Surgical options

**Option 1**

<table>
<thead>
<tr>
<th>1st treatment</th>
<th>2nd treatment</th>
<th>3rd treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Colectomy</td>
<td>• Metastasectomy (at time of colectomy or afterward)</td>
<td>• FOLFOX, or CapeOX</td>
</tr>
</tbody>
</table>

**Option 2**

<table>
<thead>
<tr>
<th>1st treatment</th>
<th>2nd treatment</th>
<th>3rd treatment</th>
<th>4th treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FOLFIRI ± bevacizumab, FOLFOX ± bevacizumab, CapeOX ± bevacizumab, or If normal KRAS/NRAS gene: – FOLFIRI ± panitumumab, – FOLFIRI ± cetuximab, or – FOLFOX ± panitumumab</td>
<td>• Colectomy</td>
<td>• Metastasectomy (at time of colectomy or afterward)</td>
<td>• Follow-up testing, or • Short course of chemotherapy</td>
</tr>
</tbody>
</table>

**Option 3**

<table>
<thead>
<tr>
<th>1st treatment</th>
<th>2nd treatment</th>
<th>3rd treatment</th>
<th>4th treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Colectomy</td>
<td>• FOLFIRI ± bevacizumab, FOLFOX ± bevacizumab CapeOX ± bevacizumab, or If normal KRAS/NRAS gene: – FOLFIRI ± panitumumab, – FOLFIRI ± cetuximab, or – FOLFOX ± panitumumab</td>
<td>• Metastasectomy</td>
<td>• Follow-up testing, or • Short course of chemotherapy</td>
</tr>
</tbody>
</table>
Research has shown that colon cancer with liver metastases can sometimes be cured. Thus, a cure is the goal when possible. Surgery is needed for a cure, but most people with liver metastases can’t have surgery. Surgery is only done when all tumors can be fully removed and your liver won’t be too small after surgery.

To enlarge your liver, your doctor may suggest 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. In some patients who have small metastatic tumors that cannot be removed with surgery, ablation can be used as treatment.

Chemotherapy is recommended with surgery if you haven’t had it before. The best order of chemotherapy and surgery is unknown, so Chart 5.3.1 presents three options.

**Option 1** starts with surgery. You will have a colectomy and metastasectomy followed by chemotherapy. FOLFOX and CapeOX are preferred regimens. Six months of chemotherapy is preferred.

**Option 2** starts with chemotherapy with or without targeted therapy. Panitumumab and cetuximab should only be used for tumors that have normal KRAS and NRAS genes. There are benefits and risks to starting with drug treatment. Some of these are:

**Benefits:**
- 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.

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

After 2 to 3 months of chemotherapy, you will have a colectomy and metastasectomy. Sometimes, more chemotherapy will be given after surgery. Together, chemotherapy given before and after surgery should not exceed 6 months.

**Option 3** starts with colectomy. Afterward, you will have chemotherapy with or without targeted therapy for 2 to 3 months. Panitumumab and cetuximab should only be used for tumors that have normal KRAS and NRAS genes. After chemotherapy, the surgery for metastases will be done. Sometimes, more chemotherapy is given after surgery. Together, chemotherapy given before and after surgery should not exceed 6 months.
Chart 5.3.2 presents the nonsurgical options for stage IV liver or lung tumors that can’t be treated with surgery. Recommended chemotherapy regimens with or without targeted therapy are listed. Panitumumab and cetuximab should only be used for tumors that have normal \textit{KRAS} and \textit{NRAS} genes.

Most people with stage IV colon cancer aren’t able to be cured of their cancer. However, for a few people, chemotherapy may shrink the tumors enough so a surgical cure is possible. Surgery is more likely possible if you only have liver metastases and have very few metastatic tumors.

After the start of chemotherapy, get tested every 2 months to see if you can have surgery. Chemotherapy should be only given for 2 to 4 months before surgery to avoid harmful side effects to the liver. Limiting chemotherapy should also reduce complications from surgery. Bevacizumab can cause bleeding and slow healing after surgery. Thus, if you will take bevacizumab, surgery should be done about 6 to 8 weeks after your last dose.

If surgery alone won’t cure your cancer, ablation may be right for you. Ablation with or without surgery should only be done when a cure is possible. You may qualify for ablation if surgery can’t be done because of other illnesses, tumor location, or the size of your liver would be too small after surgery. Ablation for this purpose has not been tested in clinical trials.

After surgery, starting follow-up testing or limited chemotherapy is an option. Together, chemotherapy before and after surgery should not exceed 6 months. The treatment regimens in Part 7 are another option for after surgery.
Chart 5.3.3 lists the follow-up tests for stage IV colon cancer found at diagnosis. Follow-up testing is for people who have no signs of cancer after treatment. It can be helpful for finding new cancer growth early.

You should receive a medical history and physical exam every 3 to 6 months for 2 years. If results are normal for 2 years, then get these tests every 6 months for 3 years.

Ongoing tests of CEA levels are mainly used to find cancer recurrences. CEA blood tests should be done every 3 to 6 months for 2 years. If results are normal for 2 years, get this test every 6 months for 3 to 5 years.

CT scans may help find metastases. Scans of your chest, abdomen, and pelvis are suggested every 3 to 6 months for 2 years. If results are normal for 2 years, then get these scans every 6 to 12 months for 3 years. CT should be done with both intravenous and oral contrast. MRI may be done if you can’t have CT.

A colonoscopy is also needed since your risk for another tumor is high within 2 years after diagnosis. You may never have had a colonoscopy of your entire colon if your gut was blocked. If so, get your first colonoscopy within 3 to 6 months after treatment. If you had a colonoscopy before, get another test 1 year after treatment.

Your second colonoscopy after treatment is based on the initial results. However, colonoscopies may be needed more often if you are younger than 50 years old or have Lynch syndrome. If results are normal, have your next colonoscopy in 3 years and then every 5 years. If the test finds an advanced adenoma, your next colonoscopy will be needed within 1 year. Advanced adenomas include a villous polyp, a polyp larger than the width of an AAA battery, or a polyp with pre-cancerous cells.

<table>
<thead>
<tr>
<th>Test</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Medical history and physical exam</td>
<td>Every 3–6 months for 2 years</td>
</tr>
<tr>
<td>• CEA blood test</td>
<td>Every 3–6 months for 2 years</td>
</tr>
<tr>
<td>• CT of chest, abdomen, and pelvis</td>
<td>Every 3–6 months for 2 years</td>
</tr>
<tr>
<td>• Colonoscopy</td>
<td>Within 1 year if colonoscopy before treatment or within 3–6 months if no colonoscopy before 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>
</tbody>
</table>
**Review**

- Surgery for stage I colon cancer with a T1 tumor is based on whether the cancer is likely to return.

- Surgery is recommended for stage I (T2), II, and III colon cancer if you are able and willing to have it. You may receive chemotherapy after surgery if the return of cancer is likely.

- Some stage IV colon cancers can be treated with surgery. If surgery isn’t possible, you can receive chemotherapy with or without targeted therapy.

- Follow-up testing is for people who have no signs of cancer after treatment and is used to find recurrences early.
Treatment guide: Recurrent treatment
Part 6 is a guide to treatment for colon cancer that returns as metastatic disease. Metastasis is the spread of cancer cells from the first tumor to one or more distant sites.

Most metastases of colon cancer occur after treatment for earlier stages. The liver is the most common site. After finding metastases, your doctor may order more tests. It may help to have a PET/CT scan to know how big the tumor is. A PET/CT scan can also find metastases other than in the liver that would make surgery not possible.

In Part 6, treatment options for metastases that can be treated with surgery are listed first. Unfortunately, most people with metastases at recurrence can’t have surgery. If you can’t have surgery, other treatment options are given.
6 Treatment guide

Recurrent treatment
6.1 Surgical options for recurrent colon cancer

If you have never had chemotherapy before, there are two options.

**Chart 6.1.1 Option 1**

<table>
<thead>
<tr>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Metastasectomy</td>
<td>• FOLFOX or CapeOX, or</td>
</tr>
<tr>
<td></td>
<td>• FLOX or Capecitabine or 5-FU/LV</td>
</tr>
</tbody>
</table>

**Chart 6.1.2 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,</td>
<td></td>
<td>– Re-start neoadjuvant regimen, or</td>
</tr>
<tr>
<td>• Capecitabine, or</td>
<td></td>
<td>– FOLFOX</td>
</tr>
<tr>
<td>• 5-FU/LV</td>
<td></td>
<td>• If neoadjuvant didn’t work:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– Treatment in Part 7, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– Observation</td>
</tr>
</tbody>
</table>

**Chart 6.1.1 Option 1** starts with surgery. A metastasectomy can be followed by chemotherapy. FOLFOX and CapeOX are preferred regimens. Other possible regimens are FLOX, capecitabine, and 5-FU/LV. Six months of chemotherapy is preferred.

**Chart 6.1.2 Option 2** starts with treating the metastases with chemotherapy. FOLFOX and CapeOX are preferred regimens. Other possible regimens are FLOX, capecitabine, and 5-FU/LV.

After 2 to 3 months of chemotherapy, a metastasectomy may be done. Treatment after surgery is based on the success of treatment before surgery. If the treatment before surgery worked, you may re-start that treatment or take FOLFOX. Together, chemotherapy given before and after surgery should not exceed 6 months. If the treatment before surgery didn’t work, you can start a treatment regimen in Part 7 or start observation. Observation is a period of testing to assess for cancer growth.
If you *have had* chemotherapy before, there are two options.

**Chart 6.1.3 Option 1**

<table>
<thead>
<tr>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Metastasectomy</td>
<td>• Observation, or</td>
</tr>
<tr>
<td></td>
<td>• Treatment in Part 7</td>
</tr>
</tbody>
</table>

**Chart 6.1.4 Option 2**

<table>
<thead>
<tr>
<th>Neoadjuvant treatment</th>
<th>Primary treatment</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Treatment in Part 7</td>
<td>• Metastasectomy</td>
<td>• If neoadjuvant worked:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– Re-start neoadjuvant regimen,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– FOLFOX, or</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>– Treatment in Part 7, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– Observation</td>
</tr>
</tbody>
</table>

**Chart 6.1.3 Option 1** starts with surgery. After surgery, you can start observation or try a treatment regimen in Part 7. Observation is a period of testing to assess for cancer growth.

**Chart 6.1.4 Option 2** starts with a treatment regimen listed in Part 7. After 2 to 3 months of chemotherapy, you can have a metastasectomy. Treatment after surgery is based on the success of treatment before surgery. If the treatment before surgery worked, you may re-start that treatment. Other options are to take FOLFOX or start observation. Together, chemotherapy given before and after surgery should not exceed 6 months. If the treatment before surgery didn’t work, you can start a treatment regimen in Part 7 or start observation. Observation is a period of testing to assess for cancer growth.
6.2 Nonsurgical options for recurrent colon cancer

Chart 6.2 Nonsurgical options

<table>
<thead>
<tr>
<th>Chemotherapy history</th>
<th>Primary treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant FOLFOX or CapeOX ≤12 months ago</td>
<td>• FOLFIRI ± bevacizumab,</td>
</tr>
<tr>
<td></td>
<td>• FOLFIRI ± ziv-aflibercept,</td>
</tr>
<tr>
<td></td>
<td>• Irinotecan ± bevacizumab,</td>
</tr>
<tr>
<td></td>
<td>• Irinotecan ± ziv-aflibercept, or</td>
</tr>
<tr>
<td></td>
<td>• If normal KRAS/NRAS gene:</td>
</tr>
<tr>
<td></td>
<td>– FOLFIRI + panitumumab,</td>
</tr>
<tr>
<td></td>
<td>– FOLFIRI + cetuximab,</td>
</tr>
<tr>
<td></td>
<td>– Irinotecan + panitumumab, or</td>
</tr>
<tr>
<td></td>
<td>– Irinotecan + cetuximab</td>
</tr>
<tr>
<td>Adjuvant FOLFOX or CapeOX &gt;12 months ago</td>
<td>• Treatments listed in Part 7</td>
</tr>
<tr>
<td>Prior 5-FU/LV</td>
<td>• Treatments listed in Part 7</td>
</tr>
<tr>
<td>Prior capecitabine</td>
<td>• Treatments listed in Part 7</td>
</tr>
<tr>
<td>Never had chemotherapy</td>
<td>• Treatments listed in Part 7</td>
</tr>
</tbody>
</table>

Chart 6.2 presents options for stage IV recurrences that can’t be treated with surgery. Treatment is based on your history of chemotherapy. If you’ve had FOLFOX or CapeOX within the past 12 months, treatment options are listed in the chart. If you haven’t had FOLFOX or CapeOX within the past 12 months, you may start a treatment regimen listed in Part 7.

Most people with stage IV colon cancer aren’t able to be cured of their cancer. However, for a few people, chemotherapy may shrink the tumors enough so a surgical cure is possible. Surgery is more likely possible if you only have liver or lung metastases and have very few metastatic tumors.

After the start of chemotherapy, get tested every 2 months to see if you can have surgery. Chemotherapy should be only given for 2 to 4 months before surgery to avoid harmful side effects to the liver. Limiting chemotherapy should also reduce complications from surgery. Bevacizumab can cause bleeding and slow healing after surgery. Thus, if you will take bevacizumab, surgery should be done about 6 to 8 weeks after your last dose.

After surgery, you may start a treatment regimen listed in Part 7. Another option is to start observation. Observation is a period of testing to assess for cancer growth.
Review

- If you have metastatic cancer, it may help to have a PET/CT scan to see if the cancer has spread to sites other than the liver.

- If you are able to have surgery, your treatment options depend on if you had chemotherapy before.

- If you are unable to have surgery, many drug treatments are available.
Treatment guide: chemotherapy pathways
Part 7 presents pathways of chemotherapy and other drugs used to treat advanced colon cancer. If one option doesn’t work or stops working, another option is given.

There are many treatment options for advanced colon cancer. Chemotherapy, targeted therapy, or both are used. Some regimes cause worse side effects than others. Your doctors will assess your health to know which side effects you can withstand. Their choice of treatment will be based on treatment goals, the type and timing of prior treatment, and which side effects the drugs cause.
There are five groups of treatment pathways listed in Part 7. The groups are based on which type of chemotherapy is given first. The first four groups may cause worse side effects than the fifth group.

The first group starts with oxaliplatin regimens, such as FOLFOX or CapeOX. The second group starts with an irinotecan-based regimen, FOLFIRI. The third group excludes both oxaliplatin and irinotecan from initial treatment. The fourth group starts with FOLFOXIRI. The fifth group includes treatments that usually result in the least harmful side effects.

You may receive targeted therapy with chemotherapy. There is good proof that cetuximab and panitumumab don’t work if the cancer cells have RAS mutations. These targeted therapies should only be used if the KRAS and NRAS genes are normal. The use of bevacizumab doesn’t depend on gene tests.
7.1 Oxaliplatin pathways

Chart 7.1 Oxaliplatin pathways

<table>
<thead>
<tr>
<th>Initial treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOLFOX,</td>
</tr>
<tr>
<td>FOLFOX + bevacizumab,</td>
</tr>
<tr>
<td>CapeOX,</td>
</tr>
<tr>
<td>CapeOX + bevacizumab, or</td>
</tr>
<tr>
<td>If normal KRAS and NRAS genes:</td>
</tr>
<tr>
<td>– FOLFOX + panitumumab</td>
</tr>
</tbody>
</table>

1st progression

| FOLFIRI,           |
| FOLFIRI + bevacizumab, |
| FOLFIRI + ziv-aflibercept, |
| Irinotecan,         |
| Irinotecan + bevacizumab, or |
| Irinotecan + ziv-aflibercept |

2nd progression

| If normal KRAS and NRAS genes: |
| – Irinotecan + panitumumab, |
| – Irinotecan + cetuximab, or |
| – Panitumumab or cetuximab if unable to take irinotecan |

3rd progression

| Regorafenib,     |
| Clinical trial, or |
| Best supportive care |

1st progression

| If normal KRAS and NRAS genes: |
| – Follow pathway on left, |
| – FOLFIRI + panitumumab, |
| – FOLFIRI + cetuximab, |
| – Irinotecan + panitumumab, or |
| – Irinotecan + cetuximab |

2nd progression

| Regorafenib, |
| Clinical trial, or |
| Best supportive care |
Chart 7.1 Oxaliplatin pathways start with oxaliplatin. You may start with either FOLFOX or CapeOX. Bevacizumab may be added either chemotherapy regimen or if the RAS genes are normal, panitumumab.

Oxaliplatin in the FOLFOX or CapeOX regimens 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 grows (progresses), oxaliplatin may be restarted if it was stopped because of side effects. You should only restart if the side effects stop.

Capecitabine in the CapeOx regimen can also 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.

The oxaliplatin regimens may not prevent the cancer from growing. If this happens, you may start to take irinotecan regimens. If the RAS genes are normal, you may also take panitumumab or cetuximab.

If panitumumab or cetuximab don’t work the first time, there is no good proof to keep taking them. Also, your doctor won’t use panitumumab after cetuximab failure or cetuximab after panitumumab failure because these drugs work in a similar way.

If oxaliplatin and irinotecan regimens fail, treatment options include regorafenib, clinical trials, and best supportive care. Supportive care treats the symptoms of cancer but not the cancer itself.
7.2 Irinotecan pathways

**Chart 7.2**  
Irinotecan pathways

<table>
<thead>
<tr>
<th>Initial treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOLFIRI,</td>
</tr>
<tr>
<td>FOLFIRI + bevacizumab, or</td>
</tr>
<tr>
<td>If normal KRAS and NRAS genes:</td>
</tr>
<tr>
<td>– FOLFIRI + panitumumab or</td>
</tr>
<tr>
<td>– FOLFIRI + cetuximab</td>
</tr>
</tbody>
</table>

1st progression

| FOLFOX,          |
| FOLFOX + bevacizumab, or |
| CapeOX, or       |
| CapeOX + bevacizumab |

2nd progression

| If normal KRAS and NRAS genes: |
|   – Irinotecan + panitumumab*, |
|   – Irinotecan + cetuximab*, or |
|   – Panitumumab* or cetuximab* if unable to take irinotecan |

<table>
<thead>
<tr>
<th>Regorafenib</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd progression</td>
</tr>
</tbody>
</table>

| Regorafenib,|
| Clinical trial, or |
| Best supportive care |

* Panitumumab and cetuximab should not be given if received before and didn’t work.
Chart 7.2 Irinotecan pathways start with irinotecan. You may start taking FOLFIRI with or without bevacizumab. If the RAS genes are normal, you may take FOLFIRI with or without panitumumab or cetuximab.

Irinotecan 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. This advice for irinotecan also applies if you have high bilirubin levels in your blood for any reason.

The irinotecan regimens may not prevent the cancer from growing. If this happens, you may start to take oxaliplatin regimens. If the RAS genes are normal, you may also take panitumumab or cetuximab.

If cetuximab or panitumumab don’t work the first time, there is no good proof to keep taking them. Also, your doctor won’t use panitumumab after cetuximab failure or cetuximab after panitumumab failure because these drugs work in a similar way.

If irinotecan and oxaliplatin regimens fail, treatment options include regorafenib, clinical trials, and best supportive care. Supportive care treats the symptoms of cancer but not the cancer itself.
# 7.3 5-FU and capecitabine pathways

## Chart 7.3
5-FU and capecitabine pathways

<table>
<thead>
<tr>
<th>Initial treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusional 5-FU/LV,</td>
</tr>
<tr>
<td>Capecitabine, or</td>
</tr>
<tr>
<td>Capecitabine + bevacizumab</td>
</tr>
</tbody>
</table>

### 1️⃣st progression
- FOLFOX,  
- FOLFOX + bevacizumab,  
- CapeOX, or  
- CapeOX + bevacizumab

### 2️⃣nd progression
- Irinotecan

### 3️⃣rd progression
If normal KRAS and NRAS genes:
- Irinotecan + panitumumab,  
- Irinotecan + cetuximab, or  
- Panitumumab or cetuximab if unable to take irinotecan

- Regorafenib

### 4️⃣th progression
- Regorafenib,  
- Clinical trial, or  
- Best supportive care

### 1️⃣st progression
- Irinotecan,  
- Irinotecan + bevacizumab,  
- Irinotecan + ziv-aflibercept,  
- FOLFIRI,  
- FOLFIRI + bevacizumab,  
- FOLFIRI + ziv-aflibercept

### 2️⃣nd progression
- FOLFOX or  
- CapeOX

### 3️⃣rd progression
If normal KRAS and NRAS genes:
- Irinotecan + panitumumab,  
- Irinotecan + cetuximab, or  
- Panitumumab or cetuximab if unable to take irinotecan

- Regorafenib

### 4️⃣th progression
- Regorafenib,  
- Clinical trial, or  
- Best supportive care
Chart 7.3 5-FU and capecitabine pathways
don’t start with either irinotecan or oxaliplatin. Instead, you may start with 5-FU/LV given by infusion. The other option is capecitabine with or without bevacizumab.

The side effects of 5-FU/LV or capecitabine aren’t usually as bad as those caused by irinotecan or oxaliplatin. Thus, if these regimens are too harsh, you should start supportive care if the cancer grows.

If you get better and then the cancer progresses, you should try regimens with irinotecan or oxaliplatin. Side effects of these drugs are discussed in the first two pathways. If the RAS genes are normal, you may also take panitumumab or cetuximab.

If cetuximab or panitumumab don’t work the first time, there is no good proof to keep taking them. Also, your doctor won’t use panitumumab after cetuximab failure or cetuximab after panitumumab failure because these drugs work in a similar way.

If oxaliplatin or irinotecan regimens fail, treatment options include regorafenib, clinical trials, and best supportive care. Supportive care treats the symptoms of cancer but not the cancer itself.
### 7.4 FOLFOXIRI pathways

**Chart 7.4 FOLFOXIRI pathways**

<table>
<thead>
<tr>
<th>Initial treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOLFOXIRI or</td>
</tr>
<tr>
<td>FOLFOXIRI + bevacizumab,</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1st progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>If normal KRAS and NRAS genes:</td>
</tr>
<tr>
<td>– Irinotecan + panitumumab,</td>
</tr>
<tr>
<td>– Irinotecan + cetuximab,</td>
</tr>
<tr>
<td>– Panitumumab or cetuximab if unable to take irinotecan</td>
</tr>
</tbody>
</table>

| Regorafenib                |

<table>
<thead>
<tr>
<th>2nd progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regorafenib,</td>
</tr>
<tr>
<td>Clinical trial, or</td>
</tr>
<tr>
<td>Best supportive care</td>
</tr>
</tbody>
</table>

**Chart 7.4 The FOLFOXIRI pathways** start with FOLFOXIRI. FOLFIRI may be taken with or without bevacizumab. You may have worse side effects with FOLFOXIRI than if you were taking FOXFIRI. Thus, this pathway is only recommended if the tumor is likely to shrink enough so surgery would be possible.

If the cancer progresses, regorafenib is an option. If the RAS genes are normal, you may also take panitumumab or cetuximab with irinotecan. If you’re unable to take irinotecan, you may take panitumumab or cetuximab alone.

If these regimens fail, treatment options include regorafenib, clinical trials, and best supportive care. Supportive care treats the symptoms of cancer but not the cancer itself.
7.5 Least toxic pathways

Chart 7.5 Least toxic pathways

<table>
<thead>
<tr>
<th>Initial treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusional 5-FU/LV or capecitabine ± bevacizumab, or</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>If normal KRAS and NRAS genes:</td>
</tr>
<tr>
<td>– Cetuximab, or</td>
</tr>
<tr>
<td>– Panitumumab</td>
</tr>
</tbody>
</table>

**Chart 7.5 The least toxic pathways** have potentially the least harmful regimens. 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. If the RAS genes are normal, a third option is to take panitumumab or cetuximab.
Review

- There are many treatment options for advanced colon cancer.
- Some treatment options may cause worse side effects than others.
- Your doctor will choose a regimen for you based on your treatment goals, the type and timing of prior treatment, and possible side effects.
Making treatment decisions
Parts 1 through 7 described the cancer and gave test and treatment options recommended by NCCN experts. These options are based on science and agreement among NCCN experts. Part 8 aims to help you make decisions that are in line with your beliefs, wishes, and values.

It's your choice

The role patients want in choosing their 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 judgement isn’t any better than your doctors’.

Your doctors will give you the information you need to make an informed choice. However, letting others decide which option is best may make you feel more at ease. But, who do you want to make the decisions? You may rely on your doctors alone to make the right decisions. You can also have loved ones help. They can gather information, speak on your behalf, and share decision–making with your doctors. Even if others decide the best option, you still have to agree to have treatment 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 but you know your concerns and goals. By working together, you are likely to get 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 will likely 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 record your talks and get copies of your medical records.

It may be helpful to have your spouse, partner, or a friend with you at these visits. They can help to ask questions and remember what was said. Suggested questions to ask include:

What’s my diagnosis and prognosis?

It’s important to know that there are different types of cancer. Cancer can greatly differ even when people have a tumor in the same organ. Based on your test results, your doctors can tell you which type of cancer you have. They 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?
2. Is this cancer common?
3. What is the cancer stage? Does this stage mean the cancer has spread far?
4. What is the grade of the cancer? Does this grade mean the cancer will grow and spread fast?
5. What other test results are important to know?
6. How often are these tests wrong?
7. Would you give me a copy of the pathology report and other test results?
8. Can the cancer be cured? If not, how well can treatment stop the cancer from growing?
What are my options?

There is no single treatment practice that is best for all patients. 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. Should I consider a clinical trial?
4. Do you consult NCCN recommendations when considering options?
5. Are you suggesting options other than what NCCN recommends? If yes, why?
6. How do my age, health, and other factors affect my options?
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? Are my chances any better for one option than another? Which option spares the most healthy tissue? Is any option less invasive? 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?
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 may also 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 many times? How long is each visit?
2. How do I prepare for treatment?
3. Should I bring someone with me when I get treated?
4. Will the treatment hurt?
5. How much will the treatment cost me?
6. Is home care after treatment needed? If yes, what type?
7. How soon will I be able to manage my own health?
8. When will I be able to return to my normal activities?
What is your experience?

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

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

Deciding which option is best can be hard. Doctors from different fields of medicine may differ 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, so science isn’t helpful. Some ways to decide on treatment are discussed next.

2nd opinion
The time around a cancer diagnosis 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, 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 on 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 patients who have walked in your shoes. Support groups often consist of people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support group meetings, you can ask questions and hear about the experiences of other patients.

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

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

Colon Cancer Alliance
www.ccalliance.org/

Fight Colon Cancer
fightcolorectalcancer.org

Hereditary Colon Cancer Foundation
www.hcctakesguts.org

National Cancer Institute
www.cancer.gov/cancertopics/types/colon-and-rectal

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.
abdomen
The belly area between the chest and pelvis.

ablation
Treatment using radiofrequency or cold to destroy cancer cells.

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

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

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

allergic reaction
Symptoms caused when the body is trying to rid itself of invaders.

angiolymphatic invasion
Cancer has spread into the lymph vessels or bloodstream.

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

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

bolus
A fast injection of a drug.

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

cancer stage
The rating of the growth and spread of cancer.

carcinoembryonic antigen (CEA)
A protein present in babies growing in the womb or when cancer forms.

carcinoma in situ
Abnormal or cancer cells have not grown into the next layer of tissue.

chemotherapy
Drugs used to stop the growth cycles of cancer cells.

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.

colecotomy
Surgery to remove a part of the colon.

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.

complete blood count (CBC)
A test that measures the parts of blood.

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

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

deoxyribonucleic acid (DNA)
A very thin and long molecule that contains genetic code. Also called the “blueprint of life.”

diagnosis
To identify a disease.

digestive system
A set of organs in the body that changes food into small parts for the body to use as energy.
**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 colon wall.

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

**familial adenomatous polyposis (FAP)**
An inherited medical condition that increases the odds of colon cancer.

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

**general anesthesia**
A controlled loss of wakefulness from drugs.

**hereditary non-polyposis colon cancer (HNPCC)**
An inherited medical condition that increases the odds of colon cancer. Also called Lynch syndrome.

**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.

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

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

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

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

**intravenous (IV)**
Receipt of a substance by a needle inserted into a vein.

**invasive cancer**
Cancer cells have grown into the supporting tissue of the colon.

**lamina propria**
Connective tissue within the mucosa of the colon wall.

**laparoscopic colectomy**
Removal of the colon using a thin, long cutting tool that is inserted through a small cut in the abdomen.

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

**laxative**
Drugs used to clean out the intestines.

**lymph**
A clear fluid containing white blood cells.

**lymphadenectomy**
Surgery to remove lymph nodes.

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

**magnetic resonance imaging (MRI)**
A test that uses radio waves and powerful magnets 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**
Abnormal changes in a DNA part that happen when DNA is making a copy of itself.

**mucosa**
The first, inner layer of the colon wall.
mucus
A sticky, thick liquid that moisturizes or lubricates.

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

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

mutation
Abnormal changes in genes.

observation
A period of testing for cancer growth.

open colectomy
Surgery to remove part of the colon through a large cut into the body.

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.

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

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

positron emission tomography/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 radiation to treat cancer.

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 disease-free period.

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

sessile polyp
A polyp that is flat.

side effect
An unhealthy or unpleasant physical or emotional response to treatment.

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

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

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

subserosa
A thin layer of connective tissue that makes fluid.

supportive care
Treatment for symptoms of a disease.

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.
**Glossary**

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

**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.

**visceral peritoneum**
The inner layer of tissue lining around the abdomen; also called the serosa.

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**Acronyms**

**CAM**
Complementary and alternative medicine

**CEA**
Carcinoembryonic antigen

**CBC**
Complete blood count

**CT**
Computed tomography

**DNA**
Deoxyribonucleic acid

**EGFR**
Epidermal growth factor receptor

**FAP**
Familial adenomatous polyposis

**HNPCC**
Hereditary non-polyposis colon cancer

**IV**
Intravenous

**MRI**
Magnetic resonance imaging

**PET/CT**
Positron emission tomography/computed tomography

**VEGF**
vascular endothelial growth factor

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**NCCN Abbreviations and Acronyms**

**NCCN®**
National Comprehensive Cancer Network®

**NCCN Patient Guidelines®**
NCCN Guidelines for Patients®

**NCCN Guidelines®**
NCCN Clinical Practice Guidelines in Oncology®
State Fundraising Notices

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# NCCN Panel Members for Colon Cancer

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<td><strong>Alan P. Venook, MD/Vice-Chair</strong></td>
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NCCN Member Institutions

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

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

City of Hope Comprehensive Cancer Center
Los Angeles, California
800.826.4673
cityofhope.org

Dana-Farber/Brigham and Women’s Cancer Center Massachusetts General Hospital Cancer Center
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877.332.4294
dfbwc.org
massgeneral.org/cancer

Duke Cancer Institute
Durham, North Carolina
888.275.3853
dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427
foxchase.org

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

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

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
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410.955.8964
hopkinskimmelcancercenter.org

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

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
800.446.2279 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/departments-centers/mayo-clinic-cancer-center

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

Moffitt Cancer Center
Tampa, Florida
800.456.3434
moffitt.org

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

Roswell Park Cancer Institute
Buffalo, New York
877.275.7724
roswellpark.org

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

St. Jude Children’s Research Hospital/The University of Tennessee Health Science Center
Memphis, Tennessee
888.226.4343 • stjude.org
901.683.0055 • westclinic.com

Stanford Cancer Institute
Stanford, California
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cancer.stanford.edu

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

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

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

University of Colorado Cancer Center
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720.848.0300
coloradooncologycenter.org

University of Michigan Comprehensive Cancer Center
Ann Arbor, Michigan
800.865.1125
michigan.org

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

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

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