LEARN, ASK, SHARE:
Your Role in Your Care as a Patient
A Patient Guide for Colorectal Cancer

This is a fundamental guide to colorectal cancer (CRC), where knowledge is strength, and strength is essential.
Colorectal cancer (CRC) is the fourth most common cancer in men and women, usually diagnosed in people aged 50 years or older. If colorectal cancer is not found at its earliest stages through preventative screenings, it can develop into metastatic colorectal cancer (mCRC), which is an advanced stage of disease. There are multiple treatment options if you have this condition.

Advances in understanding and treating colorectal cancer have improved patient outcomes. Screening for colorectal cancer is vital for spotting the disease early and preventing CRC. Early CRC can often be cured by surgery.

For patients with advanced CRC, various treatment options have been introduced in the past decade that have been shown to increase life expectancy. You can take an active role in understanding your condition in order to work efficiently with your healthcare team.

Our mission is to improve health globally, through education and advocacy, and empower patients to take an active role in fighting cancer. We work with cancer patients, their advocates and healthcare providers around the world to disseminate knowledge about antiangiogenic treatments for CRC in order to improve patient outcomes.

**TAKE ACTION**

1. **LEARN** about CRC and treatment options.

2. **SEEK** the right treatment with the help of your doctors.

3. **SHARE** knowledge about the condition and the importance of early treatment.
WHAT IS CRC?

The colon is your large intestine and makes up the final part of your digestive system. It terminates with the rectum, which is a connecting pathway between the colon and the anus. Colorectal cancer typically begins in the inner lining of the colon or the rectum. It may grow through the colon wall and may spread locally or to other areas of the body, resulting in a condition called metastatic colorectal cancer (mCRC). The most common sites of CRC metastases are the liver, lung and bone.

Most colorectal cancers develop from colorectal polyps, abnormal growths inside the colon or rectum that develop silently. Individuals with a family history of polyps may themselves be at higher genetic risk for developing polyps, and therefore at higher risk for colorectal cancer. Catching these polyps early through regular screenings by your doctor can prevent the development of CRC.

ANGIOGENESIS and CANCER

Solid cancers have been shown to depend upon angiogenesis, the growth of new blood vessels from pre-existing blood vessels, to grow beyond a few millimeters in size. These new blood vessels supply the tumor with the oxygen and nutrients needed to grow and act as lifelines to cancer cells.

A major advance in cancer treatment has been the development of drugs called angiogenesis inhibitors, or antiangiogenic drugs, which are designed to target and interfere with the tumor blood supply. In essence, they help ‘starve’ cancer cells and can slow or stop tumor growth. The specific targeted treatments are described later in this brochure.

Tumor Angiogenesis

A tumor in its early stages of development cannot grow past a few millimeters in diameter unless it is fed by blood vessels. Angiogenesis - the growth of new blood vessels - is essential for tumor growth and spread.

1. Cells in the center of the tumor mass compete with their neighboring cells for access to oxygen and nutrients. They release growth factors as "angiogenesis feeding signals" to the surrounding tissue.

2. Nearby blood vessels receive these signals and begin to sprout and grow new abnormal vessels toward the source. As long as the signal continues, the vessels will continue to grow in its direction.

3. Vessels that grow into the tumor mass nourish the tumor tissue, delivering oxygen and essential nutrients. As the tumor grows larger, signaling may increase and encourage even more blood vessel growth.

4. As the tumor expands, it invades surrounding tissue. Cancer cells spread through the blood vessels and lymph nodes, first locally and then as metastases to distant organs in the later stages of CRC progression.
Anyone can develop colon polyps, but you are at greater risk if you are age 50 or older and:

- Smoke
- Eat a high-fat diet
- Eat a low-fiber diet
- Are overweight
- Have a personal or family history of CRC, colon polyps or inflammatory bowel diseases

Polyps are small masses of cells that can develop anywhere along the inner lining of the colon and rectum. Type, location, size, and number of polyps are related to risk of developing cancer.

The most common types of colorectal polyps are adenomas, serrated, and post-inflammatory.

### Adenomatous

Adenomas are most common type of polyp (about 2/3 of the polyps found in the colon and rectum). Although most adenomas remain benign, a small percentage can develop into colorectal cancer via a process that typically takes many years.

### Villous or Tubulovillous Adenoma

This type represents approximately 15% of adenomas that are found and removed with colorectal cancer screening - they have the highest likelihood of developing into colorectal cancer.

### Serrated

Serrated lesions are a heterogeneous group of lesions including hyperplastic polyps. Certain types of less common serrated lesions have a significant risk of developing into cancer.

### Post-Inflammatory

These polyps develop most often in people with inflammatory bowel diseases such as Crohn’s disease or ulcerative colitis. The presence of post-inflammatory polyps is associated with colorectal cancer.
IMPORTANCE OF EARLY DIAGNOSIS

It's important to know that CRC can be treated and, if caught early, even cured. Preventative screenings are critical to detect CRC because it typically does not have symptoms at its early, most curable stages.

TESTS & PROCEDURES

Common tests and procedures to ensure an accurate colorectal cancer diagnosis include:

- **A Colonoscopy**, the most common procedure, is when a gastroenterologist examines the inner lining of the colon and rectum by inserting a colonoscope (a thin, long tube with a light and camera on it) through the rectum. Your doctor can then see abnormalities and take samples of tissue for biopsy and further testing.

- **A Polypectomy** is the removal of small polyps from the colon or rectum so that they can be analyzed for cancer. Although most polyps are benign, they can develop into cancer so it is safest to remove them.

- **A Barium Enema** uses dye and x-ray to visualize the colon and rectum on film. The images allow your doctor to evaluate the appearance of your entire colon and rectum.

- **A Virtual Colonoscopy** creates pictures of the inside of your colon and rectum using multiple CT images. This is an alternative if you are unable to undergo an actual colonoscopy.

If you are diagnosed with mCRC, a number of treatment options are available for you. Your doctor will help identify the best therapeutic approach for your situation, but it is important that you stay informed of all the options in order to have a productive discussion with your doctor. Knowledge and understanding of your condition equips you to take an active role in choosing and managing your treatment.

Preventative Screenings

Anyone 50 years of age and older is at greatest risk of developing CRC and is strongly encouraged to get annual screenings. If polyps are detected during screening, they are removed to avoid risk of developing cancer as some polyps may become malignant.

According to the Colon Cancer Alliance, 90% of deaths from colorectal cancer can be prevented if everybody aged 50 and older has regular screening tests.
LEARN: The Staging of CRC

Staging of cancer is the process doctors use to identify the extent and location of the cancer, including whether it has spread locally or to other parts of the body. This information is used to plan the most effective treatments for each patient. Treatments can differ based on the stage of disease.

There are five stages of colorectal cancer:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>This is the earliest stage: cancer is restricted to the innermost lining of the colon or rectum. It is also called ‘Carcinoma in Situ’.</td>
</tr>
<tr>
<td>Stage I</td>
<td>Cancer has begun to grow beyond the original site, but remains in the inner lining of the colon or rectum. This stage is also called ‘Dukes A’ colorectal cancer.</td>
</tr>
<tr>
<td>Stage II</td>
<td>Cancer has grown through the wall of the colon or rectum, but has not reached lymph nodes. This stage is also called ‘Dukes B’ colorectal cancer.</td>
</tr>
<tr>
<td>Stage III</td>
<td>Cancer has spread to one or more nearby lymph nodes but has not reached distant parts of the body. This is also called ‘Dukes C’ colorectal cancer.</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Cancer has metastasized to distant parts of the body, often to the lungs, liver, or bone. This is also called ‘Dukes D’ colorectal cancer.</td>
</tr>
</tbody>
</table>

The stage of a cancer is the designation given at the time of diagnosis. It never changes, even if the cancer progresses. A cancer that spreads or reoccurs is still referred to by the initial stage it was given when it was first diagnosed, with information about the current extent of the cancer added to it.

- Doctors gather different types of information about a cancer to determine its stage. The exact tests used for staging depend on the type of cancer.
- If colorectal cancer is found, it is highly treatable in its early stages.
- If the cancer spreads into nearby lymph nodes, chemotherapy followed by surgery has been a highly successful treatment approach.
- In the most difficult cases — when the cancer has metastasized to other organs, such as the liver or lungs — appropriate treatment can prolong life.

Lines of Therapy

Patients with mCRC often receive a sequence of different treatments, with one given after another. Each sequence is referred to as a “line of therapy.” If one line of therapy stops working, a different therapy is often effective:

1. **First-Line** therapy is the first time a patient is treated for metastatic disease.
2. **Second-Line** therapy is used if the cancer progresses or recurs during or after first line therapy.
3. **Third-Line** therapy follows second line if the cancer progresses or recurs during or after second line therapy.
To use this chart, find the column that represents your stage of CRC progression. Scan down the column to see the treatments that may be options for you, and discuss them with your doctor(s).

The doctor most familiar with your situation is in the best position to assess the stage of your cancer.

This chart lists the possible therapies and treatments you may need to discuss with your doctor according to the stage of your disease progression. Learn more at www.angio.org.
SURGERY

Surgery is standard for Stage I through Stage III colorectal cancer, where the tumor is considered local. Oftentimes, the surgeon removes not only the tumor but also the portion of the colon or rectum containing the tumor and the surrounding fat and lymph nodes. Typically the healthy sections of the colon or rectum are reconnected at the end of the surgery. If this is not possible, the surgeon will perform a colostomy, a procedure in which the colon is re-routed to an opening in the abdomen called a stoma. A colostomy is often a temporary procedure until the bowel fully heals. During the healing period, you can expect temporary diarrhea or constipation, which are common after surgery and can be alleviated with medication. Proper nutrition after surgery is important for healing and speeding recovery.

RADIATION THERAPY

Radiation therapy kills cancer cells with high-energy rays. It may be used alone or in combination with chemotherapy to shrink tumors before surgery, or to destroy any remaining cancer cells after surgery. Radiation can also be used to reduce tumor size to make a patient more comfortable, even when the cancer cannot be removed.

There is a limit to the amount of radiation a body can receive without causing irreversible damage to healthy tissues. Your doctor will take into account any previous exposure you may have had to radiation in assessing your options.

CHEMOTHERAPY (Cytotoxic, Non-targeted Therapy)

Chemotherapy (commonly referred to as ‘chemo’) is the treatment of cancer with drugs that attack and kill cancer cells. It differs from surgery and radiation therapy in that it can kill cancer cells that may have spread throughout the entire body.

Treatment of colorectal cancer has greatly evolved since the development of new chemotherapies and, as a result, patients are responding to these new therapies at higher rates. There are many different types of chemotherapy drugs used in combination to attack the cancer more aggressively. This is known as combination chemotherapy, which can also reduce the likelihood that the cancer will become resistant to any single chemotherapeutic drug.

Most chemotherapeutic drugs are liquids that are injected through an IV line (intravenous). Some chemotherapy can be taken as an oral pill. The drugs travel in the blood throughout the entire body to attack cancer cells. You can learn more about different chemo drugs and combinations at www.angio.org.

Chemotherapy can also be used for neoadjuvant therapy in order to shrink the primary tumor before surgery, facilitating the procedure. Your doctor will work with you in deciding which drug, or combination of drugs, would be best for you depending on the type and stage of your cancer, and whether surgery will be involved.

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INTRODUCTION

Beginning in 2004, treatments for mCRC were developed called “Targeted Therapies.” These new treatments capitalize on advances in our understanding of the molecular basis of cancer and are improving our ability to treat metastatic colorectal cancer. Drugs have been designed to attack specific cell pathways used by cancers to survive and grow.

By interfering with these pathways, several benefits can be achieved:

- Cancer cells are unable to grow and undergo a type of cellular “suicide,” also called **apoptosis**.
- Blood vessels that grow and feed cancer cells are halted, a process called **antiangiogenesis**.
- Tissue around the cancer, known as the tumor microenvironment, can be reverted to a more normal structure.

Together, these treatments represent an advance in cancer treatment that offers options and hope for patients with mCRC.

If you have mCRC, the type of targeted cancer therapy you may receive depends on many factors. Depending upon the targeted cancer therapy for mCRC, the therapy may be used alone or in combination with different forms of chemotherapy.

### Treatments for Stage IV Metastatic Colorectal Cancer

Because there are many treatment options for mCRC, you and your doctor will work together to select the proper treatment that will give you the most benefit.

- **Chemotherapy** attacks the cancer cells directly, causing them to die off.
- **Radiation** kills cancer cells with high-energy rays.
- **Biopsy/Genetic Test**
- **Targeted Therapies**
  - **Anti-EGFR**
    - Anti-EGFR therapy attacks the growth signals that encourage proliferation of cancer cells.
  - **Antiangiogenic Therapy**
    - Antiangiogenic therapies attack the blood vessels that feed the tumor.

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ANTIANGIOGENIC TREATMENTS

Antiangiogenic agents attack the growing blood vessels that feed the tumor, cutting its life-line. These agents are specific for treating metastatic disease and are offered as different lines of therapy to address recurrence of the cancer or treatment unresponsiveness. You and your doctor will work to identify the right dosage and duration of your treatment.

Some antiangiogenic treatments neutralize specific proteins, known as growth factors, which stimulate the growth of new blood vessels needed by the tumor to survive. Other treatments work by blocking multiple signaling pathways that drive angiogenesis, tumor cell growth and invasion, and maintenance of the tumor microenvironment.

Depending on the treatment, you may receive antiangiogenic therapy intravenously or in pill form.

ANTI-EGFR

The epidermal growth factor receptor (EGFR) is a molecule identified on cancer cells that contributes to tumor development and growth. In about 80% of malignant CRC tumors, EGFR signaling plays a role in the progression of the disease. EGFR signaling also can drive angiogenesis.

Drugs that target EGFR (anti-EGFR) can inhibit or slow cancer progression. Anti-EGFR therapy attacks specific growth signals that encourage proliferation of cancer cells.

Get informed before discussing treatment options with your doctor. It’s important to learn about possible side effects and treatment outcomes.

KRAS Screening

KRAS (pronounced kay-rass) tests determine the targeted therapies for which you may be eligible. Available EGFR inhibitors are ineffective in tumors that carry mutations of the KRAS gene. Roughly 40% of colorectal cancers have KRAS mutations while the non-mutated KRAS gene (also known as “wild type”) is found in the remaining 60%. Identifying KRAS mutation status avoids unnecessary expenses and toxicities from anti-EGFR inhibitors, which are ineffective in KRAS mutated colorectal cancers.
By reading this brochure, you’ve just taken the first step to understanding your condition and learning about treatment options that are available for mCRC. Because there are many treatment options for mCRC, you and your doctor will work together to select the proper treatment that will give you the most benefit.

Learn more at [www.angio.org](http://www.angio.org), and make sure to work with your doctor in understanding and managing your treatment.

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**Targeted Treatments - Potential Responses**

Targeted treatments can reduce the effect of growth factors released by the tumor. Outcomes may include significant to moderate tumor shrinkage.

1. **Tumor Shrinkage**
   - Metastatic tumors often shrink significantly with targeted treatments. Without a blood supply, the tumors cannot sustain themselves.

2. **Stop Tumor Growth**
   - Primary tumors are also affected by targeted treatments. As the vessels feeding the tumor shrink back, cells in the tumor mass are starved for oxygen and nutrients. Tumor growth is stopped and the surrounding environment becomes more stable.

3. **Disease Progression**
   - Tumors may continue to grow despite treatment. This is called “non-response” to treatment.

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**To Do List: After Diagnosis**

1. Understand my stage of disease
2. Learn more about my treatment options
3. Ask my doctor what is recommended for me
4. Learn about potential side effects of treatments
5. Engage my family and support network in my overall care
6. Find out if I am eligible for a clinical trial [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
7. Obtain additional patient resources

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The Angiogenesis Foundation is the world’s first and leading nonprofit organization dedicated to conquering diseases using a ground-breaking approach based on angiogenesis, the growth of new blood vessels in the body. Angiogenesis is the “common denominator” in overall health.

Understanding the science behind mCRC and its treatment empowers patients, their advocates, doctors and everyone affected by mCRC to take concrete action in preventing and effectively treating mCRC.

www.angio.org

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