

A vertical strip on the left side of the page shows a microscopic image of colon cells, with various shades of red, orange, and purple.

Colorectal Cancer

Highlights from the 2009 Annual Meeting of the American Society of Clinical Oncology

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Every year in the United States, approximately 150,000 people are diagnosed with colorectal cancer. To help choose treatment options, doctors first determine the stage of colorectal cancer—that is, to what extent the cancer has spread in the body, if at all. In this chapter, we talk about the following stages:

- **Early-stage** colorectal cancer is a tumor that is in the lining (sometimes referred to as the “wall”) of the colon or rectum.
- **Locally advanced** colorectal cancer has spread beyond the colon or rectum to the surrounding tissue. The tumor also may have reached nearby structures or lymph nodes. (Lymph nodes are a linked system of small bean-shaped structures throughout the body that filter out and destroy bacteria and other harmful substances.) When cancer cells spread to the lymph nodes, they can travel from there to other parts of the body to form new tumors.
- **Metastatic** is the most advanced stage of colorectal cancer. This is when the cancer has spread from its original spot to distant parts of the body, such as the lungs or the liver.

Early-Stage Colorectal Cancer

PREDICTING RECURRENCE

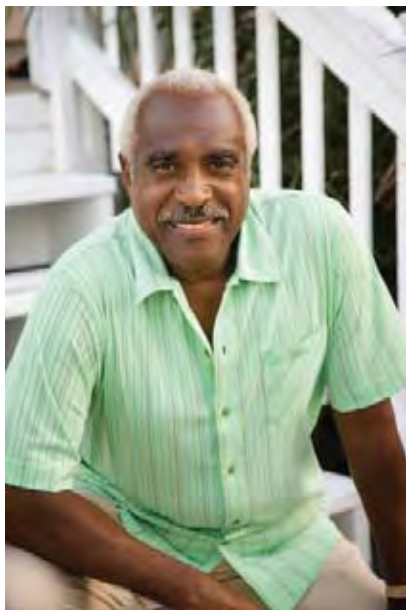
People treated for early-stage colorectal cancer seem to benefit from regular testing afterward to catch any recurrence early.

The standard treatment of colorectal cancer is surgery to remove the section of the colon containing the tumor. However, even when a tumor is removed from the body, colorectal cancer can return. Doctors have found that for people with advanced colorectal cancer who have already been treated, close monitoring with screening tests after surgery can help find any return of the cancer early. This allows the cancer to be treated again promptly, helping patients live longer. According to a new clinical study, such regular testing may also benefit people who have early-stage colorectal cancer.

Researchers studied the records of more than 850 people who had surgery years before for their colorectal cancer.

About two-thirds of them had early-stage colorectal cancer, and the others had late-stage colorectal cancer.

As expected, more people with late-stage colorectal cancer had recurrences five years after treatment than those with early-stage colorectal cancer (about 36 percent versus about 10 percent). However, there were similarities between



the two groups. For instance, the time it took for the first recurrence to appear was about the same for both groups—about one-and-a-half years. Also, in both groups, the cancer spread to the same places in the body, such as the liver or lungs.

Based on these results, researchers agreed that the outcomes of people with early-stage colorectal cancer might improve with regular testing to find any recurrence early. One of the recommended tests is the measurement of a substance called CEA (carcinoembryonic antigen), which is sometimes found in increased amounts in people who have certain cancers, such as colorectal cancer. Another way to test people for the return of cancer is a CT scan, which is a series of detailed x-ray pictures of areas inside the body taken from different angles.

A new genetic test may help doctors predict which people with colorectal cancer are more likely to have a recurrence.

If doctors could predict which people with colorectal cancer would be more likely to experience a recurrence of their cancer, they might be better able to decide who would benefit from additional treatment. One such “prognostic” test, the *Oncotype DX* breast cancer test, is already being used to help doctors decide which women with breast cancer are at a higher risk of their cancer recurring based on whether they have certain genes. The early results of an analysis of four large clinical trials show that a similar type of test may be able to do the same for doctors treating people with colorectal cancer.

Researchers used this genetic test for colon cancer to analyze more than 750 genes from about 1,400 people with early-stage disease. In these patients, the cancer had spread beyond the colon to the tissue that surrounds the colon but had not spread to the lymph nodes. These people were

treated with either surgery alone to remove their tumor or surgery plus chemotherapy.

Each person was given a recurrence score, based on the results of the genetic test. Then, doctors used the scores to help them decide the best treatment for that patient. For instance, patients who had a low recurrence score (about a 10 percent chance that the cancer would come back) would probably not be helped by chemotherapy and could thus avoid this treatment and its side effects. On the other hand, patients who had a higher recurrence score would be more likely to benefit from chemotherapy.



Researchers concluded that the results of the new genetic test may help doctors and colorectal cancer patients decide on the best treatment. This test may be available starting in 2010.

COMBINATION TREATMENT FOR EARLY-STAGE COLORECTAL CANCER

The combination treatment called FOLFOX6 still seems to be the best way to treat colorectal cancer after surgery.

The search for better cancer treatments sometimes leads researchers to try different drugs or combinations of drugs. They sometimes find that the newer treatment appears to be better than the standard treatment. However, they may also find that the standard treatment is still the best. That is what

happened in a recent clinical trial of treatments for colorectal cancer.

Over the past few years, doctors have believed that FOLFOX is the best treatment for 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 and others)

The name of this combination treatment sometimes changes when these three drugs are given in different doses or in different ways. For instance, the treatment may be referred

to as FOLFOX4, FOLFOX6, or mFOLFOX6.



Bevacizumab (Avastin), a targeted treatment, has been approved by the U.S. Food and Drug Administration (FDA) to treat colorectal, breast, and lung cancers that have spread to other parts of the body. (Unlike chemotherapy, targeted treatments block specific cell mechanisms that are thought to be important for cancer cell growth. Targeted treatments are meant to spare healthy tissues and

cause less severe side effects.) Researchers hoped that combining mFOLFOX6 with bevacizumab would be better than either treatment alone to help people go longer after surgery with no sign of the cancer.

More than 2,500 people with colorectal cancer took part in

this large clinical trial. This is the first study of bevacizumab added to standard chemotherapy after surgery for people with early-stage colorectal cancer. Half of them were treated with mFOLFOX6, and the others were treated with mFOLFOX6 plus bevacizumab.

The addition of bevacizumab did not increase the time it took for the tumor to grow and spread. But there was a brief benefit during the year of treatment with the combination. Some researchers believe that there may be better results if mFOLFOX6 and bevacizumab are given for more than one year. However, the FDA has not approved the use of bevacizumab in this way to prevent the return of colorectal cancer. So for now, mFOLFOX6 remains the best way to treat people with early-stage colorectal cancer after surgery.

Locally Advanced and Metastatic Colorectal Cancers

RADIATION AND CHEMOTHERAPY FOR LOCALLY ADVANCED RECTAL CANCER

Radiation and chemotherapy before surgery may improve the treatment of locally advanced rectal cancer.

Doctors often use radiation treatment with chemotherapy to shrink a tumor before surgery. Such treatment, which makes it more likely that surgery to remove the tumor will be successful, is called neoadjuvant therapy. According to the results of a recent clinical trial, neoadjuvant therapy may be an effective treatment for people with locally advanced rectal cancer.

Nearly 600 people who had locally advanced rectal cancer took part in this clinical trial. The promising neoadjuvant treatment consisted of radiation plus two chemotherapy drugs—capecitabine (Xeloda) and oxaliplatin. This combination treatment was given for five weeks. Then, six

weeks later, patients had surgery to remove their tumors. Shrinking the tumors before surgery was a more effective treatment than surgery alone.

Although this treatment did cause diarrhea in some patients, researchers were pleased to see that it did not interfere with the success of the surgery. They believe that this combination of radiation and chemotherapy may become a new standard of care for people with locally advanced rectal cancer.

PANITUMUMAB FOR METASTATIC COLORECTAL CANCER

The targeted drug panitumumab (Vectibix) plus the chemotherapy combination FOLFIRI may be a promising treatment for metastatic colorectal cancer.

For many people with metastatic colorectal cancer, standard chemotherapy is either ineffective or, after a while, stops working. In their search for ways to help these people, doctors have found that combining a new targeted treatment called panitumumab (Vectibix) with standard chemotherapy may be a safe new option.

More than 100 people with metastatic colorectal cancer have been given this treatment. It includes panitumumab and the chemotherapy combination known as FOLFIRI. FOLFIRI is made up of three drugs:

- 5-FU
- leucovorin
- irinotecan (Camptosar and others)

The final results of this study are not yet available. They should show whether clinical trial results with the panitumumab combination can increase survival for people with metastatic colorectal cancer.

BEVACIZUMAB AND EVEROLIMUS FOR METASTATIC COLORECTAL CANCER

When cancer no longer responds to bevacizumab treatment, adding everolimus (Afinitor) may be beneficial.

For many people with metastatic colorectal cancer, cancer may continue to grow after treatment with FOLFOX, FOLFIRI, bevacizumab, cetuximab (Erbix), or panitumumab. This type of cancer is said to be resistant to treatment. The cancer may be resistant at the beginning of treatment or may become resistant during treatment. There are few effective treatments for this type of cancer, but one promising combination is on the horizon.

Everolimus (Afinitor) is a new drug used to treat kidney cancer that is not responding to treatment with certain other anti-cancer drugs. It stops cancer cells from dividing and may block the development of new blood vessels that tumors need to grow.



In a small and early ongoing study, nearly 50 people with resistant metastatic colorectal cancer were treated with the combination of bevacizumab and everolimus. All of these patients had been previously treated with bevacizumab. The results so far show that for about five months, the cancer has remained stable, neither growing nor shrinking, in many patients.

Researchers are hopeful that this combination may be effective in treating tumors that have become resistant to

treatment with bevacizumab alone. Patients are continuing to join this study, and updated results are expected in the future.

SURGERY AND METASTATIC COLORECTAL CANCER TREATED WITH CHEMOTHERAPY

Most people who are treated with newer chemotherapy drugs may not need surgery for their metastatic colorectal cancer.

When people are first diagnosed with metastatic colorectal cancer, some doctors immediately treat them with surgery to remove the tumor and prevent complications. However, according to the results of a recent study, these people may not need to have surgery. They may be treated effectively with newer combinations of chemotherapies, such as irinotecan and oxaliplatin.

Researchers looked at the results of more than 200 people who were treated with chemotherapy (either FOLFOX or FOLFIRI) for metastatic colorectal cancer.

Ninety-three percent of these patients never developed complications that required surgery to remove the main tumor. The tumor did not block the intestines, create a hole in the wall of the

intestine, or cause bleeding. Of the seven percent who did eventually need surgery, most did not have any problems as a result of the surgery.

Based on this study, researchers believe that modern chemotherapy treatments such as FOLFOX and FOLFIRI may be the best way to treat people with newly diagnosed metastatic colorectal cancer. They also suggest that this



treatment approach without surgery should become the standard way to treat people who match the specific profile of those who took part in the clinical trial.

Please note: *Although the treatments discussed in this chapter are showing promise, most are still in clinical trials—some in earlier phases of research—and may not be available yet to the general public. Your doctor can help guide you as to which new medications could be right for you and whether you are eligible to take part in the clinical trials of these new treatments.*