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Advances in the Treatment of Colorectal Cancer

Presented by

John S. Macdonald, MD

St. Vincent's Comprehensive Cancer Center

Keith Lyons, MSW

CancerCare

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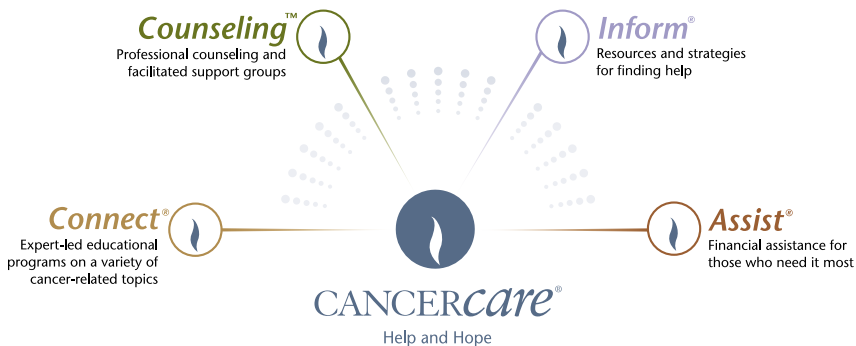
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Advances in the Treatment of Colorectal Cancer

Presented by

John S. Macdonald, MD

Professor of Medicine

Lynn Wood Neag Distinguished Professor
of Gastrointestinal Oncology

Medical Director and Chief of the
Gastrointestinal Oncology Service

St. Vincent's Comprehensive Cancer Center
New York, NY

Keith Lyons, MSW

Program Coordinator for Gastrointestinal Cancers
CancerCare

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New drug combinations improve survival, cause fewer side effects, and offer a better quality of life.

Colorectal cancer is a common disease, especially in Western societies. In the United States alone, about 150,000 people are diagnosed with the disease every year. Most cases—about 95 percent—occur in people over age 50. Doctors know that if they can detect colon or rectal cancer at an early stage, they have a much better chance of curing the patient—sometimes with surgery alone.

Colonoscopy is the most thorough test available to find the disease. Through a narrow tube equipped with a tiny camera, doctors can search the entire length of the colon for tumors. This test even helps *prevent* colorectal cancer by finding and snipping out **polyps** that can develop into tumors.

Treatment Options

Today, doctors have a variety of ways to treat colorectal cancer. The standard treatment they often begin with is surgery to remove the section of colon containing the tumor.

Once the tumor is removed, doctors can determine how likely it is that the cancer will return. Largely, that depends on whether the tumor has passed through the wall of the colon or rectum or if tumor cells have spread to the **lymph nodes**. These nodes are small “filtering stations” that remove waste and fluids and help fight infection. From the jumping-off point of lymph nodes, cancer cells can spread throughout the body to form new tumors.

Even when a tumor is removed from the body, colorectal cancer can return a year or two later. That's because it is not always possible to remove every last cancer cell during surgery. But chemotherapy given *after* surgery can greatly reduce the chance of this disease coming back. Doctors have understood this since 1990, based on large **clinical trials** performed in the United States and Europe. Known as **adjuvant chemotherapy**, drug treatment after surgery has proved especially useful for patients with tumor cells in their lymph nodes.

New Drug Combinations

Within the past three years, a newer **regimen** called **FOLFOX** became available to treat colorectal cancer after surgery.

FOLFOX is made up of three drugs:

- 5-fluorouracil (5-FU)
- leucovorin (a form of the vitamin folic acid)
- oxaliplatin (Eloxatin)

Because of clinical trials, doctors now believe that FOLFOX is the best treatment for colorectal cancer after surgery. Most people using this combination of drugs have few side effects both during treatment and afterward. And FOLFOX can prevent colorectal tumors from coming back.

Colorectal Cancer Surgery

Usually surgery for colorectal cancer requires a large opening, or incision, in the abdomen. After such an operation, patients typically spend up to a week in the hospital. But some colorectal cancers can be removed by **laparoscopic surgery**, in which a smaller incision is made and a small camera is placed into the abdomen along with miniaturized surgical instruments. In that way, the surgeon can see the tumor and remove it. Doctors don't know whether this method gives better results than conventional surgery in the long run, but the side effects are fewer and recovery is faster.

Getting Adjuvant Chemotherapy

To rid the body of any cancer cells that may have been left behind after surgery, patients receive chemotherapy:

- on an outpatient basis (no hospital stay needed);
- usually over a 6-month period;
- with office visits to the doctor two to three times a month during that period.

What about people whose cancer has already spread to other organs when their colorectal tumor is first discovered? Or those whose tumors return after surgery and spread throughout the body—for instance, to the liver or lungs? What can be done to help them? These patients also need chemotherapy. For their **metastatic** or **disseminated cancer**, doctors offer either FOLFOX or another combination known as **FOLFIRI**, which consists of 5-FU, leucovorin, and irinotecan (Camptosar).

After the first treatments with these regimens, tumors shrink about 50 percent, and many symptoms caused by the tumors fade away. When chemotherapy reduces tumors, doctors can treat them with surgery or radiation, aiming at a cure. The result is that today, people with colorectal cancer are living much longer with a better quality of life.

Targeted Treatments

Since early 2004, the U.S. Food and Drug Administration (FDA) has approved a number of new drugs for colorectal cancer treatment. These agents are not like traditional chemotherapy drugs, which attack tumors but harm healthy tissues as well. The new drugs work by specifically targeting colorectal cancer cells. These targeted treatments stem from our better understanding of what makes cancer cells grow. To rid the body of tumors, they take advantage of subtle differences between cancer cells and normal cells.

BLOCKING AGENTS

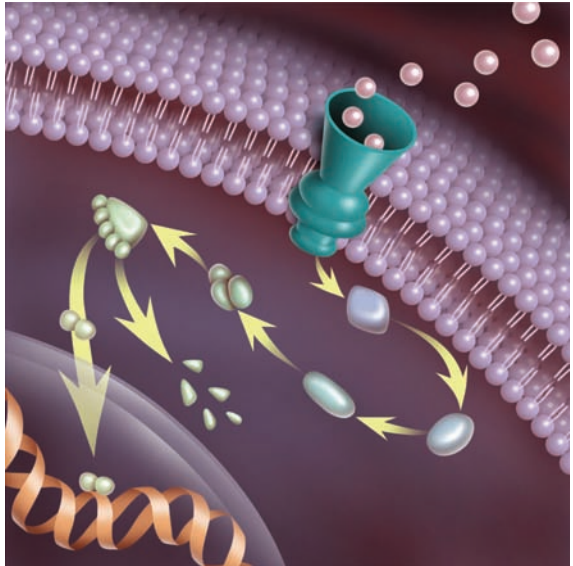
Two drugs—cetuximab (Erbix) and panitumumab (Vectibix)—are designed to bind up, or block, a **receptor** on a colorectal cancer cell. On each cell's surface, the job of receptors is to serve as docking stations or portals for specific molecules. The molecules that enter help the cell function or grow.

In this case, the receptor in question receives epidermal growth factor. Hence, it is known as **epidermal growth factor receptor**, or **EGFR**. When growth factor enters the cell via the EGFR, it encourages the cell

to grow, divide, and possibly spread as cancer. By binding to the EGFR, cetuximab and panitumumab prevent the receptor from taking in growth factor—and thus prevent the cell from growing into a tumor.

Because cetuximab and panitumumab specifically target cancer cells, generally they do not have the toxic side effects, such as nausea and vomiting, of many anti-cancer drugs. They can cause an acne-like skin rash or other allergic reactions, but generally not more than that.

The FDA approved these drugs for use in colorectal cancer that has **metastasized** (spread to other parts of the body).



On the surface of the cancer cell, a receptor (shown here as a funnel) provides an entry point for epidermal growth factor. This growth factor encourages cells to grow, divide, and possibly spread as cancer.

But scientists are beginning to explore using cetuximab, for instance, against earlier forms of the disease in the hope that it can prevent colorectal tumors from coming back. Finding the answers to this cancer is the strongest argument for conducting clinical trials (see the box at right).

STARVING TUMORS

Another drug for advanced colon or rectal cancer is bevacizumab (Avastin), which takes advantage of one of the things we know about how tumors grow. Tumors need to have a blood supply, much like normal tissues.

Blood vessels grow in several ways. One way is through the presence of a protein called **vascular endothelial growth factor**, or **VEGF**. This protein stimulates blood vessels to grow into tumors. When tumor cells spread through the body, they release VEGF to create new blood vessels. These blood vessels supply oxygen, minerals, and other nutrients to feed the tumor. Bevacizumab works by stopping VEGF from stimulating the growth of new blood vessels in tumors. Because normal tissues have an established blood supply, they are not affected by the drug.

The side effects of bevacizumab are generally mild. It may slightly increase the likelihood of a blood clot. It also sometimes raises blood pressure, which can be controlled with common high blood pressure drugs.

Managing Side Effects

In recent years the experience of chemotherapy has dramatically improved. In the past, some patients simply opted out of chemotherapy; they preferred to take their chances, rather than experience the toxic side effects of cancer treatment. But today, doctors have medications available to reduce and even prevent these symptoms. You do not have to “suffer in silence.” Talk to your doctor if you experience:

Nausea or vomiting There are drugs available to prevent

The Importance of Clinical Trials

There's no question that clinical trials have led to huge advances in cancer treatment, creating a brighter future for all people with cancer. Clinical trials are the gold standard by which we measure the worth of new treatments and quality of life as patients go through those treatments. For this reason, doctors and scientists urge patients to take part.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things you should know:

- The first patients to gain access to and benefit from new treatments are those who take part in clinical trials.
- Before you participate in a trial, you will be fully informed as to the risks and benefits of the trial.
- No patient receives a placebo or “dummy pill” if there is a standard treatment available for the disease. Most trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any additional benefit.
- You can stop taking part in a clinical trial at any time for any reason.

vomiting and quell a queasy stomach and the “anticipatory nausea” that can occur even before chemotherapy starts.

Loss of appetite Steroid medications can increase muscle and weight gain and stimulate the appetite.

Fatigue If the source of the fatigue is anemia (a low red blood cell count) or an infection, your doctor can treat that with specific medicines. Other techniques, such as taking a quick nap or doing gentle exercise, can help overcome the feeling of weariness.

Pain Pain is a symptom that can and should be managed. Some patients worry they'll become addicted to pain medications, but that belief is mistaken. New pain medications and new methods of delivering pain medicine—through a

patch, a lozenge, or a surgically implanted device—can offer relief. A procedure that blocks pain nerves has also proved highly effective.

The New “Normal”

When you’re first diagnosed with colorectal cancer, it can be like suddenly finding yourself in an unfamiliar environment. The language is new, the customs aren’t clear, you’re not sure what to expect from those around you. You and your family can feel a swirl of emotions.

The key to finding your way is to gather information and ask for help so you can make the best decisions for yourself. Here are some ways to navigate around this new terrain:

Do your research The Internet is a great place to start, but even if you’re not computer savvy, a lot of information is available through the mail and by telephone. Organizations such as CancerCare offer free—and reliable—information. Visit www.cancerca.org or call 1-800-813-HOPE (4673). CancerCare has worked with the American Society of Clinical Oncology on a website called People Living With Cancer (www.plwc.org). For more resources, see page 16.

Take your time You have some difficult medical decisions to make. Don’t rush. When you’re first diagnosed, or even if your cancer has come back, you may feel the need to act immediately. But you do have a window of time. Don’t let anybody stampede you into choices that you don’t feel comfortable with.

Speak up When you talk with your doctor, it’s important to remember: he or she is the expert in biology and medicine, but you are the expert about your own life. Don’t be afraid to bring up any topic of concern to you. Your doctor can’t treat a problem if you don’t make him or her aware of it. Doctors now understand, better than ever before, that patients are concerned about good quality of life as they go through treatment.

Questions to ask your doctor:

- What is the long-term treatment plan?
- Has there been research on this treatment?
- What are the risks and benefits of my treatment?
- What are the likely side effects?
- Who is the key nurse or doctor I can talk with if there's a problem?

Realize that it's normal to undergo changes Colorectal cancer can affect a person in body and spirit. It can affect how you see yourself and think about your future. Some medications and treatments can cause you to lose interest in your usual activities.

It's perfectly normal to feel sad, angry, scared, or frustrated by all this, but the more you learn about your condition, the better you'll be able to cope.

Seek the help of a social worker or an oncology nurse practitioner People and their families who are coping with a cancer diagnosis need someone to talk with

who can help them sort through all the complex emotions and issues that arise. These health care professionals can provide emotional support, help you manage your treatment and its side effects, and guide you to other resources. CancerCare offers free counseling from professional oncology social workers on staff.

Join a support group You and your family members may benefit from a support group, which can reduce the sense of isolation, the feeling that you are going through cancer alone. Support groups focus on coping and living with a cancer diagnosis. They provide role models, reassurance, suggestions, and insight, allowing you to share similar concerns with your peers in a safe and supportive environment.



Frequently Asked Questions

Q After surgery and chemotherapy for colorectal cancer, what are the best tests for seeing if the cancer has returned? How often should these tests be taken?

A After surgery, patients receive a **CT scan** of the chest, abdomen, and pelvis as a “before picture” to compare against later CT scans. During the first year after treatment, patients generally see their oncologist every two months for blood tests that include:

- the number of red and white blood cells and platelets;
- measurement of liver enzyme levels; and
- a test for CEA (carcinoembryonic antigen), a marker for colon cancer.

For the next two years after treatment, it’s standard for patients to see their doctor every two to three months to continue these tests.

During the first and second years, patients should also get a colonoscopy to make sure there are no other polyps.

After the second year, colonoscopies should be done every three years or so in people who have had surgery to remove a colon or rectal tumor. Unless there is some abnormality in the blood work, further CT scans aren’t needed.

Q What type of treatment is recommended for someone with cancer that has spread beyond the colon?

A People whose tumor has metastasized can be treated with the most aggressive chemotherapy—FOLFIRI or the FOLFOX combination of drugs plus bevacizumab (Avastin). Typically, these patients receive CT scans every two to three months to find out whether the chemotherapy is working and the tumor is shrinking or whether another treatment is needed.

Q Between cetuximab (Erbix), panitumumab (Vectibix), and bevacizumab (Avastin), is one better than the other?

A Cetuximab has been effective in about 25 percent of patients with colorectal tumors for whom chemotherapy did not work. Doctors are beginning to use cetuximab now at a much earlier stage in the disease and with first-line chemotherapy in advanced cancer. Panitumumab works in a similar way to cetuximab. In terms of effectiveness, there doesn't appear to be any significant difference between the two. One advantage of panitumumab is that it only needs to be given every two weeks, whereas cetuximab must be given weekly. In terms of bevacizumab, at first it was used only in patients whose disease returned. Now, doctors are starting to use it with chemotherapy after a tumor has been surgically removed to try to prevent a recurrence. Researchers continue to study all of these drugs, so it is a work in progress.

Q I've had part of my liver removed because of a colon tumor that spread. If the cancer recurred in my liver, could the surgeons remove more of that organ?

A One of the most common places for a colorectal tumor to spread is the liver, which happens to be one of the few organs that actually regenerates. That means that if you take out part of the liver, over time it grows back. You can have repeated **resections** of liver tumors if they recur.

Q What are the other options, aside from cutting out a metastasized tumor in the liver?

A In a technique known as "radiofrequency ablation," the surgeon inserts a probe into the tumor that emits microwaves to burn it away. Doctors also use a technique called SIRT (Selective Internal Radiation Therapy) to treat liver tumors. Tiny beads that contain a radioactive element are injected through

a catheter (tube) directly into the liver. There, they deliver their dose of radiation to kill the tumor. A different approach is to inject alcohol into small liver tumors to destroy them. Choosing the best procedure for each patient depends on a number of factors, including where the tumor lies in relation to major blood vessels in the liver.

Q In cases of colon cancer with lung metastasis, what do doctors recommend when the tumors show up on a CT scan, but they're too small to biopsy?

A In cases like this, doctors can perform a procedure called **bronchoscopy** to look inside the air passages leading to the lungs to see whether a biopsy can be done. Sometimes, doctors have to just wait and see whether the spots grow larger. Doctors also look for markers in the blood that would indicate these tumors are in fact metastatic colorectal tumors. If so, they can be treated with the FOLFOX or FOLFIRI chemotherapy regimens or with FOLFOX plus bevacizumab.

Q Are there any new treatments for patients with hereditary nonpolyposis colorectal cancer (HNPCC)?

A The search is on. Between two and four percent of all colorectal cancers are due to HNPCC. In families who carry the genetic mutation for HNPCC, colorectal cancer is much more common than in the general population and typically occurs among people in their 30s and 40s. Their tumors behave differently from non-hereditary colorectal cancers, but, overall, the prognosis is better—the tumors don't seem to spread as frequently as other colorectal tumors. However, they may not respond as well as a non-hereditary colorectal tumor to standard chemotherapy. So researchers are looking for other types of drugs to treat HNPCC. By better understanding the genetics of this type of tumor, we can better treat it.

Q Can diet, exercise, or vitamin supplements affect my risk of getting colorectal cancer?

A Colorectal cancer is more common among people in wealthier societies who eat more meat. So decreasing the amount of red meat you eat may be helpful. There is some evidence that exercise also decreases the risk of colon cancer. That may be because people who exercise regularly probably eat a more healthful diet. As far as supplements go, there is some evidence that suggests vitamins A, C, E, folic acid, calcium, and multivitamins can reduce the risk of colon cancer. On the other hand, research also shows that calcium may *increase* the risk of prostate cancer in men. The best course of action: Talk with your doctor and follow his or her guidelines for balanced eating.

Q Is it OK to take herbal remedies or vitamins during chemotherapy? Will they help?

A This is an important question because vitamins and products labeled “all natural” seem as though they should be harmless. But we know, for instance, that St. John’s wort—which some people use for depression—makes irinotecan (Camptosar) less effective. Before you take anything, consult with your oncologist. You can also look at a trustworthy website run by Memorial Sloan-Kettering Cancer Center that has information about all types of herbal supplements. Its address is www.mskcc.org/aboutherbs.

Q What’s coming down the pike for colorectal cancer in the next few years?

A Targeted therapies are going to be much more important. They will enable us to have more of an effect on cancer itself while causing fewer side effects. Ideally, of course, we’d like to cure this disease. But if we can control it, we could see people dying *with* their cancer at an old age, and not *because* of it.

Glossary

adjuvant chemotherapy The use of anti-cancer drugs after surgery to prevent the return of a tumor that has been removed surgically.

bronchoscopy Performed under anesthesia, this examination looks inside the air passages (“bronchi”) leading to the air sacs in the lungs. The doctor inserts into the nose a thin instrument with a light on the end.

CT scan CT stands for “computed tomography.” It’s a special type of x-ray study used to detect the spread of disease or track the progress of treatment.

clinical trials Research studies that test new treatments in patients, under carefully controlled conditions. Clinical trials are the gold standard by which doctors and scientists measure the worth of new therapies.

colonoscopy A screening test for colorectal cancer in which the doctor explores the colon and rectum through a narrow tube with a small light and camera.

disseminated cancer See **metastatic**.

EGFR Stands for “epidermal growth factor receptor,” a portal on a cell’s surface. When growth factor enters the cell via the EGFR, it encourages the cell to grow, divide, and possibly spread as cancer. The drugs cetuximab (Erbix) and panitumumab (Vectibix) block EGFR and the spread of colorectal cancer.

FOLFIRI A combination of three anti-cancer drugs: 5-fluorouracil (5-FU), leucovorin, and irinotecan (Camptosar). In addition to FOLFOX (see next page), this is an effective choice for treating advanced colorectal cancer.

FOLFOX A powerful combination of three anti-cancer drugs: 5-fluorouracil, leucovorin (a form of the vitamin folic acid), and oxaliplatin (Eloxatin), often used for the adjuvant treatment of colorectal cancer.

laparoscopic surgery In this procedure, surgeons are able to remove a tumor by making a small opening in the skin and operating through a tube inserted through the opening. A miniature television camera is placed into the abdomen through a tube so that the surgeon can see the tumor and remove it.

lymph nodes Small “filtering stations” that remove waste and fluids and help fight infection. When invaded by cancer cells, lymph nodes are a jumping-off point from which tumors can spread throughout the body.

metastasis The spread of cancer from its original tumor site to other parts of the body.

metastatic (metastasized) A tumor that has spread to distant parts of the body.

polyps Small pieces of usually benign (non-cancerous) tissue jutting out from the inner lining of the colon or rectum. A polyp can sometimes turn into a tumor if it is not removed.

receptor On each cell’s surface, the job of receptors is to serve as docking stations or portals for specific molecules. These molecules enter the cell to help it function or grow.

regimen A recommended program of drug treatment, describing what drugs will be used, in what doses, and how often they should be given.

resection Surgical removal, in this case, of a tumor.

VEGF A protein called “vascular endothelial growth factor.” This protein stimulates blood vessels to grow in tumors. When tumor cells spread through the body, they release VEGF and create new blood vessels to supply the tumor cells with oxygen, minerals, and other nutrients.

Resources

CancerCare

1-800-813-HOPE (4673)

www.cancercares.org

Colon Cancer Alliance

1-877-422-2030

www.ccalliance.org

Colorectal Cancer Network

1-301-879-1500

www.colorectal-cancer.net

The Jay Monahan Center for Gastrointestinal Health

www.monahancenter.org

National Colorectal Cancer Research Alliance

www.nccra.org

American Cancer Society

1-800-227-2345

www.cancer.org

People Living With Cancer

(Patient Website of the American Society of Clinical Oncology)

www.plwc.org

National Cancer Institute

Cancer Information Service

1-800-422-6237

www.cancer.gov



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The information presented in this patient booklet is provided for your general information only. It is not intended as medical advice and should not be relied upon as a substitute for consultations with qualified health professionals who are aware of your specific situation. We encourage you to take information and questions back to your individual health care provider as a way of creating a dialogue and partnership about your cancer and your treatment.

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Medical illustration on page 5 © Mark Lefkowitz Biomedical Visuals.

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