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# Medical Update on Colorectal Cancer

## *Understanding KRAS*

Presented by

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*Learn about:*

- Advances in tumor research
- Personalizing treatment
- Coping with side effects
- How CancerCare helps



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# As we understand the KRAS gene better, personalized treatment for colorectal cancer is becoming possible.

In the United States, about 150,000 people are diagnosed with colorectal cancer every year. Studies show that between 1991 and 2005, survival rates for this cancer improved by 30 percent. And now doctors have developed a way to personalize treatment for patients, which they hope will further increase survival and improve quality of life.

In this new approach to treating colorectal cancer, doctors are moving away from “one-size-fits-all” treatments.



Instead, they are trying to determine the best approach for each patient based on his or her tumor’s genes, or genetic makeup.

Every cell in the body contains approximately 30,000 genes. These genes create a blueprint for the human body and its functions. In the same way, the cells of colorectal cancer tumors have their own distinct gene patterns.

As doctors learn more about these patterns, they are finding ways to predict how some patients will respond to certain

treatments. This kind of information helps doctors as they make decisions about what treatments to recommend.

## Treatment Options

### **SURGERY AND CHEMOTHERAPY**

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

When a tumor is removed, doctors determine how likely it is that the cancer will return. In part, this 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. The lymph nodes are small organs located throughout the body that remove waste and fluids and help fight infection. Once cancer cells reach the lymph nodes, they may metastasize, or spread, to form new tumors in other parts of the body. Chemotherapy given after surgery can significantly reduce the chance of colorectal cancer spreading.

For patients whose cancer has spread to the lymph nodes, the current standard of care is six months, or 12 cycles, of a chemotherapy combination called FOLFOX. This combination is composed of 5-fluorouracil (5-FU), leucovorin calcium (folinic acid), and oxaliplatin (Eloxatin and others).

For people with metastatic disease—that is, cancer that has spread beyond the colon or rectum to the liver or lungs, for example—doctors often treat with chemotherapy alone. In some cases, surgery may benefit patients with metastatic colorectal cancer.

### **TARGETED TREATMENTS**

Unlike chemotherapy, targeted treatments attack specific cell mechanisms thought to be important for cancer cell survival

and growth. This specific targeting helps to spare healthy tissues and causes less severe side effects. Bevacizumab (Avastin) is one type of targeted treatment used to treat colorectal cancer. Called a VEGF inhibitor, it works by cutting off the blood and oxygen supplies that tumors need to grow.

Cetuximab (Erbix) and panitumumab (Vectibix) are another type of targeted treatment called EGFR inhibitors. They work by blocking certain kinds of receptors, or “doorways,” found on the surface of cancer cells. These receptors allow substances to enter the cells and stimulate their growth. By blocking the receptors, drugs such as cetuximab and panitumumab prevent cancer cells from growing into larger tumors.

Doctors often combine chemotherapy with targeted treatments. Research shows such combinations are an effective way to kill cancer cells.

## **CLINICAL TRIALS**

Clinical trials offer an important treatment option for people with colorectal cancer. These studies play an especially vital role for patients with metastatic cancer whose standard treatment has not worked or is no longer working.

Doctors conduct clinical trials because they believe the drugs or techniques they are studying could be more effective or safer than the treatments they’re using now. This means that patients in the trials may have access to new cancer treatments and techniques (such as a better way of delivering treatment) before they are widely available.

People who take part in clinical trials also have the benefit of being very closely observed by their health care team. Clinical trials must follow a strict protocol, or plan, and researchers monitor patients closely so they can be sure that the information they get from the study is accurate and complete.

## Questions to Ask About Clinical Trials

If you are considering joining a clinical trial, there are a number of questions to ask, including:

- What is the purpose of the study?
- What kinds of tests and treatments are involved?
- How do the possible risks, side effects, and benefits of the treatment being tested in this study compare with my current treatment?
- How might this study affect my daily life?
- How many visits per week or month will I need to make?
- How long will the study last?
- Is a hospital stay required?
- Who will pay for the treatment? Will the trial sponsor or my insurance cover all or part of it?
- What will I need to pay for myself?
- Will I be reimbursed for related expenses such as transportation?
- What type of long-term follow-up care is part of this study?
- How will I know if the treatment being studied is working?
- Will the results of the trial be given to me?
- Who will be in charge of my care?
- Is there someone I can talk with about this study if I have more questions?



If you think you would like to take part in a clinical trial, ask your doctor or nurse about the trials available for colorectal cancer. You can also search online using the websites in our resource list on page 16. There are toll-free numbers available as well, so you can talk to someone who can guide you.

## Personalizing Treatment: The Role of KRAS

One important area of cancer research is understanding how tumor cells behave, what makes them grow and multiply, and whether they are likely to respond to treatment or return after treatment. Each tumor has its own biological profile, based on the genes found in its cells. Knowing more about that profile allows doctors, in some cases, to choose the right treatment for a particular tumor. This approach is much more effective than using the same treatment for everyone, because some treatments don't work for certain types of tumors.

To better understand what type of tumor a patient has, doctors look at its genes in search of "tumor markers." There are two main types of



markers. One is called a *predictive marker*. It predicts whether a given treatment will be effective against that type of tumor. The other type is a *prognostic marker*. It can tell what the likely outcome of treatment will be, and whether or not there is a high risk of the tumor returning.

A key tumor marker that has been found in colorectal cancer is the KRAS gene. Through clinical trials, researchers have



learned that people who have a mutation (or change) in the KRAS gene *do not* benefit from treatment with EGFR inhibitors, such as cetuximab or panitumumab. About 40 percent of all people with colorectal cancer have this mutation. However, having the KRAS mutation does not appear to affect the benefit these patients *do* get from chemotherapy.

The other 60 percent of people with colorectal cancer have what is known as the KRAS wild-type gene—a normal, unchanged form of the KRAS gene. These patients *do* tend to benefit from treatment with EGFR inhibitors.

Knowing whether you have a KRAS mutation or the KRAS wild-type gene is important to your health care team in deciding the best treatment for your specific type of cancer. Because people with KRAS mutations will not benefit from cetuximab or panitumumab, they need not waste valuable time taking those drugs. Instead, they can use other treatments that will be more helpful to them—or consider taking part in clinical trials.

Because tumor markers are such an important step on the road toward personalized medicine, researchers conduct many clinical trials on them. They are looking for new treatments that will work for people with KRAS mutations.

They are also continuing to study people with the KRAS wild-type gene. Even though most people in this group are more likely to benefit from EGFR inhibitors, not everyone does. Doctors need to understand why. There may be other tumor markers that can give clues as to what treatments will work best for these individuals.

## Managing Treatment Side Effects

To effectively treat any cancer, doctors must be able to give patients their full dose of medications, on schedule. But side effects of chemotherapy and targeted treatments can

# Keeping a Side-Effect Journal

When you keep a log of your side effects, you don't have to rely on your memory. Remember that specific information will help your medical team provide the best possible treatment. Having a written record makes it easier for you to discuss with your doctor or nurse any concerns you might have.

Here are some of the things you should record:

- When and where your symptom(s) occurs.
- Specifics about what it feels like.
- Whether anything seems to trigger the symptom.
- Whether anything makes the side effect feel better or worse.
- How much relief you are getting from medications or other methods you use.
- How the symptom is affecting your everyday life.



interfere with treatment. That is why it is so important to prevent side effects, or to treat them promptly if they do develop. If you are experiencing any side effects, you *can and should* seek help. If your doctor doesn't ask you about side effects, be sure to bring them up.

Here is a list of some common side effects and how they are prevented and managed:

**Nausea and vomiting** are common concerns when it comes to chemotherapy. But the management of these symptoms has improved so much that most patients are

able to avoid them. Doctors can prescribe a number of different drugs to prevent and reduce nausea and vomiting: ondansetron (Zofran and others), granisetron (Kytril and others), and dolasetron (Anzemet). These medications are usually given on the same day as chemotherapy. The steroid dexamethasone is also sometimes used, as is aprepitant (Emend).

**Infections** can result when the level of white blood cells drops as a result of chemotherapy. To raise the level of these blood cells, doctors sometimes prescribe medications such as filgrastim (Neupogen) or pegfilgrastim (Neulasta).

**Anemia**, caused by a lowered level of red blood cells, often occurs in patients with colorectal cancer who develop blood in the stool. It can be treated with prescription medications.

**Fatigue** (an extreme tiredness that isn't usually eased by sleep) is a main symptom of anemia.

**Blood clots** may affect some cancer patients. Blood clots occur when a solid mass of blood forms and lodges in a blood vessel or in the heart, for example. Blood clots are serious and may be life-threatening. Blood thinners such as warfarin (Coumadin and others) and medications known as LMWHs (low molecular weight heparins) effectively treat blood clots. For patients in the hospital who have had cancer surgery, doctors also use a mechanical cuff to prevent blood clots. The cuff is placed on the legs; it gently squeezes every few minutes to help keep blood flowing.



**Mucositis** (sores inside the mouth and on the lining of the throat and digestive tract) can result from radiation treatments and from some types of chemotherapy. Mucositis can be a serious problem because it can cause pain and

infections, making it difficult to eat, drink, and swallow. Once treatment ends, mouth sores do disappear. But before they fade, it's important that you work closely with your health care team to manage this side effect of cancer treatment with good oral care and prescription medications such as Gelclair or Miracle Mouthwash.

**Skin rash** and other bothersome skin and nail conditions often result from the use of EGFR inhibitors such as

cetuximab and panitumumab. The symptoms are actually a sign that these drugs are working. If you are taking EGFR inhibitors, talk with your health care team about the possible side effects and the various ways to treat them.



**Pain** can greatly affect your quality of life—that is, your daily activities, eating habits, ability to get a good night's sleep, and even your outlook and how you interact with others. But your health care team can help control cancer pain. Controlling different types of pain may require different approaches, which is why it is so important for your health care team to understand the cause of your pain and for you to have good communication with them.

## The Role of Diet and Exercise

Another part of personalizing your care is choosing the best diet and activity level for your own health. It's important to talk with your medical team, both during and after treatment, about which lifestyle changes may be right for you. Find out if your doctor has a registered dietitian (RD) on staff or can recommend one. RDs are experts in diet and nutrition and can advise you about eating right.

The information here should serve as a general guideline for healthy choices:

### EATING RIGHT

The most healthful diet is one that is low in fat and rich in plant foods. That means eating plenty of whole grains, vegetables, and fruits. With more of these foods in your diet, you increase the amount of fiber. Fiber is important for both preventing and managing constipation, which may result from some treatments or medications for side effects.

Diarrhea is another possible side effect of colorectal cancer treatment. Talk to your doctor or an RD about the right diet if you are experiencing diarrhea after receiving treatment. There are many foods that can nourish you without contributing to diarrhea. When you have diarrhea, be sure to drink extra fluids with electrolytes so that you do not get dehydrated. Electrolytes are the body's salts that must stay in balance in order for cells to work properly. Ask your doctor if sports drinks such as Gatorade would be helpful to you.

As you eat a more plant-based diet, you increase your intake of needed nutrients. So do you need to take vitamin supplements? Although most people get enough vitamins and minerals through their diet, many people take calcium in pill or liquid form because they find it difficult to maintain high enough levels of this important mineral. Calcium is most abundant in dairy and fortified soy products; low- and nonfat milk, yogurt, and cheese are recommended. If you cannot tolerate dairy or soy products, talk with your doctor and RD about



the exact amount and type of calcium supplement they recommend for you.

Many people also have trouble getting enough vitamin D. There is now some evidence that suggests vitamin D protects the body against colorectal cancer and may improve survival. However, before you take any supplements, consult with your medical team.

### **INCREASING YOUR PHYSICAL ACTIVITY**

Experts recommend that, ideally, everyone should try to engage in at least 30 minutes of physical activity each day.

The activity can be anything you enjoy doing: walking, swimming, riding a bike, or playing a sport such as golf or tennis. Of course, during cancer treatment, it may be necessary to have a lighter schedule of activity, especially if you feel fatigued. That is fine; go at your own pace. You will find that staying as active as possible can help you regain your energy.



Try to stay active for at least 10 minutes at a time and then build from there. Remember that increasing physical activity is a lifelong lifestyle change.

## **CancerCare<sup>®</sup> Can Help**

If you or a loved one has been diagnosed with colorectal cancer, contact CancerCare. We are a national nonprofit organization that provides free professional support to anyone affected by cancer. Our services are provided by oncology social workers and include individual counseling, support groups, education, financial assistance, and referrals. To learn more, call us at 1-800-813-HOPE (4673) or visit [www.cancercare.org](http://www.cancercare.org).

## Frequently Asked Questions

**Q Is there a promising treatment for people with the KRAS mutation?**

**A** In clinical trials around the world, researchers are looking for such treatments right now. The key is to study individual patient's tumor samples. These samples offer the best way to evaluate new medications. That is why it's so important for people with colorectal cancer to talk to their doctors about seeking out these clinical trials. The clinical trials process is the only way we are going to find new treatment approaches.

**Q During chemotherapy, do I need to eat more protein?**

**A** We know that if the body does not have enough nutrients, it is weaker and more susceptible to infection. Chemotherapy and the cancer itself can rob the body of nutrients. One way to manage this loss is by eating as much protein as possible. There are a number of recommended low-fat foods that contain lots of protein, such as beans, lentils, and quinoa (a high-protein, high-fiber grain).

Other high-protein foods include dairy products (preferably low- or nonfat), soy milk, tofu, edamame (baby soybeans), soy nuts, walnuts, almonds, cashews, and nut butters (such as almond or peanut butter). Chicken and turkey are also excellent protein sources, as is fish. Be sure that the fish and shellfish are well cooked. Small amounts of lean red meat are fine, too, especially if you need a good source of iron during treatment.

Of course, what you eat will depend on which foods you can tolerate. Sometimes, chemotherapy leaves a metallic taste in the mouth, making certain foods unpalatable. Try experimenting with protein shakes and other foods. By eating protein, you will help maintain your immune system and reduce some of the side effects of cancer and its treatment.

**Q Since I have been on oxaliplatin, my kidneys have been weakened. Is it likely that this medication is to blame, or could there be some other reason for it?**

**A** A decline in kidney function can be caused by a number of things. However, it rarely occurs as a result of taking oxaliplatin (Eloxatin and others). However, when other conditions such as high blood pressure are present, the kidneys can be affected. After rectal cancer treatment, especially if radiation is used, scar tissue can block the ureter, one of the tubes that lead from the kidneys to the bladder. Talk with your doctor. You may need to consult a kidney specialist (nephrologist).

Your question brings up another important issue, though: how doctors are able to make the right diagnosis for a particular problem. To narrow down the list of possible causes, doctors rely on tests they perform and the information that you provide about your symptoms—when they started and how they affect your daily activities, for example. They also take into account other illnesses that you may have at the same time. Doctors call this making a differential diagnosis—that is, ruling out what *is not* causing the symptom in order to find out what *is* causing it.



**Q What are multidisciplinary health care teams, and why are they important?**

**A** Sometimes, it takes many specialties or “disciplines” within medicine to evaluate a problem and manage it. This is especially true with cancer, where caring for patients is a complex process that requires a team approach. For people with colorectal cancer, a number of different types of medical issues often arise, each of which is best managed by a specialist. Patients may need a surgeon, medical oncologist, radiation oncologist, nurse, pain management expert, and a registered dietitian, for example. One member of the team—usually the medical oncologist—coordinates the care a patient receives from various members of the team.

Many people also need help coping with the emotional or practical concerns that come up during treatment. Oncology social workers, counselors, financial specialists, and other non-medical professionals are available to help. They also form part of the multidisciplinary team. CancerCare® can help you find resources in each of these areas. Call us at 1-800-813-HOPE (4673) or visit [www.cancercares.org](http://www.cancercares.org).

# Resources

## **CancerCare**

1-800-813-HOPE (4673)  
[www.cancer.org](http://www.cancer.org)

## **American Cancer Society**

1-800-227-2345  
[www.cancer.org](http://www.cancer.org)

## **Cancer.Net**

Patient information from the American Society of Clinical Oncology  
[www.cancer.net](http://www.cancer.net)

## **Cancer Support Community**

1-888-793-9355  
[www.cancersupportcommunity.org](http://www.cancersupportcommunity.org)

## **Colon Cancer Alliance**

1-877-422-2030  
[www.ccalliance.org](http://www.ccalliance.org)

## **National Cancer Institute**

1-800-422-6237  
[www.cancer.gov](http://www.cancer.gov)

## **National Library of Medicine (MedlinePlus)**

[www.medlineplus.gov](http://www.medlineplus.gov)

## **To find out about clinical trials:**

Coalition of Cancer Cooperative Groups  
[www.CancerTrialsHelp.org](http://www.CancerTrialsHelp.org)

National Cancer Institute  
[www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials)



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