



Cancer Reference Information


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Detailed Guide: Colon and Rectum Cancer Chemotherapy

Use of chemotherapy after surgery can increase the survival rate for patients with some stages of colon cancer and rectal cancer. This is called *adjuvant* (additional) chemotherapy. It is given when there is no evidence of cancer but there is a chance that it might come back. Chemotherapy can also help shrink tumors and relieve symptoms of advanced cancer. This is called *palliative* chemotherapy.

Systemic chemotherapy uses anticancer drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body. This treatment is useful for cancers that have metastasized (spread) beyond the organ they started in. In *regional chemotherapy*, drugs are injected directly into an artery leading to a part of the body containing a tumor. This approach concentrates the dose of chemotherapy reaching the cancer cells. It reduces side effects by limiting the amount reaching the rest of the body. *Hepatic artery infusion* is an example of regional chemotherapy sometimes used for colon cancer that has spread to the liver.

Fluorouracil (5-FU) is the drug most often used to treat colon cancer. In adjuvant therapy, it is often given together with another drug, *leucovorin*, which increases its effectiveness. In the past, 5-FU was usually injected slowly into a vein over about 5 minutes and then followed by the leucovorin. These injections were given daily for 5 days, followed by 3 weeks off chemotherapy or weekly for 6 weeks, followed by 2 weeks off treatment.

Recently it has been found that a different way of giving these drugs may be better. In this regimen, called the de Gramont regimen, the 5-FU is given continuously over 2 days as well as by rapid injection on the first day. The leucovorin is given on the first and second day over 2 hours. The de Gramont regimen is given every other week.

In all of these schedules, alternating periods of treatment and recovery are repeated over a period of 6 months to 1 year. In some regimens the 5-FU is

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given continuously and patients wear a small battery-operated pump that continuously infuses 5-FU into an intravenous catheter. Leucovorin and 5-FU are also used for palliative treatment (to control the growth of the cancer or relieve symptoms). Generally, 5-FU/leucovorin is given for 6 months.

Capecitabine (Xeloda) is an oral chemotherapy drug that is changed to 5-FU once it gets to the tumor site. This drug can be used instead of intravenous 5-FU and acts as if the 5-FU were being given continuously. The side effects of treatment with this drug are nausea, diarrhea, and a syndrome of hand and foot redness that is sometimes accompanied by skin peeling.

Irinotecan (Camptosar) is often used to help control colorectal cancer. It formerly was used in patients no longer responding to palliative 5-FU therapy. But it has been found that irinotecan combined with 5-FU and leucovorin is more effective than 5-FU and leucovorin alone as the first treatment in people with metastatic colorectal cancer, so it is now often used as the first treatment in this situation. This combination may also be more effective as an adjuvant therapy after surgery. Clinical trials have begun to study whether irinotecan would be effective in preventing recurrence.

Although adding irinotecan to the standard chemotherapy combination of 5-FU and leucovorin makes the treatment more effective, it may also make your side effects (such as diarrhea, nausea, and low white blood cell counts) more severe. Irinotecan can cause severe diarrhea, so you must tell your doctor right away if you develop diarrhea. Your doctors may not recommend irinotecan if you are elderly or have other serious health problems. If these severe side effects are uncontrolled, they may lead to death.

These side effects are not as much a problem in patients who do well with the first treatment. If you are already on this combination and have not had any major problems, you are probably safe.

Oxaliplatin (Eloxatin) is another drug recently approved by the FDA for use in colorectal cancer. Oxaliplatin is very effective when combined with 5-FU and leucovorin (LV). The major side effect of oxaliplatin is that it causes numbness and tingling -- and extreme sensitivity to temperature -- in various parts of the body, mostly arms and legs. This can last for months but almost always goes away.

Patients with more advanced cancers, which includes some with stage II and all with stage III have a higher chance that the cancer will return, often at a distant site. Many clinical trials have tested different combinations of drugs to prevent this recurrence. The most effective adjuvant treatment seems to be a chemotherapy combination called FOLFOX (*Folinic acid, 5-FU, Oxaliplatin*). This is a combination of 5-FU and leucovorin (also called folinic acid) given by the de Gramont method along with oxaliplatin. Another regimen gives the 5-FU and leucovorin weekly by rapid intravenous infusion along with the oxaliplatin. Although this may be as effective as FOLFOX 4, it appears to have more side effects, mainly causing severe diarrhea. Other regimens that may be used are combinations of 5-FU and leucovorin.

Side effects of chemotherapy: Chemotherapy drugs kill cancer cells but also damage some normal cells. Your doctor and other health providers can help to avoid or minimize side effects, which will depend on the type of drugs, the amount taken, and the length of your treatment. You might temporarily experience nausea and vomiting, loss of appetite, loss of hair, hand and foot swelling and rashes, and mouth sores. Diarrhea can be troubling, especially if you are receiving irinotecan (Camptosar), but it can also occur with 5-FU/leucovorin treatment. Nerve damage from oxaliplatin can also be troubling but eventually disappears.

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Because chemotherapy can damage the blood-producing cells of the bone marrow, you may develop low blood cell counts. This can result in an increased chance of infection (due to a shortage of white blood cells), bleeding or bruising after minor cuts or injuries (due to a shortage of blood platelets), and fatigue (due to low red blood cell counts). Please talk with your doctor if you have any unrelieved side effects.

Most side effects disappear once treatment is stopped. Your hair will grow back after treatment ends, though it may look different. There are remedies for many of the temporary side effects of chemotherapy -- for example, *antiemetic* drugs that can prevent or reduce nausea and vomiting.

Elderly people seem to be able to tolerate chemotherapy for colorectal cancer. There is no reason to withhold treatment in otherwise healthy people because of age.

Targeted Therapies

Targeted therapies are those that specifically attack some part of cancer cells that make them different from normal cells. Because of this, they should cause fewer side effects than chemotherapy drugs.

Cetuximab (Erbix) was the first targeted therapy approved for treating colorectal cancer. It is a manmade protein called a monoclonal antibody that specifically attacks the epidermal growth factor receptor (EGFR), a molecule that often appears in high amounts on the surface of cancer cells.

The FDA has approved cetuximab for use with irinotecan or without irinotecan in those who can't take irinotecan or whose cancer is no longer responding to it. In about 10% of patients whose cancers continue to grow despite other treatments, cetuximab will cause tumor shrinkage. This figure is doubled when cetuximab is combined with irinotecan, even if the patients have already been treated with irinotecan and are no longer responding.

Cetuximab is given by intravenous injection. The most serious side effect of cetuximab is an allergic reaction during the first infusion, which could cause problems with breathing and low blood pressure. Other less serious side effects may include an acne-like rash, dry skin, tiredness, fever, and constipation.

Bevacizumab (Avastin), another monoclonal antibody, is approved for first-line use against metastatic colorectal cancer. It is used along with chemotherapy drugs. This antibody is directed against vascular endothelial growth factor (VEGF), a protein that helps tumors form new blood vessels to get nutrients (a process known as angiogenesis). In one study, when bevacizumab was given along with an irinotecan-containing chemotherapy regimen, it increased the shrinkage rate in tumors by 30% compared to patients who were given the same chemotherapy without bevacizumab. It also nearly doubled the time it took for the tumors to grow back. Bevacizumab is the first anti-angiogenesis drug approved to treat colorectal cancer. It is given by intravenous infusion.

Rare but possibly serious side effects include bleeding, holes forming in the colon (requiring surgery to correct), and slow wound healing. More common side effects include high blood pressure, tiredness, blood clots, low white blood cell counts, headaches, mouth sores, loss of appetite, and diarrhea.

Clinical trials are in progress that are testing whether adding either bevacizumab or cetuximab to chemotherapy will further lower the chance of

recurrence.

Cost of Drugs

Some of the cancer drugs described are very expensive. 5-FU and leucovorin are inexpensive, but 8 weeks of treatment with a combination that includes oxaliplatin or irinotecan and either bevacizumab or cetuximab will cost at least \$20,000-30,000. Patients on Medicare without any other insurance will need to pay for 20% of this cost.

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