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Update on the Treatment of Liver Cancer

Presented by

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Learn about:

- Types of liver cancer
- Treatment options
- Managing side effects
- Emotional and practical support



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As treatments improve, men and women with liver cancer are surviving longer and with a better quality of life.

Liver cancer affects nearly 24,000 people in the United States each year. Surgery to remove the cancer or a liver transplant is the most effective treatment. But not all patients are candidates for these methods. When liver cancer cannot be treated with surgery or a transplant, doctors often prescribe chemotherapy or other anti-cancer drugs. In the past, doctors had to rely on medications used for other types of cancer to treat liver cancer. But newer drugs specifically for liver cancer are now available, along with better ways to deliver the drugs directly to the cancer with fewer side effects.



For example, a drug called sorafenib (Nexavar) is now available for people with hepatocellular carcinoma, the most common form of liver cancer. Sorafenib is a pill that patients can take at home. It is a targeted treatment, which means it attacks mainly cancer cells, sparing healthy tissues. Along with sorafenib, researchers are studying other promising targeted treatments for liver cancer—everolimus (Afinitor), bevacizumab (Avastin), and erlotinib (Tarceva). New radiation treatments also offer hope for people with liver cancer.

Types of Liver Cancer

There are three main types of liver cancer:

- **Hepatocellular carcinoma** is the most common, accounting for about 90 percent of all liver cancers. Some hepatocellular carcinomas spread tentacle-like growths throughout the liver. Others start as one tumor that may spread to other parts of the liver. Still others start as small swellings or masses in several parts of the liver.
- **Cholangiocarcinoma** develops from cells that line the bile ducts of the liver. The bile ducts are tubes that connect the liver to the small intestine. Cholangiocarcinomas make up approximately nine percent of liver cancers.

Your Health Care Team

Liver cancer is usually treated by a multidisciplinary team of experts. Working together, your team will set up a personalized treatment plan for you. The doctors treating your liver cancer may include a:

- **Hepatologist**—an expert in the treatment of liver disease
- **Surgeon**—an expert in surgical procedures of the liver
- **Medical oncologist**—to coordinate all aspects of cancer care, especially chemotherapy and other drug treatments
- **Radiologist**—to locate the tumors in the liver and determine whether they have spread to other organs, using CT scanning or MRI
- **Interventional radiologist**—to perform radioembolization, chemoembolization, or radio-frequency ablation or to take tissue samples from tumors in the liver or elsewhere

Other health care professionals, such as oncology nurses, pain specialists, registered dietitians, psychologists, and social workers, can also form part of your health care team.

- **Angiosarcoma** is the rarest type, accounting for about one percent of liver cancers. Angiosarcoma develops in the cells that line the walls of blood vessels in the liver.

Treatments for Liver Cancer

Before deciding how to treat your liver cancer, your team of experts will go over all the information it has gathered about your health. One of the most important factors in determining the best treatment (or combination of treatments) for you is the current status of your liver. The factors your team will consider are:

- whether there are tumors in more than one lobe of your liver (the liver is divided into four sections, or lobes);
- whether the cancer has spread beyond your liver to other parts of the body;
- how much your liver has been damaged by the cancer;
- how much, if any, underlying liver damage, such as cirrhosis, is present from other conditions.



SURGICAL OPTIONS

Surgery is used to remove tumors (with either a standard “open” procedure or with laparoscopy, sometimes called “keyhole” surgery). When tumors cannot be removed, in some cases surgery is used to transplant a new liver.

Standard surgery, or hepatectomy, is the surgical removal of the part of the liver affected by cancer. This procedure can only be performed in people who do not have severe liver damage and whose cancer has not spread

to other areas of the body. Your doctor will do a series of tests to determine whether the area of the liver not affected by cancer is healthy enough to carry out its functions after the surgery. Generally, this type of surgery works best in people whose tumors are small.

Laparoscopic, or keyhole, surgery enables doctors to remove some tumors using three to four tiny incisions rather than one large incision. People who have this type of surgery experience faster recovery than those who have standard surgery. They report much less pain and are usually sent home from the hospital on the second day after surgery. A laparoscopic approach is not offered for all liver cancers, as some can only be safely removed through standard surgery.



Liver transplants are done most often in people who have one tumor—usually a small one—that cannot be removed because of its location. Only a select percentage of people with liver cancer are candidates for transplantation. To receive a transplant, a suitable donor with a healthy liver must be found. Recently, changes in the organ donor system have increased the availability of organs, reducing the waiting time for people with hepatocellular cancer who are transplant candidates.

CHEMOTHERAPY

Chemotherapy may also be used to treat people with liver cancer, especially when surgery is not an option. The kind of chemotherapy that is usually used is systemic treatment, which means that the chemotherapy travels through the bloodstream to reach cells throughout the body. Some people with liver cancer are candidates for a procedure called chemoembolization. With chemoembolization, the

blood supply to the tumor is blocked, and chemotherapy is administered directly into the tumor at a higher concentration for a longer period of time. This approach can slow or stop the tumor from growing.

TARGETED TREATMENTS

Targeted treatments are drugs that attack specific cell mechanisms that are important for cancer cells to survive and grow. These medications spare healthy cells and result in different side effects than traditional chemotherapy.

Sorafenib was approved for people with hepatocellular carcinoma by the U.S. Food and Drug Administration in 2007. It works by blocking the action of a substance called vascular endothelial growth factor, or VEGF. This protein stimulates the growth of new blood vessels that tumors need to grow. 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.



Sorafenib also blocks the action of platelet-derived growth factor (PDGF). Like VEGF, PDGF is a protein that plays an important role in the growth of new blood vessels that feed tumors. By preventing the formation of these blood vessels, sorafenib slows or stops the growth of tumors. Also, sorafenib is the first drug to target another protein, called RAF kinase, which helps signal cancer cells to grow and multiply.

Researchers believe it is the combination of these actions that makes sorafenib effective at slowing the growth of liver cancer. Currently, clinical trials are studying sorafenib

in combination with the drugs capecitabine (Xeloda) and doxorubicin to see whether using them together is more beneficial than using sorafenib alone. Researchers are also studying sorafenib in people receiving chemoembolization. Researchers also want to find out whether sorafenib prevents liver cancer from returning in people whose tumors were removed surgically.

Everolimus also works by starving the tumor of the blood supply and nutrients it needs to grow. This drug is currently approved for treating kidney cancer, but researchers are studying it in clinical trials for people with liver cancer.

Bevacizumab and erlotinib are being studied in clinical trials alone and in combination as a treatment for liver cancer. Bevacizumab is already used to treat people with lung, colon, and other cancers that have spread to other parts of the body.

Like sorafenib, this targeted drug works by stopping VEGF from stimulating the growth of new blood vessels in tumors. Currently, erlotinib is used to treat people with advanced lung and pancreatic cancers. It works by blocking a different substance—endothelial growth factor receptor (EGFR), which encourages cancer cells to grow.

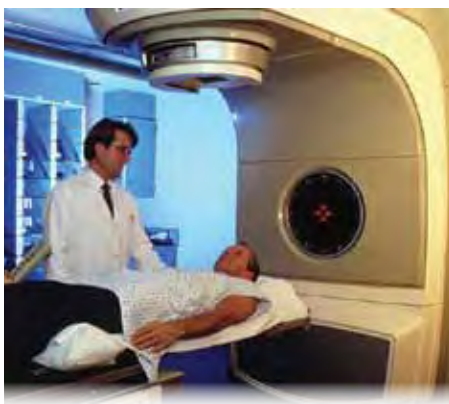


RADIATION TREATMENT

Radiation is sometimes used when a liver cancer cannot be removed by surgery. Although radiation kills liver cancer cells, very high doses can damage non-cancerous tissue as well. So now doctors use devices that deliver radiation beams more directly to the tumor, helping to spare healthy tissue.

Intensity-modulated radiation therapy (IMRT) uses advanced computer technologies to map and plan a precise dose of radiation to the liver, based on individual tumor size, shape, and location. IMRT modulates, or controls, very thin beams of radiation at varying intensities and from various angles. This allows the radiation beams to conform to, or fit, the three-dimensional shape of the tumor for a custom tailored radiation dose.

Radioembolization In this procedure, the radiation specialist injects small radioactive beads into the main artery of the liver, which allows concentrated amounts of radiation to attack the tumor sites. This method delivers an intense dose of radiation to the tumor with less damage to healthy tissue. Patients remain awake during this procedure, which is usually performed in a hospital's radiology suite.



Radiofrequency ablation, sometimes referred to as RFA, kills cancer cells with heat. An imaging technique such as ultrasound or CT scan is used to help guide a needle into the tumor. High-frequency electrical currents are then passed through the needle, creating heat that destroys the cancer cells.

Managing Side Effects

As you are being treated for liver cancer, it's important that you let your health care team know about any side effects you experience. The more detailed and precise you can be, the more it will help your team treat you quickly and effectively. Consider keeping a journal of your symptoms—

The Importance of Clinical Trials

Clinical trials are essential to advancing our knowledge of how best to treat cancer. They are the standard by which we measure the worth of new treatments and their impact on quality of life as patients go through those treatments. That is why doctors and researchers urge people with cancer to take part in a clinical trial.

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:

- People who take part in clinical trials often gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial.
- No patient receives a placebo (a look-alike medication containing no active ingredient) when there is a standard treatment available. Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

when they occur, how severe they are, how they feel, and whether you get relief from prescribed medications.

Some of the side effects you may experience include:

Skin problems Although targeted treatments generally cause less severe side effects than chemotherapy, some of the new drugs lead to skin problems, such as a rash. Development of a rash can actually mean the treatment is working effectively. The rash may cause peeling skin on the hands or feet, but it can also spread to other parts of the body.

Usually a rash develops within the first six weeks of starting a targeted treatment. Mild rashes can be treated with creams applied to the skin. A steroid cream, such as hydrocortisone valerate (Westcort and others), may help reduce the inflammation, pain, and discomfort of the rash. If the rash becomes severe, it may be necessary to stop taking the medication, something you should discuss with your doctor.

If you are taking a targeted treatment, when you spend time outdoors, be sure to use a sunscreen, especially if a rash has already developed.



High blood pressure This side effect can be managed with diet and medication. Your doctor and a registered dietitian can advise you on how to manage high blood pressure.

Pain Another side effect that people with liver cancer may experience is pain. Because certain pain relievers, such as acetaminophen (Tylenol and others), may further damage the liver, pain management is specialized for people with liver cancer. It's essential that you let your health care team know when you are having any pain, as effective treatments are available and can make a big difference in your quality of life. You should not take any pain relievers without talking with your doctor first.

Loss of appetite If you find you don't feel like eating or you become full very quickly, try to have small but frequent meals; drink a liquid supplement, such as Ensure, as one of your small meals; and avoid sweet foods, sweet liquids, and greasy, fried, or highly spiced foods. Talk with a registered dietitian for guidance on eating specific foods.

Nausea, with or without vomiting Talk to your doctor about anti-nausea medications. There are effective treatments available. Here are some things you can do on your own to get relief from nausea: Eliminate offending odors; foods served at room temperature or colder give off fewer offending smells. Snack on dry crackers or toast. Try tart or sour flavors.

Diarrhea This symptom should be taken seriously. If it becomes severe, talk with your doctor about the right medication for you. Often prescribed for pain, opioids reduce diarrhea by slowing movement through the intestines. Loperamide (Imodium A-D, for example) causes fewer side effects than other opioids, making it a common treatment choice. Other types of drugs such as aspirin, bismuth subsalicylate (Pepto-Bismol, for example), corticosteroids, and octreotide (Sandostatin) can help make stools more firm and can reduce fluid loss from the body. Do not treat yourself with any of these drugs without talking to your doctor first.

Changes to your diet that may help include limiting or avoiding lactose (found in milk and cheese), insoluble fiber such as wheat bran and whole-grain products, alcohol, and sugar-sweetened beverages.

Increase your use of active yogurt culture, soluble fibers such as oats, high-potassium foods such as bananas, and beverages such as Gatorade to replace lost electrolytes.

Fluid in the abdomen (ascites) Eat small but frequent meals and reduce the amount of sodium in your diet to help decrease the fluid retention.

Encephalopathy (impaired brain function from the liver's inability to remove toxins from the body) is usually



treated with medication, but it's important to consume an adequate amount of protein, spread evenly throughout the day. A registered dietitian can help determine what is adequate for you.

How CancerCare® Helps

When you are being treated for liver cancer, you may have many concerns. It's perfectly normal to feel sad, worried, or upset. But the more you learn about what's involved and what to expect, the better you'll feel about your treatment. Help is available to you as you consider your options. Your most important support will likely come from your health care team, family members, and friends. But CancerCare offers these free resources as well:

Counseling Our oncology social workers can speak with you one-on-one to help you find ways to cope with the emotional and practical challenges of cancer. Counseling services are available in person or over the phone.

Support groups Connect with other people who are in a similar situation in our free telephone and online



support groups led by professional oncology social workers.

Connect® Education Workshops Leading experts in oncology provide the latest treatment information in these free, one-hour workshops over

the telephone. Listen in live to learn about cancer-related issues from the convenience of your home or office. Past workshops are also available as podcasts on our website and on telephone replay 24 hours a day, seven days a week.

Publications Our free booklets and fact sheets offer up-to-date, easy-to-read information about the latest treatments, managing side effects, and coping with cancer.

Financial help Our staff helps you manage financial concerns and provides referrals. Limited aid is also available to eligible individuals and families for cancer-related costs such as transportation and child care.

Referrals to resources CancerCare can help you learn about other organizations in your community and nationwide that can assist you in finding information and help.

To learn more about how we help, call 1-800-813-HOPE (4673) or visit www.cancercare.org.

Frequently Asked Questions

Q How do viruses affect the development of liver cancer in different people?

A The most common viral risk for developing liver cancer is either hepatitis B or hepatitis C virus. Hepatitis C plays an important role in liver cancer in the United States and in some European countries, such as Spain and Italy. In Southeast Asia, China, and Indonesia, hepatitis B is more prevalent in leading to liver cancer. It's also important to note that cirrhosis—scarring of the liver and poor liver function that result from chronic liver disease—leads to at least 60 percent of all the cases of liver cancer in the United States.

Q I have biliary cancer and I've been on sorafenib (Nexavar) with gemcitabine (Gemzar) for about five months, with minimal side effects. Are any studies looking at sorafenib in situations like mine?

A Based on the results of clinical trials, cisplatin (Platinol and others) plus gemcitabine is now a standard treatment. But research continues. There are several large trials of sorafenib in combination with other drugs such as gemcitabine and capecitabine (Xeloda) that show promise in biliary cancers. Researchers are also looking at methods such as chemoembolization to deliver treatments with more accuracy and fewer side effects.

Q I have a rare kind of liver cancer called fibrolamellar carcinoma. What kind of treatment is recommended for this type of cancer?

A Fibrolamellar carcinoma is a rare form of liver cancer, most often seen in people between the ages of 20 and 40. If possible, the preferred treatment is surgery. But as with other hepatocellular carcinomas, the options include liver transplant, chemoembolization, sorafenib, and clinical trials. If the tumor is successfully treated but returns, this form of liver cancer tends to grow very slowly.

Resources

CancerCare

1-800-813-HOPE (4673)

www.cancercares.org

American Cancer Society

1-800-227-2345

www.cancer.org

American Liver Foundation

1-800-465-4837

www.liverfoundation.org

Cancer.Net

Patient information from the American Society of Clinical Oncology

www.cancer.net

National Cancer Institute

1-800-422-6237

www.cancer.gov

National Coalition for Cancer Survivorship

See especially their Cancer Survival Toolbox®

1-877-650-9127

www.canceradvocacy.org

National Organization for Rare Disorders

1-203-744-0100

www.rarediseases.org

To find out about clinical trials:

Coalition of National Cancer Cooperative Groups

www.CancerTrialsHelp.org

National Cancer Institute

www.cancer.gov/clinicaltrials



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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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the difference comes from:

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