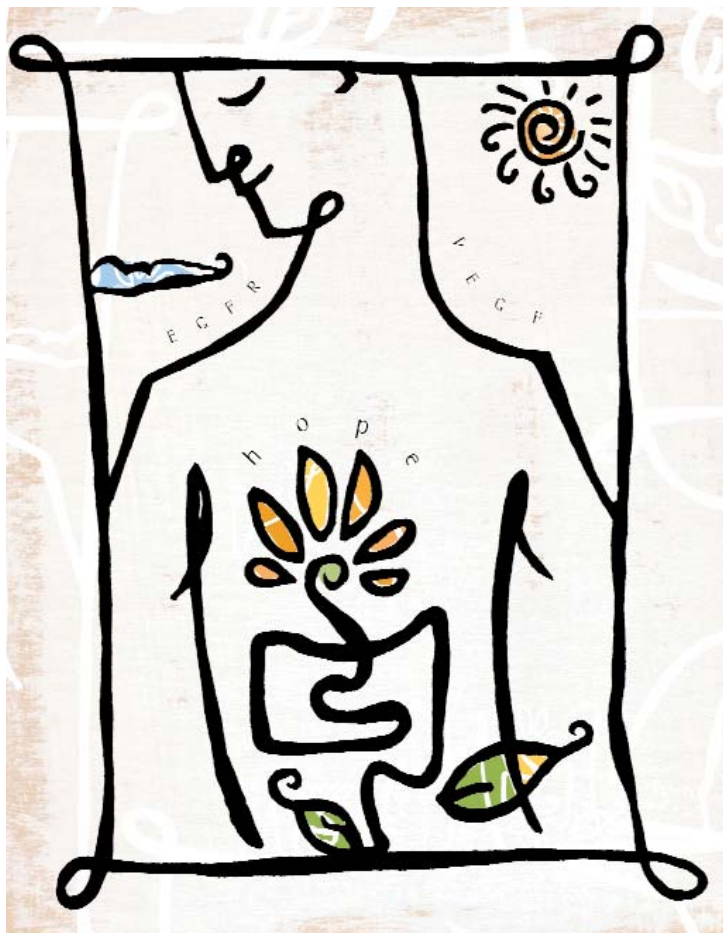


A Patient's **Guide** to **Colorectal Cancer**



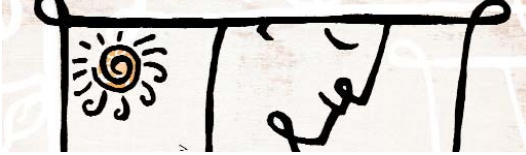
Screening ■ **Treatment Overview** ■ **Chemotherapy Drugs** ■ **Side Effects**
■ **Clinical Trials** ■ **Questions To Ask** ■ **Staging** ■ **Resources** ■ **and More**

cure
CANCER UPDATES, RESEARCH & EDUCATION

Based on science, but filled with humanity,
CURE makes cancer understandable.

QUESTIONS TO ASK YOUR ONCOLOGIST

- 1.** Explain my diagnosis to me. What is staging and why is it important?
- 2.** What are my treatment options?
- 3.** What are the benefits and risks of each treatment option?
- 4.** What are the side effects of each treatment? How can these side effects be managed/prevented?
- 5.** Are there any new treatments available? Should I participate in a clinical trial?
- 6.** Do you recommend a second opinion?
- 7.** What follow-up testing do I need after completing treatment?
- 8.** What are my options if the cancer comes back?
- 9.** How will treatment affect my quality of life? Should I make any lifestyle changes?
- 10.** Will I have bowel problems? Should I speak to a registered dietician?
- 11.** Who at your office can I contact if I have questions or concerns?
- 12.** Is my cancer caused by genetic factors? Do you recommend genetic counseling?
- 13.** Can you recommend any local support groups or emotional/financial/spiritual resources?



A Patient's Guide to Colorectal Cancer

MORE THAN 100,000 Americans are diagnosed with colon cancer each year and an additional 42,000 are diagnosed with rectal cancer. Colorectal cancer remains the fourth most common cancer in the United States, excluding skin cancers. However, new medicines and new combinations show great promise in fighting the disease. **This guide will provide you with the information you need if you've just been diagnosed with colorectal cancer** or if you or a family member are at risk for the disease. By educating yourself about colorectal cancer and the available options, you can make informed decisions about your care.

What is colorectal cancer?

FOOD BEGINS IN THE STOMACH and moves to the small intestine. From there it moves through the cecum, which connects the large and small intestines, and into the large intestine. The first part of the large intestine is called the ascending colon, followed by the transverse colon. The sigmoid colon, the last part of the small intestine, empties into the rectum, the last 4 to 5 inches of colon, before it ends at the anus.

The colon is divided into four layers of tissue: the mucosa (the most superficial layer that comes in contact with the colonic contents and stool), the submucosa (lies just below the mucosa), the muscularis mucosa (the muscular layer) and the outer layer called the serosa. Most colorectal cancers start as a polyp in the mucosa, which, if detected and removed early, will prevent it from becoming cancer.

Some common symptoms of colorectal cancer include:

- ▶ A change in bowel habits
- ▶ Diarrhea, constipation or feeling that the bowel does not empty completely
- ▶ Blood (either bright red or very dark) in the stool
- ▶ Stools that are narrower than usual
- ▶ General abdominal discomfort (frequent gas pains, bloating, fullness and/or cramps)
- ▶ Unexplained weight loss
- ▶ Abdominal and pelvic pain

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Since other health problems can cause the same symptoms, anyone with these symptoms should see a doctor so that any problem can be diagnosed and treated as early as possible.



Screening Options

POLYPS, small growths in the colon, are usually benign but can become cancerous over time.

Finding and removing polyps may prevent colorectal cancer, and treatment is likely to be more effective when the disease is found early. Generally, people age 50 and older should be screened for colorectal cancer and polyps. Those at higher-than-average risk due to a family history of colon cancer, a history of ulcerative colitis or other risk factors should talk to their doctor about whether to undergo screening before age 50.

Fecal occult blood test (FOBT)

This test checks for presence of blood in the stool, which may be the first sign of a bleeding polyp or cancer. Using a home kit, you collect stool smears and send them to your doctor or lab for analysis. If properly done, FOBT can detect about 50 percent of colorectal cancers. The test is relatively non-specific and needs to be followed by a sigmoidoscopy or colonoscopy if positive.

Frequency: Annual

Flexible sigmoidoscopy

This test examines the bottom 10 inches of the colon and rectum using a sigmoidoscope, a thin, flexible tube typically fitted with a tiny video camera to display images. A biopsy of suspicious lesions can be obtained at the same time. It can be done in the physician's office without sedation.

Frequency: Every five years

Colonoscopy

Considered the gold standard, colonoscopy uses a long, flexible tube to examine the

entire colon. Polyps can be biopsied or removed during the procedure. Preparation includes extensive cleaning of the colon using laxatives. The procedure causes minimal discomfort and can be done as an outpatient procedure using a mild sedative.

Frequency: Every five to 10 years

Virtual colonoscopy

This procedure takes a series of X-ray images of the colon and rectum and turns them into multi-dimensional views with computer software. Air is introduced into the colon to distend it and an oral contrast substance is administered. If a polyp is found, colonoscopy must be performed to confirm its presence and remove it. This test is still considered investigational.

Frequency: Every five to 10 years

DNA stool testing

Ultra-sensitive lab tests can detect changes in the DNA of cells shed from polyps or cancers into stool, without the need for invasive scopes. Positive results would trigger colonoscopy for further evaluation. No special diet, medication changes or bowel preparation are required, and studies have shown these tests, which are still investigational, can detect 50 to 60 percent of colorectal cancer cases.



Staging Colon Cancer

STAGE 0 (carcinoma in situ)

As the most superficial of all the lesions, it is limited to the lining of the colon or rectum. These cancers are usually detected in a polyp that has been removed using a colonoscope. These are almost always considered curable.

STAGE 1

Cancer has spread from the mucosa down to the muscularis mucosa layers, but is still within the colon or rectum. Cancer has not spread to either the lymph nodes or outside of the colon. These lesions are treated by surgery (without the need for chemotherapy) and have a cure rate of as high as 93 percent.

STAGE 2

Divided into two subcategories, surgery is the primary treatment for this stage, although some patients with stage 2B disease may be considered for chemotherapy after surgery (called adjuvant chemotherapy).

2A: Cancer has grown close to but not penetrated the outermost layer (serosa) of the colon. It has not spread to the lymph nodes. Five-year survival rate is up to 84 percent.

2B: The cancer has grown through the outer layer of the colon into nearby tissues or organs. It has not yet spread to the lymph nodes or distant sites. Five-year survival rate is about 72 percent.

STAGE 3

This stage is divided into three subcategories with all stage 3 patients treated with a combination of surgery

followed by six or more months of chemotherapy.

3A: The cancer has grown close to but not penetrated the outermost layer of the colon and has also spread to one to three nearby lymph nodes but not distant sites. Five-year survival rate is about 80 to 85 percent.

3B: The cancer has grown through the wall of the colon into nearby tissues or organs and has also spread to one to three nearby lymph nodes but not distant sites. Five-year survival rate drops to 64 percent.

3C: Once the cancer has spread to four or more nearby lymph nodes but not distant sites, it is considered stage 3C. Five-year survival rate drops further to 44 percent.

STAGE 4

This is the term given to advanced cancer that has spread to distant organs, such as the liver and lungs. These patients are primarily treated with chemotherapy, including biological agents such as Avastin™ (bevacizumab) and Erbitux™ (cetuximab).



Surgical & Other Invasive Treatment Options

Surgical removal of the tumor, along with adjacent parts of the colon and the draining lymph nodes (called a partial colectomy) is the primary treatment for all stages of colon cancer.

After removal of the cancerous areas, the surgeon performs an anastomosis (sewing the healthy parts of the colon together). Colostomy, in which stool is diverted through a hole in the abdomen after removal of part of the colon, is less frequently done. If a colostomy is needed at the time of surgery, most patients can undergo closure of the colostomy a few months after surgery, thus obviating the need for a long-term colostomy bag. Even if the doctor removes all visible cancer during the operation, some patients may be given chemotherapy or radiation after surgery to kill any remaining cancer cells.

LAPAROSCOPIC COLECTOMY:

This newer surgical technique is less invasive but possibly just as effective as traditional open surgery. The procedure involves a video endoscope and other surgical instruments being inserted into the abdomen through four or five very small incisions. These instruments are then used to remove the part of the colon with the adjacent lymph nodes as well as reconnect the remaining sections of the colon.

HEPATIC RESECTION:

This procedure is used to remove colon cancer deposits that have reached the liver. It can usually be done in patients with fewer than five deposits that are not too

large and are located in one lobe of the liver.

RADIOFREQUENCY ABLATION:

This is a new technique used to shrink tumor deposits in the liver that are either too big or too numerous for surgical resection. A special probe with tiny electrodes is introduced into the tumor using ultrasound or computed tomography guidance. Radiofrequency waves generated by the probe heat and kill the tumor deposits. This technique is relatively non-invasive compared with a surgical hepatic resection.

CRYOSURGERY:

This is another technique in which a cryoprobe (a thin needle that can freeze the tumor) is inserted into the tumor. Using liquid nitrogen, the tumor is frozen into an "iceball," thus killing it.



Chemotherapy for Colorectal Cancer

CHEMOTHERAPY is given following surgery to patients with stage 3 (and some patients with stage 2) colon cancer to eliminate any remaining cancer cells and decrease the risk of recurrence. All patients with stage 4 colon cancer that has spread to other organs are also candidates for chemotherapy. Standard and novel chemotherapy treatments include:

5-FU/LEUCOVORIN:

5-FU, the oldest chemotherapy drug for colorectal cancer, was developed more than 40 years ago. 5-FU kills cancer cells by interrupting their DNA-making capabilities and is almost always given with leucovorin (also called folinic acid) in order to enhance its effectiveness. This combination, typically delivered as an intravenous (I.V.) injection or by a continuous infusion using a portable infusion pump, has remained the mainstay of treatment of both surgically resected and advanced colorectal cancer. Common side effects include diarrhea, mouth sores and lowered white blood cell counts. Patients with a deficiency of the DPD enzyme may have severe side effects with 5-FU.

CAMPTOSAR® (IRINOTECAN):

First available in the United States in 1996, Camptosar works by interfering with the unwinding of the DNA chain during replication of the cell by blocking an enzyme called topoisomerase-1. It is given either by itself or in combination with

5-FU/leucovorin to patients with advanced colorectal cancer. Initial studies used Camptosar with 5-FU/leucovorin given via a brief injection (sometimes called the Saltz regimen), but more recently, Camptosar is being given with 48-hour infusions of 5-FU/leucovorin (FOLFIRI regimen). This seems to improve efficacy while reducing side effects as compared with the Saltz regimen. Camptosar is also approved for use with targeted agents, such as Avastin and Erbitux. The main side effect of Camptosar is diarrhea, which can sometimes be severe. Other side effects include low blood counts that can increase the risk of infections.

XELODA® (CAPECITABINE):

Xeloda is an oral pill (approved by the FDA in 2001) that is converted in the body to 5-FU. The drug has the potential to be as active as traditional 5-FU but with the convenience of a pill rather than I.V. infusions or injections. Xeloda is the first oral medication for metastatic colorectal cancer. It has recently been shown to be as effective as intravenous 5-FU/leucovorin when given as adjuvant therapy for surgically resected disease. A side effect called hand-foot syndrome—swelling, dryness and cracking of the skin on the palms and feet—can necessitate decreasing the dosage or interrupting treatment. This condition also can occur with intravenous 5-FU, but usually only when given as a prolonged infusion. Xeloda can also cause diarrhea, mouth sores and low blood counts. Patients need to be vigilant about these side effects and stop taking Xeloda for a few days if side effects worsen.

ELOXATIN® (OXALIPLATIN):

Eloxatin is the latest chemotherapy drug approved in August 2002 in combination with infused 5-FU/leucovorin (known as FOLFOX regimen). The first platinum agent approved for metastatic colorectal cancer, it has recently been approved for adjuvant chemotherapy. Unlike Camptosar, Eloxatin is not particularly active by itself, but the drug can shrink tumors in more than 50 percent of patients with advanced colorectal cancer when given with 5-FU/leucovorin. The main side effect of Eloxatin is peripheral nerve damage (neuropathy), which can cause numbness, tingling and pain in the extremities. Eloxatin-induced neuropathy is characterized both by sensitivity to cold and cumulative sensory nerve damage, which can result in numbness of the hands and feet after prolonged use of the drug. Other side effects of Eloxatin include diarrhea and low blood counts.

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ANTIBODIES AND BIOLOGICAL AGENTS

A number of agents targeting various biological pathways like blood vessel growth (angiogenesis) and cell growth (epidermal growth factor [EGF]) have been developed for colorectal cancer. Two of these drugs, **Avastin** and **Erbix**, were approved in 2004 for colorectal cancer. A number of other drugs, including **PTK787** (vatalanib), an angiogenesis inhibitor, and **ABX-EGF** (panitumumab), an antibody blocking EGF receptor (EGFR), are in advanced development for colorectal cancer.

AVASTIN™ (bevacizumab):

Approved in February 2004, Avastin is not only the first angiogenesis inhibitor drug to be approved for the treatment of advanced colorectal cancer, it was the first targeted agent to show a significant survival benefit as first-line therapy in advanced colorectal cancer patients. Avastin stops the process of angiogenesis, the development and growth of new blood vessels, which feeds the tumor. It is an intravenous monoclonal antibody that targets an important protein called vascular endothelial growth factor (VEGF), which is responsible for new blood vessel growth in normal cells as well as cancerous tumors. Once bound to VEGF, Avastin renders it inactive, and thereby shuts down the hungry tumor cells' ability to stimulate blood vessel growth. Without proper nutrients brought to them by blood vessels, the tumor cells can no longer grow. Initial studies with Avastin were done using Camptosar-containing chemotherapy. More recently, Avastin has also been successfully combined with the FOLFOX regimen. It is approved for previously untreated patients with colorectal cancer, but has also been shown to be of benefit in patients with relapsed disease. Overall, Avastin is very well tolerated with side effects that include high blood pressure and an increase risk of blood clots, which can in rare instances cause stroke. A rare complication seen with Avastin was perforation of the intestinal wall.

ERBITUX™ (cetuximab):

Erbix is a monoclonal antibody that binds to EGFR, which is involved in stimulating a cell's growth. Erbix binds to EGFR on the colorectal cancer cells and slows their

growth. It is the first in a class of EGFR-blocking drugs to be approved for colorectal cancer. Under their accelerated approval program, the FDA approved Erbitux on Feb. 12, 2004. The drug, given intravenously once a week, has been shown to cause a 50 percent shrinkage of tumors in about 10 to 11 percent of the patients whose cancer has progressed after two prior chemotherapy regimens. When given in combination with chemotherapy drugs like Camptosar, Erbitux has caused 50 percent tumor shrinkage in about one-quarter of patients. Recent studies have shown Avastin can be combined with Erbitux to further increase its activity. Common side effects of Erbitux include acne-like rash, which can sometimes be severe. A few patients may develop an allergic reaction to Erbitux, especially during their first treatment, so patients need to be carefully observed during their first infusion.



Managing Side Effects

SIDE EFFECTS of chemotherapy depend mainly on the type and extent of the treatment. Side effects may not be the same for each person, and they may change from one treatment session to the next. Talk to your healthcare team if you are experiencing these or other side effects.

CHEMOTHERAPY-INDUCED DIARRHEA (CID)

The cells of the small and large intestines divide rapidly and are, therefore, vulnerable to cancer drugs like 5-FU, Camptosar, Xeloda and Eloxatin. Diarrhea frequently occurs during chemotherapy, but diet and medication can help alleviate this side effect.

CID can sometimes be improved without medication through diet. Over-the-counter medications such as Imodium® (loperamide) are useful for mild diarrhea, but the manufacturer's recommended dosage is ineffective for diarrhea caused by chemotherapy. Much higher doses (as much as four times the usual dose) of Imodium are recommended for diarrhea caused by chemotherapy. Imodium, typically the treatment of choice at the initial onset of CID, has few side effects, is limited to the gastrointestinal tract and is inexpensive. Lomotil® (diphenoxylate and atropine), a drug combination used as an alternative to Imodium, has an efficacy similar to Imodium but is only effective for mild to moderate cases.

For severe cases, Sandostatin® (octreotide), an injectable drug, is used to treat CID. This synthetic analog, which decreases the production of growth hormone, is also used to treat acromegaly (a disease caused by overproduction of growth hormone). The drug is usually given three times a day, although a long-acting preparation that can be given once a month is also available and has been studied for the treatment of CID. And although the FDA has not approved Sandostatin for CID, it has shown encouraging benefit in this condition.

Tips for managing CID:

- Drink a variety of clear liquids—as much as three to four liters a day—and avoid caffeine.
- Avoid fried foods and dairy products.
- Use the BRAT diet (bananas, rice, applesauce and toast) until the diarrhea begins to resolve.

NEUROPATHY

Neuropathy, an injury to the peripheral nerves, is a fairly common side effect of some chemotherapy agents, particularly Eloxatin. In most patients, the effect is not permanent. Sensory neuropathy is more common than motor neuropathy and may result in pain as well as numbness and a tingling or loss of sensation. Motor nerve damage results in a disruption of signals to the body and can result in symptoms such as muscle weakness, problems with balance and foot drop. For cancer patients, the legs, feet, arms and hands are most commonly affected. The feet are almost always affected first.

Neuropathy may occur weeks or months after treatment ends, but patients receiving Eloxatin usually develop neuropathy during treatment or soon thereafter. Patients receiving Eloxatin may develop a cold-sensitive neuropathy within the first few days of treatment. This may be related to the drug binding with calcium, causing a hyperactive state in the nerves. Eloxatin-induced cold neuropathies often resolve within a couple of weeks after completing treatment and do not become permanent.

Physicians have had some success in reducing the incidence and intensity of neuropathy symptoms by giving calcium and magnesium infusions prior to Eloxatin.

The infusion supplements the calcium bound with the drug, decreasing the risk of the hyperactive state. The magnesium may help maintain adequate calcium levels.

Treatment for established neuropathy can include anticonvulsants and tricyclic antidepressants. Anticonvulsants, such as Neurontin® (gabapentin), and antidepressants, including nortriptyline or amitriptyline, are often prescribed “off-label,” meaning the FDA has not approved these drugs for treating neuropathy, but in practice, physicians have found they often bring patients some relief. Tricyclic antidepressants relieve neuropathy by decreasing the chemicals in the brain that transmit pain signals.

A topical cream containing the active ingredient in Neurontin for application to the skin produces fewer side effects. Also available topically is lidocaine patch (Lidoderm®), although it must be used cautiously in patients with a history of abnormal heart rhythms. Lidoderm is applied to intact skin in the area with the most pain.

HAND-FOOT SYNDROME

Both 5-FU, when given as an infusion, and Xeloda, can cause redness and swelling of the palms and soles of the feet. This can be painful and can interfere with daily activities. Following administration of chemotherapy, small amounts of the drug can leak out of very small blood vessels in the palms of the hands and soles of the feet. Exposure of your hands and feet to heat as well as friction on your palms and soles of your feet increase the amount of drug in the capillaries and increase the amount of drug leakage. Patients should



About Clinical Trials

recognize the side effect early, as stopping Xeloda for a few days or reducing the dose can minimize it. Emollients and lotions can also be helpful.

ORAL MUCOSITIS

Oral mucositis, or inflammation of the tissue lining the nose and throat, is common in patients being treated for colon cancer. Because the mucosa acts as a barrier to pathogens, like bacteria, individuals with oral mucositis not only have difficulty tasting, eating and drinking, but also are susceptible to opportunistic infections. Certain chemotherapeutic agents like 5-FU, Camptosar and Xeloda have a much higher incidence of oral mucositis.

Early intervention and prompt treatment of mucositis may lessen the degree of these symptoms and potential complications. It is important to take good care of the mouth and throat by keeping your mouth and teeth clean. Examine the mouth at least once daily and report changes to your doctor or nurse. Specifically, these changes include ulcers, pimples, sores, red areas, patches or other changes in the mouth.

In December 2004, the FDA approved Kevivance™ (palifermin) for severe oral mucositis in patients with blood cancers undergoing bone marrow transplant. The safety and efficacy of the drug is being investigated in patients with solid tumors.

In addition, a new agent, Gelclair™ (hyaluronate), exerts its pain-relieving effect by forming a protective barrier, hydrating and coating the oral mucosa without numbing or drying.

CLINICAL TRIALS are research studies in which patients participate to assess the safety and efficacy of newer drugs for cancer. Each study tries to answer scientific questions and to find better ways to prevent, diagnose or treat cancer.

Most clinical research that involves the testing of a new drug progresses in an orderly series of steps called phases. Clinical trials are classified into one of three phases:

PHASE I: These first studies in humans usually only involve a small number of patients. The primary goal of the trial is to determine how best to administer the drug, the maximum tolerated dose and how often it can be given.

PHASE II: A phase II trial continues to test the safety of the drug and begins to evaluate how well the new drug works. Phase II studies usually focus on a particular type of cancer.

PHASE III: These studies test a new drug, a new combination of drugs or a new surgical procedure in comparison to the current standard. A participant will usually be assigned to the standard group or the new group at random (called randomization). Phase III trials often enroll large numbers of people.

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The process of finding a clinical trial requires clear communication between the patient, healthcare provider and research team in a number of areas. But physicians may not have access to every open clinical trial, so patients need the tools to research their own clinical trial options.

RESOURCES

Colorectal Cancer Network

301-879-1500

www.colorectal-cancer.net

Colon Cancer Alliance

877-422-2030

www.ccalliance.org

American Cancer Society

800-ACS-2345

www.cancer.org

National Cancer Institute

800-4-CANCER

www.cancer.gov

Cancer Care

800-813-HOPE

www.cancercare.org

United Ostomy

Association, Inc.

800-826-0826

www.uoa.org

American College of

Gastroenterology

703-820-7400

www.acg.gi.org

Foundation for Digestive

Health and Nutrition

301-654-2635

www.fdhn.org

American Society of Colon & Rectal Surgeons

847-290-9184

www.fascrs.org

CDC's Screen for Life:

National Colorectal Cancer Action Campaign

www.cdc.gov/cancer/screenforlife

National Council on the Aging

www.benefitscheckup.org

Resources for

Finding Clinical Trials

Include:

National Cancer Institute

www.cancer.gov

800-4-CANCER or

888-NCI-1937

National Institutes of Health's ClinicalTrials.gov

www.clinicaltrials.gov

CenterWatch

www.centerwatch.com

Coalition of National Cancer Cooperative

Groups, Inc.

www.cancertrialshelp.org

Travel and Accommodation Resources Include:

Angel Flight America

www.angelflightamerica.org

800-446-1231

Corporate Angel Network

www.corpangelnetwork.org

866-328-1313

National Association of Hospital Hospitality Houses

www.nahhh.org

800-542-9730