TREATMENT UPDATE:

Liver Cancer

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All people depicted in the photographs in this booklet are models, used for illustrative purposes only.

Each year, approximately 42,000 people in the United States are diagnosed with primary liver cancer. As treatments improve, people 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.

If primary liver cancer is suspected, imaging tests such as CT and MRI scans can often confirm or rule out the diagnosis. In some cases, a biopsy may be required, in which a tissue sample from the liver is obtained through a thin needle and examined by a pathologist.

Treatment Options

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).

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 following evaluation by a transplant surgery team. In the United States, the most common type of liver transplant is "orthotopic," meaning the diseased liver is replaced by all or part of a normal liver from a living or deceased donor.

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 made of gelatin sponges or beads 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.

If chemotherapy is injected into the catheter along with the particles, the procedure is called transarterial chemoembolization (TACE). 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 in TACE 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 different methods, such as heat, freezing or microwaves, 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 people for whom surgery is not an option, and whose tumors are small.

Tyrosine Kinase Inhibitors

Tyrosine kinase inhibitors (TKIs) are a class of drug that focus 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.

There are four TKIs approved by the U.S. Food and Drug Administration (FDA) for the treatment of HCC:

- **Lenvatinib (Lenvima)** is used as a first-line (initial) treatment of unresectable (inoperable) HCC. Lenvatinib inhibits the growth of cancer cells and blood vessels by blocking certain enzymes. (Blood vessels carry oxygen, minerals and other nutrients that tumors need to grow.)
- **Sorafenib (Nexavar)** works by blocking the action of proteins that promote the growth of new blood vessels. Sorafenib also blocks some of the proteins on cancer cells that help them grow and multiply.

- **Regorafenib (Stivarga)** is approved for the treatment of people 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.
- **Cabozantinib (Cabometyx)** is approved for the treatment of people with HCC who previously received sorafenib. Cabozantinib targets multiple enzymes that are part of many cell functions, including growth and division.

Immunotherapy

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 recent years, immunotherapy has emerged as an important treatment option for HCC.

There are three immunotherapies for advanced HCC previously treated with the TKI sorafenib. Called immune checkpoint inhibitors, they interfere with molecular "brakes" that prevent the body's immune system from attacking tumors. Nivolumab (Opdivo) and pembrolizumab (Keytruda) work by interfering with the PD-1 brake. The combination of nivolumab and ipilimumab (Yervoy) interferes with the PD-1 and CTLA-4 brakes.

In 2020, the FDA approved atezolizumab (Tecentriq) in combination with bevacizumab (Avastin) as an initial treatment for HCC that has spread beyond the liver or is inoperable. Atezolizumab interferes with a molecular brake called PD-L1. Bevacizumab works by blocking the action of VEGF (vascular endothelial growth factor), a protein released by tumors which promotes the formation of blood vessels. By blocking this protein, bevacizumab "starves" tumors.

In October 2022, the FDA approved tremelimumab (Imjudo) in combination with durvalumab (Imfinzi) for the treatment of unresectable (inoperable) HCC. Both tremelimumab and durvalumab are monoclonal antibodies, a type of immunotherapy. Anticancer monoclonal antibodies are made in the laboratory and then administered intravenously to target cancer cells.

Radiation

Radiation is sometimes used to shrink liver tumors or to relieve pain. The types of radiation used in the treatment of liver cancer include:

- **Stereotactic body radiation therapy (SBRT)** is a technique that delivers the highest appropriate dose in the fewest 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.
- **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.

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.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth 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 valuable 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.
- 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.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects 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 may improve your quality of life and allow you to maintain your treatment plan. It's important to remember that not all people experience all side effects, and people may experience side effects not listed here.

Side Effects of Embolization

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

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)

Side Effects of Tyrosine Kinase Inhibitors

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

Specific TKIs may have unique side effects. It's important to have a discussion with your health care team to understand what these potential side effects are, how to reduce the risk of their occurring, and how to minimize their impact should you experience them.

Side Effects of Immunotherapy

Immunotherapy helps to prompt an immune response against 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. These effects can be mild, moderate or severe. In some cases, immunotherapy may be temporarily halted. Additionally, steroids may be given to stop an immune response against healthy cells.

Side Effects of Radiation Therapy

Changes to the skin is the most common side effect 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 area, 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 that are chilled, 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. 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.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. 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.

Constipation

- As hydration is important to avoid constipation, make sure to drink plenty of fluids. Also, limit your intake of caffeine and alcoholic beverages, as they can cause dehydration.
- Include foods high in fiber in your daily diet, such as fruit (especially pears and prunes), vegetables and cereals. If your health care team approves, you may want to add synthetic fiber to your diet, such as Metamucil, Citrucel or FiberCon.
- Be as physically active as you can, after checking with your health care team on the level of physical activity that is right for you.
- If your doctor has prescribed a "bowel regimen," make sure to follow it exactly.

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 during the day.
- 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 they think 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 it is 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 liver 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 (either on paper or in a digital format) 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.

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

Bring someone with you to your appointments or have them be present during telehealth sessions. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person you bring 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. You can also ask the person who accompanies you to take notes for you. If you have a mobile device, ask if you can use it to take notes. Keeping 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 liver cancer treatment and any test results.
- 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.

Cancer*Care*'s Free Support Services and Programs

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

Cancer*Care*® 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 Cancer*Care* helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network, composed 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: Cancer can spread to the liver after originating in another part of the body, such as the colon, stomach or breast. Treatment for these tumors depends on where the cancer originated. Surgery is a potential option for both primary liver cancer and cancer that has spread to the liver from another place in the body, depending on the number, size and location of the tumors.

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 screenings, including diagnostic ultrasound, 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 people 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

Cancer*Care*®
800-813-HOPE (800-813-4673)
www.cancercare.org

American Liver Foundation
800-465-4837
www.liverfoundation.org

American Cancer Society
800-227-2345
www.cancer.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

National Cancer Institute
800-422-6237
www.cancer.gov

National Coalition for Cancer Survivorship
877-622-7937
www.canceradvocacy.org

Imerman Angels
866-463-7626
www.imermanangels.org

Medicine Assistance Tool
www.medicineassistancetool.org

CLINICAL TRIALS WEBSITES

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