

TREATMENT UPDATE:

Liver Cancer

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Treatment Update: Liver Cancer

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Each year, approximately 40,000 people in the United States are diagnosed with cancer that originates in the liver. As treatments improve, men and women with this type of cancer are living longer and with a better quality of life.

The liver is the body's largest internal organ. Located below the right rib cage, it has many vital functions related to digestion, metabolism, and the storage of nutrients. The liver also makes proteins that help the blood to clot, and clears the blood of drugs and other harmful substances.

Primary liver cancers originate in the liver, rather than spreading to the liver from another part of the body. Hepatocellular cancer (HCC) is the most common type of primary liver cancer, accounting for about 90 percent of cases. It forms in hepatocytes, the main cells of the liver.

After your diagnosis, you and your health care team will discuss the best way to proceed with your treatment. Factors that influence the choice of treatment include the number of tumors in the liver, whether the cancer has affected blood vessels, how much the liver has been damaged by the cancer, and whether the cancer has spread to other parts of the body (metastasized).

Treatment Options

Surgery

A partial hepatectomy is the surgical removal of the part of the liver affected by cancer. This procedure may be an option for people whose tumor (or tumors) are confined to a small section of the liver, are not near blood vessels, and whose liver is not damaged by cirrhosis.

Transplant

A liver transplant is a possible option for people whose tumors are very small, few in number, do not involve blood vessels, and have not spread outside the liver. To receive a transplant, a suitable donor with a healthy liver must be found.



Embolization

A minimally-invasive procedure called transarterial embolization (TAE) may be considered in cases where surgery is not an option. In TAE, an interventional radiologist injects tiny particles into a catheter (small plastic tube) that has been placed into the hepatic artery, the main source of blood for most liver tumors. This kills tumors by blocking their blood supply.

The procedure is called transarterial chemoembolization (TACE) if chemotherapy is injected into the catheter along with the particles. The chemotherapy is targeted directly to the tumors, sparing healthy tissue from the effects of the drug. Chemotherapies that may be used alone or in combination include cisplatin, doxorubicin, and mitomycin.

Treating primary liver cancer with TAE or TACE may allow for future surgery or transplant.

Ablation

Ablation is a treatment that uses heat to destroy cancer cells. In radiofrequency ablation (RFA) and microwave ablation (MWA), the doctor uses an imaging technique, such as an ultrasound or CT scan, to guide a needle into the tumor. High-frequency electrical currents (in RFA) or microwaves (in MWA) are passed through the needle, creating a small region of heat that destroys the tumor.

Cryoablation is a technique similar to RFA and MWA, but uses cold instead of heat to destroy tumors.

Ablation may be an effective option for patients for whom surgery is not an option, and whose tumors are small.

Targeted Therapy

Targeted therapy focuses on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how cancer cells grow.

Two targeted therapy drugs are approved by the U.S. Food and Drug Administration (FDA) for the treatment of HCC:

- **Sorafenib (Nexavar)** was approved by the FDA in 2007. It works by blocking the action of proteins that promote the growth of new blood vessels; these blood vessels carry oxygen, minerals, and other nutrients that tumors need to grow. Sorafenib also blocks some of the proteins on cancer cells that help them grow and multiply.
- **Regorafenib (Stivarga)** was approved by the FDA in 2017 for the treatment of patients who had been previously treated with sorafenib. Like sorafenib, regorafenib is designed to block the formation of new blood vessels, as well as block proteins that contribute to the growth of cancer cells.

Immunotherapy

Immunotherapy has recently emerged as a new treatment option for HCC.

Our immune system is constantly working to keep us healthy. It recognizes and fights against danger, such as infections, viruses, and growing cancer cells. In general terms, immunotherapy uses our own immune system as a treatment against cancer.

In September 2017, the FDA granted accelerated approval to the immunotherapy drug nivolumab (Opdivo) for patients with advanced HCC who were previously treated with the targeted therapy sorafenib. Nivolumab works by interfering with a molecular “brake” known as PD-1 that prevents the body's immune system from attacking tumors.

Radiation

Radiation is sometimes used to shrink liver tumors or to relieve pain, but because radiation can easily damage healthy liver tissue, it is not a common treatment approach, and is given only in low doses.

Types of radiation therapy used in the treatment of liver cancer include:

- **Stereotactic body radiation therapy (SBRT)** is a technique that can deliver the highest appropriate dose in a fewer number of treatment sessions. The radiation is precisely targeted to the tumor, sparing healthy tissue.
- **Intensity-modulated radiation therapy (IMRT)** is a form of external beam radiation therapy (EBRT) that directs a beam (or multiple beams) of radiation through the skin to the tumor. Unlike standard EBRT, IMRT allows a higher dose of radiation to be directed to the tumor, while minimizing the amount of radiation received by healthy tissue in the liver.
- **3-dimensional conformal radiation therapy (3D-CRT)** uses a computer to create a 3-dimensional picture of the tumor, allowing for the highest appropriate dose of radiation to be directed to the tumor, while sparing healthy tissue as much as possible.

Radioembolization

Radioembolization is a procedure that combines embolization and radiation therapy to treat liver cancer. Small radioactive beads are placed inside the blood vessels that feed tumors, allowing concentrated amounts of radiation to attack the tumor. Radioembolization delivers an intense dose of radiation to the cancer cells while minimizing the effect on healthy tissue.

Chemotherapy

Liver cancer does not generally respond to “systemic” chemotherapy (treatment that is given orally or injected into a vein), whether used as single drug or as a combination of drugs. A few chemotherapy drugs, including doxorubicin, 5-fluorouracil, and cisplatin, have had some limited effectiveness in shrinking tumors.



Treatments Being Studied

Targeted Therapy

Lenvatinib. In September 2017, the FDA accepted a new drug application for the targeted therapy lenvatinib (Lenvima) as a treatment for patients with advanced HCC. Lenvatinib, which inhibits the growth of cancer cells by blocking certain enzymes, has shown promising results in a late-stage clinical trial. The FDA is expected to announce the results of its review by the end of 2018.

Cabozantinib. Findings from a phase III clinical trial presented in January 2018 showed that cabozantinib (Cabometyx, Exelixis) significantly improved outcomes in patients with advanced HCC. Cabozantinib is a vascular endothelial growth factor receptor (VEGFR)-2 inhibitor.

FGF19-driven HCC. There are a number of targeted therapy drugs being assessed for the subgroup of HCC patients who have an “overexpression” of a protein called fibroblast growth factor 19 (FGF19).

Treatments for HCC that has other types of genetic alterations are also being studied in early-stage clinical trials.

Immunotherapy

Tumor cells often have “immune checkpoint” molecules that act as a shield, allowing the cancer to evade an attack by the immune system. This can be countered by immune checkpoint inhibitors—drugs designed to remove the shield and allow the immune system to attack the cancer cells. There are a number of clinical trials underway to test immune checkpoint inhibitors in the treatment of HCC.

Hepatic Artery Infusion

Because of HCC's poor response to systemic chemotherapy, researchers are studying hepatic artery infusion (HAI), in which chemotherapy drugs are injected directly into the hepatic artery. Early studies have shown that HAI can be effective in shrinking tumors, but additional research is needed.



The Importance of Clinical Trials

Clinical trials are the standard by which we measure the safety and effectiveness of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials 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, including any possible side effects.
- Many clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- Participation is voluntary and does not affect your access to treatment in other settings. You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all patients experience all side effects, and patients may experience side effects not listed here.

Side Effects of Embolization

Post-embolization syndrome (PES), which can cause flu-like symptoms such as pain, fever, and nausea, is a common side effect of transarterial embolization (TAE) and transarterial chemoembolization (TACE).

Chemotherapy-related side effects may be experienced with TACE. Those side effects may include:

- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Chemotherapy can cause changes in the way food and liquids taste, including causing an unpleasant metallic taste in the mouth. Many people find that switching to plastic utensils helps. It may also help to avoid eating or drinking anything that comes in a can, and to use enamel-coated pots and pans for food preparation.

Side Effects of Targeted Therapy

Common side effects of targeted therapy include diarrhea, rash, liver problems (such as hepatitis and elevated liver enzymes), problems with blood clotting and wound healing, and high blood pressure.

Side Effects of Immunotherapy

Immunotherapy helps to prompt an immune response against the cancer cells. Because the immune system may attack healthy cells as well as cancer cells, certain side effects may be experienced, including fatigue, digestive tract symptoms, shortness of breath, and rash.

Side Effects of Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy; those changes can include dryness, swelling, peeling, redness, and blistering. Sun exposure should be avoided, as it can worsen this side effect. If a reaction occurs, contact your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful areas, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried, or highly seasoned food.
- Eat meals cold or at room temperature, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes as well as liquid. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits, and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Managing loss of appetite

- Weight loss is common in people being treated for cancer. To help maintain your weight, eat small meals throughout the day, and try to include protein in every meal.

- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna, or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis, and depression. So be sure to ask your doctor if he or she thinks any of these conditions may be contributing to your fatigue.

Managing Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs.
- When the pain occurs.
- How long it lasts.
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense.
- What makes the pain feel better and what makes it feel more intense.

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication, to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture, and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.



Communicating with Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurse practitioners, physician assistants, nurses, dietitians, social workers, and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with cancer and treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first, and be as specific and brief as possible.

Bring someone with you to your appointments. It's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears. He or she may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, ask if you can use it to take notes. Writing notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team.

Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Because some potential treatment side effects affect the digestive system, it is a good idea to have a gastroenterologist as part of your multi-disciplinary team.
- Your local pharmacist is a great source of knowledge about the medications you are taking; have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have, or any pain you are experiencing, so that they can consult with your primary care physician or specialists as needed.

Remember, there is no such thing as over-communication.

CancerCare's Free Support Services and Programs

Receiving a diagnosis of cancer can be very difficult, and adjusting to the necessary changes in your life can be challenging.

CancerCare can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and provide information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercares.org.

You will likely also build your own personal support network, comprised of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q. What are the treatments for liver cancer that has spread from another location in the body?

A. Liver cancer often begins in another location in the body, such as the colon, stomach, or breast. These tumors are treated with the specific drugs used when the tumors began (before they spread). Depending on the number, size, and location of the tumors, surgery is a potential option for both primary liver cancer and cancer that has spread to the liver from another place in the body.

Q. Should a person diagnosed with liver cancer seek a second opinion?

A. At the time of diagnosis, it makes sense to seek a consultation from a major cancer center or a group of physicians who are experts in managing primary liver cancer. Another time to seek a consultation or second opinion is if the cancer is not responding to treatment and/or if a change in treatment is warranted. Discussions can include possible changes in treatment approaches, and if participation in a clinical trial should be considered.

Q. I've had hepatitis C. Should I be tested for liver cancer?

A. Hepatitis C is a condition characterized by inflammation of the liver, resulting from infection with the hepatitis C virus. Over the course of many years, this inflammation can lead to cirrhosis (scarring throughout the liver), a risk factor for primary liver cancer. People with cirrhosis should get regular ultrasound screenings to check for liver tumors.

Q. What is ascites and how is it treated?

A. Ascites is the accumulation of protein-containing (ascitic) fluid in the abdomen. It may develop in patients with HCC who also have liver damage. The basic treatment for ascites is a low-sodium diet along with bed rest. In some cases, diuretics (medications designed to increase the amount of water and salt expelled from the body) are prescribed; more rarely, a surgical procedure may be needed to remove the fluid.



Resources

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www.cancercares.org

American Cancer Society

800-227-2345

www.cancer.org

American Liver Foundation

800-465-4837

www.liverfoundation.org

Cancer.Net

Patient information from

the American Society of

Clinical Oncology

888-651-3038

www.cancer.net

Cancer Support Community

888-793-9355

www.cancersupportcommunity.org

CLINICAL TRIALS WEBSITES**EmergingMed**

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National Cancer Institute

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National Cancer Institute

800-422-6237

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**National Coalition
for Cancer Survivorship**

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