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✓ Designed to help you discuss cancer treatment with your doctors

NCCN Guidelines for Patients®: Liver Cancer, 2020
These NCCN Guidelines for Patients® are based on the NCCN Guidelines® for Hepatobiliary Cancers (Version 4.2020, June 19, 2020).

NCCN Guidelines for Patients®
Liver Cancer, 2020

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Global Liver Institute

An essential element of patient empowerment is accessible, actionable, high-quality information. The Global Liver Institute is proud to work with the NCCN Foundation to provide this information to support liver and bile duct cancer patients in the hope that together we can make the cancer journey easier and more successful.

Donna R. Cryer, JD, President & CEO, Global Liver Institute
globalliver.org

The Bili Project Foundation

The Bili Project Foundation is honored to work with the NCCN Foundation to provide this information to support bile duct, liver and gallbladder cancer patients and their families in our goals together to raise awareness and access to educational information to make informed decisions about their care.

Susan Acquisto/Joy Stephenson Laws, Co-Founders
thebiliproject.org

To make a gift or learn more, please visit NCCNFoundation.org/donate or e-mail PatientGuidelines@nccn.org.
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The liver is the largest organ in the body. The liver, gallbladder, and bile ducts work together to make, store, and secrete bile. Bile is a fluid that helps digest fat in the food you eat. The liver also filters your blood. This chapter will discuss the liver and give an overview of liver cancer.

The liver

The liver is the largest organ in the body. It is located on the right side of the body under your rib cage. The liver filters blood, helps with blood clotting, makes bile, breaks down fats, and helps process sugar for energy. The liver also produces lymph. Inside the liver is a network of blood and lymph vessels.

The liver has two lobes, a right and left lobe. Blood enters the liver from the hepatic artery and the portal vein. Blood leaves the liver through the hepatic veins before entering the inferior vena cava and returning to the heart.
**Bile**
Liver cells make bile. Bile is a yellow or green fluid made up of cholesterol, bilirubin, salts such as potassium and sodium, water, and other elements found in the body. It flows into small channels that drain into thin tubes called ducts. These ducts form larger and larger channels that flow into the left and right hepatic ducts. The left and right hepatic ducts join to form the common hepatic duct. The common hepatic duct joins with the cystic duct that connects to the gallbladder to form the common bile duct. The common bile duct is joined by the pancreatic duct just before it enters the small intestine.

**The gallbladder**
The gallbladder is a small, pear-shaped organ found under the liver. It is sometimes described as sac-like because it holds bile from the liver. Bile is stored in the gallbladder, and when you eat, it then passes through the bile ducts into the small bowel to help digest food.

**The hepatobiliary system**
The liver is part of the hepatobiliary system. Hepato means liver and biliary refers to the gallbladder and bile ducts. Together, they form the hepatobiliary system. The hepatobiliary system makes bile and is a part of the digestive system. The digestive system takes in food, breaks it down (digestion), absorbs nutrients, and removes waste from the body. Some doctors consider the pancreas to be a part of this system.

**The hepatobiliary system includes the liver, gallbladder, and bile ducts. It is part of the digestive system.**
Risk factors

A risk factor is anything that increases your chances of having a disease like cancer. Risk factors can be activities that people do, things in the environment, or traits passed from parents to children through genes. Genes are coded instructions for the proteins your cells make. A mutation is when something goes wrong in the genetic code. Mutations can be passed down in families or can occur spontaneously. In other words, they may be present before you are born (inherited) or caused by genetic damage (acquired) later in life. For a list of risk factors, see Guide 1.

Risk is based on:

- Those with cirrhosis
- Those without cirrhosis

Cirrhosis

Cirrhosis is scarring of the liver. It is a type of long-term (chronic) liver disease where liver cells are replaced by scar tissue. If you have cirrhosis, you should be screened for liver cancer.

Cirrhosis can be caused by:

- Hepatitis B
- Hepatitis C
- Alcohol
- Non-alcoholic fatty liver disease (NAFLD)
- Genetic hemochromatosis
- Stage 4 primary biliary cholangitis
- Alpha-1-antitrypsin deficiency
- Other causes of cirrhosis

Guide 1

Risk factors for liver cancer

Those with cirrhosis or chronic hepatitis B should be enrolled in a liver cancer screening program

Risk factors for those with cirrhosis:

- Hepatitis B
- Hepatitis C
- Alcohol
- NAFLD
- Genetic hemochromatosis
- Stage 4 primary biliary cholangitis
- Alpha-1-antitrypsin deficiency
- Other causes of cirrhosis

Risk factors for those without cirrhosis:

- Hepatitis B
- Additional risk factors include HBV carrier with family history of liver cancer, Asian males 40 years of age or over, Asian females 50 years of age or over, and African/North American Blacks with hepatitis B
Hepatitis
Hepatitis is a type of liver disease. Viruses called hepatitis A, hepatitis B (HBV), and hepatitis C (HCV) are the most common causes of hepatitis. HBV and HCV are spread by contact with blood and other bodily fluids. HBV and HCV can cause scarring of the liver (cirrhosis), liver failure, and liver cancer. If you have chronic HBV, you should be screened for liver cancer.

Other risk factors
Drinking too much alcohol can cause damage to the liver. Having NAFLD may lead to cirrhosis in people who drink little or no alcohol. NAFLD is seen in obese people or those with diabetes, high cholesterol, and a few other conditions. Diabetes, obesity, or other problems processing sugar may put someone at risk for liver cancer. Genetic hemochromatosis is an inherited condition that causes the liver to store too much iron from food.
Screening

People at risk for liver cancer may have screening tests. Screening is when tests are done on a regular basis to detect a disease in someone without symptoms. The earlier the cancer is found, the earlier treatment can start. For screening tests, see Guide 2.

For screening:

- An ultrasound (US) is recommended
- An alpha-fetoprotein (AFP) test is optional

An ultrasound is a test that uses sound waves to take pictures of the inside of the body. A blood test checks for the protein AFP. An elevated or rising AFP might be a sign of primary liver cancer. This is cancer that starts in the liver. If a blood test shows a high AFP and/or there is a liver nodule (lump) 10 millimeters (mm) or larger, a CT (computed tomography) scan or MRI (magnetic resonance imaging) scan of the abdomen is recommended. A CT scan uses x-rays and computer technology to take pictures of the inside of the body. An MRI scan uses radio waves and powerful magnets to take pictures of the inside of the body.

Follow-up steps after a screening ultrasound may include:

- If AFP is elevated or an ultrasound finds nodules that are 10 mm or larger, you will have more tests such as a CT or MRI.
- If ultrasound finds nodules that are smaller than 10 mm, repeat ultrasound and AFP in 3 to 6 months.
- If the ultrasound is negative, repeat ultrasound and AFP in 6 months.

Guide 2
Screening tests

Ultrasound (US) is recommended
- It should be done by qualified sonographers or physicians. Liver dynamic CT or dynamic MRI may be performed as an alternative to US.

Alpha-fetoprotein (AFP) is optional
- It would be done in addition to an ultrasound. A CT or MRI will follow a positive or rising AFP, regardless of what the ultrasound shows.
Liver cancer basics

Liver cancer

Cancer that starts in the liver is called primary liver cancer. Secondary liver cancer is when other cancer types spread to the liver. For example, cancer can start in the intestines (colon) and spread to the liver. This is called metastatic colon cancer.

There is more than one type of primary liver cancer in adults. The most common type is hepatocellular carcinoma (HCC). There is a subtype of HCC called FLHC (fibrolamellar hepatocellular carcinoma). FLHC affects a small number of people and usually occurs at a younger age.

The second most common type of primary liver cancer is called intrahepatic cholangiocarcinoma, which is a cancer of the bile ducts. Other primary liver cancers in adults include rare types of sarcoma that start in the blood vessel cells of the liver. Another rare type is made of both hepatocellular carcinoma and cholangiocarcinoma (this is called a mixed-type tumor).

Information on bile duct and gallbladder tumors can be found in NCCN Guidelines for Patients: Gallbladder and Bile Duct Cancers, available at NCCN.org/patientguidelines.

Information on sarcomas in the liver can be found in NCCN Guidelines for Patients: Soft Tissue Sarcomas, available at NCCN.org/patientguidelines.

This patient guideline will focus on HCC and its treatment.
How liver cancer spreads

Liver cancer can spread throughout the liver. It can also spread to a body part far from the primary tumor called a distant metastasis. This is metastatic liver cancer.

Cancer can spread to distant sites through blood. Liver cancer can travel through the hepatic vein into the inferior vena cava and metastasize in other parts of the body. It most often metastasizes to the lung or bone.

Cancer can also spread through the lymphatic system. The lymphatic system has a clear fluid called lymph. Lymph gives cells water and food. It also has white blood cells that fight germs. Lymph nodes filter lymph and remove the germs. Lymph travels throughout the body in vessels like blood does. Lymph vessels and nodes are found everywhere in the body. Although possible, HCC does not commonly spread to nearby lymph nodes.

Cancer stages

A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. The American Joint Committee on Cancer (AJCC) created this to determine how much cancer is in your body, where it is located, and what subtype you have. AJCC is just one type of staging system. Staging is needed to make treatment decisions. Once treatment starts, staging does not change.

Human liver anatomy

Liver cancer can invade nearby veins, arteries, and bile ducts. It can spread to the gallbladder and other parts of the body.
Liver cancer basics

Cancer stages

TNM scores
The tumor, node, metastasis (TNM) system is sometimes used to stage liver cancer. In this system, the letters T, N, and M describe different areas of cancer growth. Based on surgery and lab results, your doctor will assign a score or number to each letter. The higher the number, the larger the tumor or the more the cancer has spread. These scores will be combined to assign the cancer a stage. A TNM example might look like this: T1N0M0 or T1, N0, M0.

- **T (tumor)** - Size of the main (primary) tumor
  - **T1** One tumor 2 cm or smaller, or one tumor larger than 2 cm without vascular invasion
    - **T1a** One tumor 2 cm or smaller
    - **T1b** One tumor larger than 2 cm, but blood vessels do not have cancer
  - **T2** One tumor larger than 2 cm with vascular invasion, or multiple tumors, no tumors are larger than 5 cm
  - **T3** Multiple tumors with at least one that is larger than 5 cm
  - **T4** Single tumor or multiple tumors of any size involving a major branch of the portal vein or hepatic vein, or tumor(s) that involve nearby organs (other than the gallbladder) or have invaded the peritoneum (lining of the abdomen)

- **N (node)** - If cancer has spread to nearby (regional) lymph nodes
  - **N0** means no cancer is in regional lymph nodes
  - **N1** means cancer in the regional lymph nodes is found

- **M (metastasis)** - If cancer has spread to distant parts of the body or metastasized

Keep in mind, TNM scores are not always used to describe liver cancer. Doctors may explain your cancer stage in different ways to make it less confusing.

- **N = Node**
  - There are hundreds of lymph nodes throughout your body. They work as filters to help fight infection and remove harmful things from your body. Regional lymph nodes are those located near the liver. These include the hilar, hepatoduodenal ligament, inferior phrenic, inferior vena cava lymph nodes, and the hepatic artery and portal vein lymph nodes. Cancer in the lymph nodes is called nodal disease.
  - **N0** means no cancer is in regional lymph nodes
  - **N1** means cancer in the regional lymph nodes is found

T= Tumor
The primary tumor size is measured in centimeters (cm). A large pea is 1 cm. A golf ball is 4 cm.

- **T1** One tumor 2 cm or smaller, or one tumor larger than 2 cm without vascular invasion
  - **T1a** One tumor 2 cm or smaller
  - **T1b** One tumor larger than 2 cm, but blood vessels do not have cancer
- **T2** One tumor larger than 2 cm with vascular invasion, or multiple tumors, no tumors are larger than 5 cm
- **T3** Multiple tumors with at least one that is larger than 5 cm
- **T4** Single tumor or multiple tumors of any size involving a major branch of the portal vein or hepatic vein, or tumor(s) that involve nearby organs (other than the gallbladder) or have invaded the peritoneum (lining of the abdomen)
M = Metastatic
Cancer that has spread to distant parts of the body is shown as M1. Common sites for metastasis include the lung and bone.

- **M0** means no distant metastasis
- **M1** means distant metastasis is found

Grade
Another factor used in staging is the cancer grade. Grade describes how abnormal the tumor cells look under a microscope (called histology). Higher-grade cancers tend to grow and spread faster than lower-grade cancers. GX means the grade can’t be determined, followed by G1, G2, G3, and G4. G4 is the highest grade for liver cancer. Well differentiated means the cancer cells look similar to normal cells. Poorly differentiated means the cancer cells look very different compared to normal cells. Undifferentiated means the cells are abnormal and don’t look like the cells in the organ where cancer started.

- **GX** Grade cannot be determined
- **G1** Well differentiated
- **G2** Moderately differentiated
- **G3** Poorly differentiated
- **G4** Undifferentiated

Numbered stages
Number stages range from stage 1 to stage 4, with 4 being the most advanced. Doctors write these stages as stage I, stage II, stage III, and stage IV. See Guide 3.

### Guide 3
#### Liver cancer stages

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Stage 1A</th>
<th>• T1a, N0, M0</th>
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<tbody>
<tr>
<td></td>
<td>Stage 1B</td>
<td>• T1b, N0, M0</td>
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<tr>
<td>Stage 2</td>
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<td>Stage 3A</td>
<td>• T3, N0, M0</td>
</tr>
<tr>
<td></td>
<td>Stage 3B</td>
<td>• T4, N0, M0</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Stage 4A</td>
<td>• Any T, N1, M0</td>
</tr>
<tr>
<td></td>
<td>Stage 4B</td>
<td>• Any T, Any N, M1</td>
</tr>
</tbody>
</table>
Stage 1
In stage 1 liver cancer, there is only one tumor up to 2 cm in size or a tumor larger than 2 cm that does not involve blood vessels found in the liver. It may have grown into veins, arteries, or bile ducts. Cancer has not spread to lymph nodes (N0) or other parts of the body (M0).

Stage 2
In stage 2 liver cancer, there is one tumor larger than 2 cm that has grown into veins, arteries, or bile ducts. There might be multiple tumors that are smaller than 5 cm. Cancer has not spread to lymph nodes (N0) or other parts of the body (M0).

Stage 3
In stage 3a liver cancer, there are multiple tumors. One of these tumors is larger than 5 cm. Cancer has not spread to lymph nodes (N0) or other parts of the body (M0).

In stage 3b liver cancer, there is a single tumor or multiple tumors of any size involving a major branch of the portal vein or hepatic vein, or tumor(s) that involve nearby organs (other than the gallbladder), or the peritoneum (lining of the abdomen). Cancer has not spread to lymph nodes (N0) or other parts of the body (M0).

Stage 4
In stage 4A liver cancer, the cancer is any size and there may be more than one tumor in the liver. It may have grown into blood vessels or the organs around the liver. Cancer has spread to lymph nodes (N1), but not to other parts of the body (M0).

Stage 4B liver cancer is cancer that has spread to distant parts of the body (M1). The tumor can be any size and there may be more than one tumor in the liver. Cancer might be in the lymph nodes. This is metastatic liver cancer.

Review
- The liver, gallbladder, and bile ducts are part of the hepatobiliary system.
- A risk factor is anything that increases your chances of having a disease like cancer.
- Screening is when tests are done on a regular basis to detect a disease in someone without symptoms. If you have cirrhosis or chronic hepatitis B, then you should be enrolled in a liver cancer screening program.
- Cancer staging is a rating by your doctors of the extent of the cancer at the time you are first diagnosed.
- Staging is based on the number of tumors, tumor size(s) and location(s), and if the tumor(s) involves any blood vessels, bile ducts, or nearby organs.
- TNM scores are not always used to describe liver cancer. Doctors may explain your cancer stage in different ways to make it less confusing.
2

Testing for liver cancer

18 General health tests
20 Blood tests
21 Imaging tests
23 Biopsy
24 Test results
25 Review
Treatment planning starts with testing. This chapter presents an overview of the tests you might receive and what to expect.

**General health tests**

**Medical history**
A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter medicines, herbs, or supplements you take. Tell your doctor about any symptoms you have. A medical history will help determine which treatment is best for you.

**Family history**
Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.

**Physical exam**
During a physical exam a doctor will check your body for signs of disease.

A health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Weigh you

Bring a list of any medications, vitamins, over-the-counter drugs, herbs, or supplements you are taking.

- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched. Tell your doctor if you feel pain.
- Feel for enlarged lymph nodes in your neck, underarm, and groin. Tell the doctor if you have felt any lumps or have any pain.

Doctors should perform a thorough physical exam along with a complete health history. A list of tests can be found in Guide 4.
Guide 4
Tests for liver cancer

Evaluation by a multidisciplinary team of doctors to assess liver health and to stage cancer

Medical history and physical exam

Hepatitis panel

Bilirubin, transaminases, alkaline phosphatase

Prothrombin time (PT) or international normalized ratio (INR), albumin, blood urea nitrogen (BUN), and creatinine

Complete blood count (CBC) and platelet count

Alpha-fetoprotein (AFP)

Chest CT

Bone scan, if needed

Abdominal and pelvic CT or MRI with contrast
Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of your blood, which is removed through a needle placed into your vein.

**Complete blood count**
A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. Your doctor will want to know if you have enough red blood cells to carry oxygen throughout your body, white blood cells to fight infection, and platelets to control bleeding.

**Comprehensive metabolic panel**
A comprehensive metabolic panel (CMP) is a test that measures 14 different substances in your blood. A CMP provides important information about how well your kidneys and liver are working, among other things.

**Blood urea nitrogen**
Blood urea nitrogen (BUN) is a waste product filtered out of the blood by the kidneys. A high level of BUN can be a sign your kidneys aren’t working well.

**Creatinine**
Creatinine is a waste produced in the muscles. It is filtered out of the blood by the kidneys and tells how well the kidneys are working.

**Liver function panel**
Liver function tests (LFTs) look at the health of your liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver is not working well or the bile ducts might be blocked.

**Bilirubin**
One of the liver function tests that is measured is bilirubin, a chemical that gives bile its color. There may be too much bilirubin in the blood if a tumor is blocking a bile duct and preventing the free flow of bile from the liver into the intestines or the liver is not working as well as it should. Too much bilirubin causes a yellowing of the eyes and skin called jaundice.

**Other**
Tests to measure the following might be done:

- Albumin
- Transaminases such as aspartate aminotransferase (AST) and alanine transaminase (ALT)
- Alkaline phosphatase (ALP)
- Prothrombin time (PT)
- International normalized ratio (INR)

Some of these tests are used to determine your Child-Pugh class. Levels that are too high or low may be a sign of liver damage or cancer spread.

**Hepatitis panel**
Hepatitis is a type of liver disease. Viruses called hepatitis A, hepatitis B (HBV), and hepatitis C (HCV) are the most common causes of hepatitis. A hepatitis panel is a blood test that checks to see if you have a hepatitis infection caused by one of these viruses. Chronic (long-term) hepatitis B and a current or past infection with hepatitis C increase the risk for liver cancer and biliary tract cancers. Hepatitis causes the liver to become inflamed and not work as it should. HBV can cause scarring of the liver, liver failure, and cancer.
A hepatitis panel will tell your treatment team if you had hepatitis in the past or if you have it today. You may be referred to a hepatologist if you have positive results. A hepatologist is a doctor who specializes in the care of the liver, biliary tract, gallbladder, and pancreas.

**Fibrosis score**
Fibrosis is scored from 0 to 6. Fibrosis is mild scarring of liver tissue. Cirrhosis is when this scarring becomes severe.

This F scoring system is another important factor for determining prognosis. Prognosis is the likely course and outcome of a disease based on your age and blood tests.

- **F0** Fibrosis score of 0 to 4 is none to moderate fibrosis
- **F1** Fibrosis score of 5 to 6 is severe fibrosis or cirrhosis

A fibrosis score is based on a biopsy or surgery sample. There are ultrasound tests that can estimate fibrosis, as well.

**Child-Pugh class**
The Child-Pugh score measures the severity of liver disease such as cirrhosis. This score helps your treatment team see how the liver is working, decide if surgery is an option, and plan treatment.

This system includes:

- Class A (lowest surgery risk)
- Class B (intermediate surgery risk)
- Class C (highest surgery risk)

The class is based on signs, symptoms, and blood test results. Those with a Child-Pugh Class A have the lowest risk of complications or death from surgery. In some cases, those with Child-Pugh Class B might be recommended for surgery.

**Imaging tests**
Imaging tests take pictures (images) of the inside of your body. These tests are used to find and treat liver cancer. Imaging tests show the primary tumor, or where the cancer started, and look for cancer in other parts of the body. Imaging tests also look to see if the tumor involves any veins, arteries, or organs.

A radiologist, an expert who looks at test images, will write a report and send this report to your doctor. Your doctor will discuss the results with you. Feel free to ask as many questions as you like.

**CT scan**
A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the images are combined to make one detailed three-dimensional (3D) picture.

A CT scan of your chest, abdomen, and/or pelvis may be one of the tests to look for cancer. In most cases, contrast will be used. Contrast material is used to improve the pictures of the inside of the body. Contrast materials are not dyes, but substances that help certain areas in the body stand out. Contrast is used to make the pictures clearer.
The contrast is not permanent and will leave the body in your urine.

Tell your doctors if you have had bad reactions to contrast in the past. This is important. You might be given medicines, such as Benadryl® and prednisone, for an allergy to contrast. Contrast might not be used if you have a serious allergy or if your kidneys aren’t working well.

**Dynamic CT scan**
In a dynamic CT scan, there are two scans: one without contrast and one with contrast. First, a scan is done without contrast. Then, contrast is injected into a vein and another scan is done.

**Multiphasic CT scan**
A multiphasic CT scan is similar to a dynamic CT scan. It starts without contrast. Then contrast is added and multiple sets of pictures are taken as the contrast moves through the arteries and veins of the liver. This allows doctors to see where the tumor is in the liver and if the tumor involves any veins, arteries, or organs.

**MRI scan**
A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. Contrast might be used.

**Dynamic MRI scan**
In a dynamic MRI scan, there are two scans: one without contrast and one with contrast. First, a scan is done without contrast. Then, contrast is injected into a vein and another scan is done.

**MRCP**
A magnetic resonance cholangiopancreatography (MRCP) is a type of MRI scan that makes very clear pictures of the pancreas and bile ducts. No contrast is used because bile and other fluids act as their own contrast. An MRCP is usually done with an MRI scan.

**Ultrasound**
An ultrasound (US) uses high-energy sound waves to form pictures of the inside of the body. A probe will be pressed onto your abdomen. Ultrasound is good at showing small areas of cancer that are near the surface of the body. Sometimes, an ultrasound or MRI is used to guide a biopsy.

A contrast-enhanced ultrasound (CEUS) might be used in addition to other tests to learn more about nodules or very small tumors.

**PTC**
A percutaneous transhepatic cholangiography (PTC) uses contrast and an x-ray to take pictures of the biliary tract. A needle or small catheter (thin, flexible tube) is placed through the skin (percutaneous) into a bile duct and contrast is injected. X-rays that use small amounts of radiation are then taken to make pictures of the bile ducts. If necessary, a catheter can be inserted to drain fluid from the biliary tract into a bag outside of the body or into the small intestine. A metal stent may also be placed for an obstruction or blocked bile duct.

For this test, you will be given medicine to help you feel relaxed.
Biopsy

A biopsy is a procedure that removes samples of fluid or tissue. Tissue or fluid may be removed from your body and tested to diagnose cancer. If you are at high risk for liver cancer, sometimes findings on CT or MRI are enough to make the diagnosis and a biopsy may not be needed.

A biopsy may be considered because you are not at high risk (no cirrhosis, no HBV) or imaging results are unclear. You may have a biopsy if the cancer has spread to another area in the body, also known as metastatic cancer. Your doctor may want to assess the cell type of the cancer before starting treatment.

Types of possible biopsies include:

- **Fine-needle aspiration (FNA)** uses a thin needle to remove a sample of tissue or fluid. An ultrasound (US) may guide the FNA biopsy.

- **Core needle biopsy** removes tissue samples with a hollow needle about the same size as a needle used for an IV (intravenous) line.

- **Laparoscopy** uses a device that passes through a small cut in the abdomen. A tool then takes samples of tissue.

The biopsy samples will be sent to a pathologist. A pathologist is an expert in examining cells under a microscope to find disease.

Tumor tests

A sample from a biopsy of your tumor will be tested to look for biomarkers or proteins. This information is used to choose the best treatment for you. It is sometimes called molecular testing. Cancer antigen 19-9 (CA 19-9), carcinoembryonic antigen (CEA), and alpha-fetoprotein (AFP) are examples of biomarkers. Some biomarkers are found in your blood. Others can be found in tumors.

Tumor mutation testing

A sample of your tumor or blood may be used to see if the cancer cells have any specific mutations. Some mutations can be targeted with specific therapies such as NTRK gene fusion. This is separate from the genetic testing for mutations that you may have inherited from your parents.
Test results

Results from blood tests, imaging studies, and biopsy will determine your treatment plan. It is important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a great way to access your test results.

Whether you are going for a second opinion, test, or office visit, keep these things in mind:

- Bring someone with you to doctor visits. Encourage this person to ask questions and take notes. Perhaps they can record the conversation with your doctor.
- Write down questions and take notes during appointments. Don’t be afraid to ask your care team questions. Get to know your care team and let them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have. It will be helpful when getting a second opinion.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your binder or notebook. Hang the list on your fridge or keep it by the phone.

Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- Create folders for insurance forms, medical records, and tests results. You can do the same on your computer.
- Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- Organize your binder in a way that works for you. Add a section for questions and to take notes.
- Bring your medical binder to appointments. You never know when you might need it!
Review

- The liver, gallbladder, and bile ducts are part of the hepatobiliary system.
- Tests are used to find cancer, plan treatment, and check how well treatment is working.
- Your health history and physical exam inform your doctor about your overall health.
- Blood tests check for signs of disease and how well organs are working.
- Imaging tests take pictures of the inside of your body.
- A biopsy removes tissue or fluid from your body to diagnose cancer.
- Fibrosis score and Child-Pugh class are used to see how well the liver is working, decide if surgery is an option, and plan treatment.
- Results from blood tests, imaging studies, and biopsy will determine your treatment plan. Online portals are a great way to access your test.
Liver cancer treatments

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28 Liver transplant
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31 Arterially directed therapy
32 Radiation therapy
33 Systemic therapy
34 Clinical trials
35 Supportive care
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37 Review
Liver cancer is treatable. Treatment can be local, systemic, or a combination of both. It is important to have regular talks with your doctor about your goals for treatment and your treatment plan.

There are 2 types of treatment:

- **Local therapy** focuses treatment on a certain area. It includes surgery, ablation, embolization, and radiation therapy.

- **Systemic therapy** works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.

There are many treatment options. However, not everyone responds to treatment in the same way. Some people will do better than expected. Others will do worse. Many factors play in a role in how you respond to treatment.

## Surgery

Surgery is a form of local treatment. It is an operation or procedure to remove cancer from the body. This is only one part of a treatment plan.

Surgery can be used to:

- Remove all of the tumor
- Provide supportive care (relieve pain or discomfort)

Surgery is the main or primary treatment for liver cancer. The goal of surgery is to remove all of the cancer. Surgery may also be used to reduce symptoms caused by the cancer or extend life.

The type of surgery you receive depends on size, location, and number of tumors in the liver. It also depends on if there is cancer in any surrounding organs and tissues, if there is cirrhosis, and how severe the cirrhosis is.

Liver surgery can be complex. The tumor might have grown into veins and arteries in such a way that makes it unsafe to remove. Surgery may not be an option if the cancer has spread, the liver is not healthy enough for surgery, or if other medical conditions exist.

When preparing for surgery, you should seek the opinion of an experienced surgeon. The surgeon should be an expert in performing these types of surgery. Seek care or ask for a referral to a hospital or cancer center that has experience in treating liver cancer.
Liver cancer treatments

Tumor resection
Imaging tests will be used to see if your cancer is resectable (can be removed completely with surgery) or unresectable (cannot be removed with surgery). The goal of surgery or tumor resection is to remove all of the cancer. To do so, the tumor is removed along with some normal-looking tissue around its edge. The normal-looking tissue is called the surgical margin. A clear or negative margin (R0) is when no cancerous cells are found in the tissue around the edge of the tumor. In an R1 positive margin, the surgeon removes all of the visible tumor, but the microscopic margins are still positive for tumor cells. In an R2 positive margin, the surgeon does not or is unable to remove all of the visible tumor.

A negative margin (R0) is the best result. Your surgeon will look carefully for cancer not only along the surgical margin, but in other nearby areas. It is not always possible to find all of the cancer. Sometimes, surgeons can’t safely remove the tumor with a cancer-free margin.

You might have more than one surgery. You might also have a wound drain to prevent fluid from collecting in the body after surgery.

Partial hepatectomy
If the tumor is resectable, then you might have a partial hepatectomy. This is surgery to remove a portion of the liver. It might be a small wedge resection or removal of an entire lobe. The part of the liver that remains will keep working, and the missing section will regrow. A partial hepatectomy is different than a liver transplant. A partial hepatectomy is not for everyone. Liver damage, such as cirrhosis or fibrosis, can make surgery more difficult. The size and location of the tumor, as well as your liver function (Child-Pugh score), will play a role in if tumor resection is the best option for you. You must also have a working liver and be healthy enough for surgery.

Liver transplant
In a liver transplant, the entire diseased liver is removed and replaced with a healthy, donor liver. The new liver may be donated from a person who recently died or a section of liver may be donated from a living person. A liver transplant is based on certain size limits and tumor locations.

The liver is divided into 8 sections or segments based on portal vein and bile duct locations. It is possible for someone to donate a portion of the liver. Structures such as the inferior vena cava, portal vein, hepatic artery, and bile ducts are reconnected to the new liver. Remember, a liver transplant can be a whole liver replacement or just a portion.

A liver transplant may be an option for people who can’t have a partial hepatectomy. However, not everyone is a candidate for a liver transplant.

Other treatments may be given if you are waiting for a transplant. These treatments are called bridging therapy and include ablation and embolization.
There is still a chance that cancer will return after a liver transplant. It is also possible your body will reject the donor liver. You will be given medicine to prevent rejection.

**UNOS**

United Network for Organ Sharing (UNOS) is the non-profit organization that manages the organ transplant list in the United States.

Those with hepatocellular carcinoma (HCC) must meet certain criteria to be eligible for a liver transplant:

- One tumor of 5 cm or less, or
- 2 or 3 tumors of 3 cm or less
- Sometimes exceptions are made at select transplant centers

**MELD**

Model for End-Stage Liver Disease (MELD) is a score determined by 3 blood tests:

- Total bilirubin, a measure of jaundice
- Prothrombin time, a measure of clotting ability
- Creatinine, a measure of kidney function

The poorer the liver function, the higher the MELD score. The person with the highest MELD score is at the top of the transplant list. Lists are organized by blood type. Your blood type must match the donor’s blood type.

---

**Liver transplant**

The liver is divided into 8 sections or segments based on the location of the portal vein, hepatic vein, and bile ducts.
Ablation

Ablation is a type of local treatment that uses extreme cold or heat, radio waves, microwaves, or chemicals such as ethanol (a type of alcohol) or acetic acid to destroy cancer cells. It can destroy small tumors with little harm to nearby tissue.

There are 3 types of ablation used to destroy cancer cells:

- **Chemical** includes percutaneous ethanol injection (PEI) or acetic acid injection.
- **Thermal** includes radiofrequency ablation (RFA) or microwave ablation (MWA). RFA kills cancer cells by heating them with high-energy radio waves. MWA uses microwaves.
- **Cryoablation** kills cancer cells by freezing them with a very cold substance.

All types of ablation use a special needle, called a probe, which is inserted into the tumor. With cryotherapy, a medical gas is passed through the probe to cause below-freezing temperatures. This freezes the tumor to destroy it. With RFA, the probe emits radio waves to heat the tumor and destroy it. The probe can be guided into place with a CT scan, ultrasound, or other imaging tests. The probe will be removed when treatment is done.

Your doctor will check the tumor size and location, and how well your liver is working before doing this treatment. Ablation can be done through the skin (percutaneous), through small cuts (laparoscopic), or using a large incision like in surgery (open approach). RFA and MWA are the most common types of ablation used.

Ablation is often used with smaller tumors of 3 cm or less. Tumors must be in an area that can be reached with ablation and not be near other organs, major blood vessels, or bile ducts.
Arterially directed therapy

Arterially directed therapy includes embolization (TAE), chemoembolization (TACE), drug-eluting bead embolization (DEB-TACE), and radioembolization (Y90 or TARE). It treats tumors by injecting particles, chemotherapy, or radioactive beads directly into the blood vessels that supply the tumor(s). A small catheter is inserted into the artery and is guided to the tumor. Once in place, the particles, chemotherapy, or beads are injected.

The common types of arterially directed therapy include:

- Transarterial bland embolization (TAE) involves blocking the blood supply to the tumor by injecting tiny particles into the blood vessels feeding the tumor(s). Stopping the blood flow cuts off the oxygen supply to the tumor and causes cancer cells to die. TAE has risks. It might not be used if your bilirubin level is above 3 mg/mL.

- Chemoembolization (also known as TACE or transarterial chemoembolization) involves injecting a chemotherapy mixture into the tumor and blocking the feeding blood vessels to the tumor(s). TACE has risks. It might not be used if your bilirubin level is above 3 mg/mL.

- DEB-TACE (drug-eluting bead transarterial chemoembolization) uses tiny particles loaded with chemotherapy that are injected into the blood vessels feeding the tumor(s). The particles give off small amounts of chemotherapy to the tumor over several days. It might not be used if your bilirubin level is above 3 mg/mL.

- Transarterial radioembolization (TARE) uses tiny glass or resin beads filled with the radioactive isotope yttrium-90 that are injected directly into the tumor(s). TARE has risks. It might not be used if your bilirubin level is above 3 mg/mL.

Depending on the circumstances, arterially directed therapy may be used as bridging treatment before a liver transplant, as definitive treatment, or for palliation. Definitive treatment is defined as the best treatment after all choices have been considered. The type of arterially directed therapy recommended will depend on the size, number, and location of tumors as well as your previous medical history and the expertise of your treating physicians.
Radiation therapy

Radiation therapy (RT) uses high-energy radiation from x-rays, gamma rays, protons, and other sources to kill cancer cells and shrink tumors. It is given over a certain period of days to weeks. RT can be given alone, or before or after surgery, or with other therapies to treat or slow the growth of cancer. Sometimes, radiation is given with certain systemic therapies such as chemotherapy. It may be used as supportive care to help ease pain or discomfort caused by cancer.

RT may be a treatment for all tumors, regardless of location.

In general, radiation may be given:

- As the primary (first) treatment
- Before surgery, called neoadjuvant therapy, to shrink the tumor before surgery
- During surgery, called intraoperative radiation therapy (IORT)
- After surgery, called adjuvant treatment, to kill any cancerous cells that remain

External beam radiation therapy

External beam radiation therapy (EBRT) uses a machine outside of the body to aim radiation at the tumor(s). There is more than one type of EBRT used in the treatment of liver cancer. These allow for safer, higher doses of radiation.

Types of EBRT that may be used to treat your cancer include:

- **Stereotactic body radiation therapy (SBRT)** uses high-energy radiation beams to treat cancers. The goal is to kill or ablate the tumor. SBRT can be done with either photons or protons.
- **Proton beam radiation therapy** uses particles called protons to treat and kill tumor cells. Protons reduce the dose of radiation to surrounding normal tissues.
- **Three-dimensional conformal radiation therapy (3D-CRT)** uses computer software and CT images to aim beams that match the shape of the tumor. This limits the amount of radiation to normal tissues.
- **Intensity-modulated radiation therapy (IMRT)** uses small beams of different strengths so that the radiation matches the shape of the tumor. This limits the amount of radiation to normal tissues.
- **Image-guided radiation therapy (IGRT)** uses a computer to create a picture of the tumor. This helps guide the radiation beam during treatment. It is used with IMRT and 3D-CRT. Tumors can shift slightly within the body and can change shape and size between and during treatment visits. Because of this, IGRT can improve how well 3D-CRT and IMRT target the tumor.
- **Intraoperative radiation therapy (IORT)** uses radiation treatment aimed directly at the tumor during surgery.
- **Palliative EBRT** is used to treat pain caused by cancer.
Systemic therapy

A cancer treatment that affects the whole body is called systemic therapy. Traditional chemotherapy is still the most common type of systemic therapy, but now there are other cancer treatments like targeted therapy and immunotherapy. Each works differently to shrink the tumor and prevent recurrence. Systemic treatments may be used alone or together.

Systemic therapies that might be used include:

- Chemotherapy – attacks rapidly dividing cells in the body
- Targeted therapy – focuses on specific or unique feature of cancer cells
- Immunotherapy – uses your body's natural defenses to find and destroy cancer cells

Chemotherapy
Chemotherapy is a type of drug therapy that kills fast-growing cells throughout the body, including cancer cells and normal cells. All chemotherapy drugs affect the information inside genes called DNA (deoxyribonucleic acid). Genes tell cancer cells how and when to grow and divide. Chemotherapy disrupts the life cycle of cancer cells.

Targeted therapy
Targeted therapy is a form of systemic therapy that works throughout your body. It is drug therapy that focuses on specific or unique features of cancer cells.

Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop the action of molecules that help cancer cells grow and/or survive. A tyrosine kinase inhibitor (TKI) is a type of targeted therapy that blocks the signals that cause liver cancer to grow and spread.

The following are some targeted therapies that might be used to treat liver cancer:

- Sorafenib
- Lenvatinib
- Atezolizumab
- Bevacizumab

Targeted therapies may be used to treat other tumors that have certain gene mutations such as NTRK gene fusion.

Immunotherapy
Immunotherapy is a type of systemic treatment that increases the activity of your immune system. By doing so, it improves your body’s ability to find and destroy cancer cells. Immunotherapy can be given alone or with other types of treatment. Pembrolizumab, ipilimumab, and nivolumab are types of immunotherapy.

An immune checkpoint inhibitor is a type of immunotherapy that blocks proteins called checkpoints that are made by some types of immune system cells and some cancer cells. Sometimes, immune checkpoint inhibitors are used to treat liver cancer.
Clinical trials

Clinical trials study how safe and helpful tests and treatments are for people. Clinical trials find out how to prevent, diagnose, and treat a disease like cancer. Because of clinical trials, doctors find safe and helpful ways to improve your care and treatment of cancer.

Clinical trials have 4 phases.

**Phase I trials** aim to find the safest and best dose of a new drug. Another aim is to find the best way to give the drug with the fewest side effects.

**Phase II trials** assess if a drug works for a specific type of cancer.

**Phase III trials** compare a new drug to a standard treatment.

**Phase IV trials** evaluate a drug’s safety and treatment results after it has been approved.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial often are alike in terms of their cancer and general health. This helps to ensure that any change is from the treatment and not because of differences between patients.

If you decide to join a clinical trial, you will need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits. Even after you sign a consent form, you can stop taking part in a clinical trial at any time.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you’re getting treatment or at other treatment centers nearby. Discuss the risks and benefits of joining a clinical trial with your care team. Together, decide if a clinical trial is right for you.

NCCN experts encourage patients to join a clinical trial when it is the best option for the patient.
Supportive care

Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. It might include pain relief (palliative care), emotional or spiritual support, financial aid, or family counseling. Supportive care is given during all cancer stages. Tell your care team how you are feeling and about any side effects. Best supportive care is used with other treatments to improve quality of life. Best supportive care, supportive care, and palliative care are often used interchangeably.

Treatment side effects

All cancer treatments can cause unwanted health issues. Such health issues are called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant.

Ask for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects.

Trouble eating

Sometimes side effects from surgery, cancer, or other treatments might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth. Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who is an expert in nutrition and food can help. Speak to your care team if you have trouble eating or maintaining your weight.

For more information, read the NCCN Guidelines for Patients: Nausea and Vomiting, available at nccn.org/patientguidelines.

Blocked bile duct

A tumor in the liver may grow large enough to block your bile duct. A bile duct is a small tube that drains digestive fluid (bile) from the liver. The common bile duct carries bile from the liver through the pancreas and into the first part of the small intestine (duodenum). A blocked duct causes bile to build up in the liver. As a result, you may have pain, itching, discomfort, and/or yellowing of the skin and eyes. This is called jaundice. This blockage can cause an infection of the bile duct called cholangitis.

A blocked bile duct may be treated by placing a biliary stent or doing a biliary bypass. A biliary stent is a tiny tube that is placed in the bile duct to unblock it or keep it open. Before the stent can be placed, bile may need to be drained through an opening in the side of the body. You may need a new or second stent during or after cancer treatment if the tumor grows. A biliary bypass is a surgery to re-route the flow of bile from the common bile duct into the small intestine. The result is that the bile flow avoids (bypasses) the blocked part of the duct.
Treatment team

Treating cancer takes a team approach. Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and let them get to know you.

Depending on your diagnosis, your team might include the following specialists:

- **Your primary care doctor** handles medical care not related to your cancer. This person can help you express your feelings about treatments to your cancer care team.
- **A pathologist** interprets the cells, tissues, and organs removed during a biopsy or surgery.
- **A diagnostic radiologist** reads the results of x-rays and other imaging tests.
- **An interventional radiologist** performs needle biopsies, ablations, and arterially directed therapies, and places ports for treatment.
- **A surgical oncologist** performs operations to remove cancer.
- **A medical oncologist** treats cancer in adults using systemic therapy. Often, this person will lead the overall treatment team and keep track of tests and exams done by other specialists. A medical oncologist will often coordinate your care. Ask who will coordinate your care.
- **A radiation oncologist** prescribes and plans radiation therapy to treat cancer.
- **An anesthesiologist** gives anesthesia, a medicine so you do not feel pain during surgery or procedures.
- **A gastroenterologist** is an expert in digestive diseases. A specific type of gastroenterologist that focuses on liver disease is called a hepatologist.
- **A palliative care specialist** is an expert in the treatment of symptoms caused by the cancer with the goal of improving a patient’s quality of life and easing suffering.
- **Advanced practice providers** are an important part of any team. These are registered nurse practitioners and physician assistants who monitor your health and provide care.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Nutritionists** can provide guidance on what foods or diet are most suitable for your particular condition.
- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you feel.

You know your body better than anyone. Help other team members understand:

- How you feel
- What you need
- What is working and what is not
Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

Get to know your care team and let them get to know you.

Review

- Local therapy focuses treatment on a certain area. It includes surgery, radiation therapy, ablation, and arterially directed therapy.

- Surgery is a main treatment option for liver cancer.

- Doctors may consider a liver transplant for those who meet certain criteria for this treatment.

- Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.

- Arterially directed therapy treats tumors by injecting particles, chemotherapy, or radioactive beads directly into the blood vessels that supply the tumor(s).

- Targeted therapies can block the ways cancer cells grow, divide, and move in the body.

- Immunotherapy uses your body’s natural defenses to find and destroy cancer cells.

- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.

- Supportive care is health care that relieves symptoms caused by cancer or cancer treatment and improves quality of life.
4
Resectable

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40 Surveillance
40 Review
A tumor that can be removed with surgery is called resectable. This is different than a liver transplant, which removes the liver and replaces it with a donor liver. This chapter is for those whose tumor might be resectable or for whom a liver transplant is an option. Together, you and your doctor will choose a treatment plan that is best for you.

Overview

Surgery is not for everyone. You must be healthy enough for surgery and not have other serious health issues. Depending on the size and location of the tumor(s), how well your liver functions, or if the cancer has spread outside the liver or invaded other structure such as veins, arteries, or ducts, surgery might not be an option.

There are 2 types of surgery:

- Resection is surgery to remove a tumor. Sometimes, a partial hepatectomy is referred to as resection. A partial hepatectomy removes part of the liver.
- Transplant is surgery to remove all of your liver and replace it with a donor liver.

Your doctor will talk to you about the options and ask if you want surgery. Not everyone wants surgery. Your wishes about treatment are important.

Resection

Resection may be an option when the following criteria are met:

- Child-Pugh Class A (Child-Pugh Class B only in certain cases)
- No portal hypertension
- Suitable tumor location
- Adequate liver reserve
- Suitable liver remnant

When possible surgery to remove the tumor is preferred. However, resectable tumors can also be treated with ablation, arterially directed therapy, or radiation therapy. For resectable treatment options, see Guide 5.

Guide 5

Resectable treatment options

<table>
<thead>
<tr>
<th>Treatment Options</th>
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<tbody>
<tr>
<td>Surgery to remove tumor (preferred)</td>
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<tr>
<td>Ablation</td>
</tr>
<tr>
<td>Arterially directed therapy</td>
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<tr>
<td>External beam radiation therapy (EBRT)</td>
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</tbody>
</table>
Transplant

Transplant may be an option if the following UNOS criteria are met:

- Tumor is 2 to 5 cm in diameter or 2 to 3 tumors that are 3 cm or less
- No large veins, arteries, or bile ducts have cancer (no macrovascular involvement)
- No disease outside the liver (extrahepatic)

If transplant is not an option, see Guide 5.

If transplant is an option, then

- Refer to a liver transplant center that has an experienced transplant team
- Consider bridging therapy

Bridging therapy is treatment given while waiting for a transplant to prevent cancer from growing or spreading. If cancer grows or spreads, you might not be able to have a liver transplant. Bridging therapy options include ablation, embolization, radiation therapy, or systemic therapy.

Surveillance

After treatment, you will start surveillance. Surveillance consists of testing on a regular basis to watch for signs that cancer has returned. Imaging tests and blood tests to look for alpha-fetoprotein (AFP) are needed. You might be referred to a hepatologist to discuss antiviral treatment options if you have hepatitis. See Guide 6.

Review

- A tumor that can be removed with surgery is called resectable. In a resectable tumor, surgery to remove the tumor is preferred. However, resectable tumors can be treated with ablation, arterially directed therapy, or radiation therapy.
- A liver transplant might be an option if you meet certain UNOS criteria.
- If a liver transplant is an option, you might have bridging therapy while waiting for a transplant. Bridging therapy might include ablation, embolization, radiation therapy, or systemic therapy.
- Surveillance consists of testing on a regular basis to watch for tumor growth.

Guide 6

Surveillance

- Imaging tests every 3 to 6 months for 2 years, then every 6 to 12 months
- Alpha-fetoprotein (AFP) every 3 to 6 months for 2 years, then every 6 to 12 months
- Refer to a hepatologist for a discussion of antiviral therapy for those with hepatitis
5

Unresectable

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43 Treatment without surgery
45 Review
Surgery for liver cancer is not always possible. Sometimes, the location of the tumor prevents surgery or the liver is not healthy enough for resection. A tumor that cannot be removed with surgery is called unresectable. A liver transplant might be an option for some. Together, you and your doctor will choose a treatment plan that is best for you.

Overview

Surgery to remove a tumor is called resection. Surgery that removes the tumor with part of the liver is called partial hepatectomy. Sometimes, surgery is not possible because of where the tumor is located or the liver is too damaged. In addition, sometimes liver transplant is not an option.

There are treatments if a partial hepatectomy or liver transplant are not options.

Transplant

Transplant may be an option if the following UNOS criteria are met:

- Tumor is 2 to 5 cm in diameter or 2 to 3 tumors are 3 cm or less
- No large veins, arteries, or bile ducts have cancer
- No disease outside the liver (extrahepatic)

If transplant is an option, then

- Refer to a liver transplant center that has an experienced transplant team
- Consider bridging therapy

Bridging therapy is treatment given while waiting for a transplant to prevent cancer from growing or spreading. If cancer grows or spreads, you might not be able to have a liver transplant. Bridging therapy options include ablation, embolization, radiation therapy, or systemic therapy.

Surveillance

After a liver transplant, you will start surveillance. Surveillance consists of testing on a regular basis to watch for signs that cancer has returned. Imaging tests and blood tests to look for alpha-fetoprotein (AFP) are needed. See Guide 7.

Guide 7

Surveillance after liver transplant

Imaging tests every 3 to 6 months for 2 years, then every 6 to 12 months

Alpha-fetoprotein (AFP) every 3 to 6 months for 2 years, then every 6 to 12 months
Treatment without surgery

Not everyone is healthy enough for a liver transplant. You may not want a liver transplant. There are treatments if surgery or a liver transplant are not options. For treatment options, see Guide 8.

Locoregional therapy
Locoregional therapy focuses on the area or region where the cancer is. It includes ablation, arterially directed therapy, and radiation therapy. These are the preferred treatment options for those not receiving a liver transplant.

Best supportive care
Best supportive care is used to relieve symptoms caused by cancer or cancer treatment and improve quality of life.

Clinical trial
A clinical trial might be an option. Ask your doctor if a clinical trial is right for you.

Systemic therapy
Systemic therapy is drug therapy that works throughout the body. Preferred treatment options will be based on your Child-Pugh class. Ask your medical oncologist why one drug might be chosen over another.

First-line options are the treatments tried first. The preferred systemic therapies are sorafenib, lenvatinib, or atezolizumab with bevacizumab. Nivolumab and FOLFOX (fluorouracil, leucovorin, and oxaliplatin) are used in some cases. For first-line systemic therapy options, see Guide 9.

Guide 8
Unresectable treatment options for those not receiving a liver transplant

Locoregional therapy (preferred):
• Ablation
• Arterially directed therapy
• External beam radiation therapy (EBRT)

Clinical trial

Best supportive care

Systemic therapy (see Guide 9)
Progression
When cancer grows or spreads, it is called disease progression. When first-line systemic therapy doesn’t stop the growth or spread of cancer, then more lines of therapy might be tried. Treatment is based on the type of systemic therapy you had before.

For next-line systemic therapy options, see Guide 10.

Guide 9
First-line systemic therapy options

<table>
<thead>
<tr>
<th>Preferred options</th>
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</thead>
<tbody>
<tr>
<td>• Sorafenib (Child-Pugh Class A or B7)</td>
<td></td>
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<tr>
<td>• Lenvatinib (Child-Pugh Class A only)</td>
<td></td>
</tr>
<tr>
<td>• Atezolizumab with bevacizumab (Child-Pugh Class A only)</td>
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</table>

<table>
<thead>
<tr>
<th>Useful in some cases</th>
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</tr>
</thead>
<tbody>
<tr>
<td>• Nivolumab (if tyrosine kinase inhibitors [TKIs] or other anti-angiogenic agents are not an option)</td>
<td></td>
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<tr>
<td>• FOLFOX</td>
<td></td>
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</tbody>
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Guide 10
Next-line systemic therapy options: Disease progression

• Regorafenib (Child-Pugh Class A only)
• Cabozantinib (Child-Pugh Class A only)
• Ramucirumab (only if AFP is 400 ng/mL or more)
• Lenvatinib (Child-Pugh Class A only)
• Sorafenib (Child-Pugh Class A or B7)

For those who have not been previously treated with a checkpoint inhibitor:
• Nivolumab (Child-Pugh Class A or B)
• Nivolumab with ipilimumab (Child-Pugh Class A only)
• Pembrolizumab (Child-Pugh Class A only)

• Larotrectinib and entrectinib are treatment options for HCC that is NTRK gene fusion-positive
Review

- A tumor that cannot be removed with surgery is called unresectable.

- A liver transplant might be an option if you meet certain criteria.

- After a liver transplant, you will undergo surveillance. Surveillance consists of testing on a regular basis to watch for tumor growth.

- If a liver transplant is not an option, or to prevent the tumor from growing while you are on a transplant list, then locoregional therapy such as ablation, arterially directed therapy, or EBRT are preferred.

- Systemic therapy, a clinical trial, or best supportive care are other options for those not undergoing a liver transplant.
6 Inoperable

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47 Treatment options
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In inoperable liver cancer, resection and a liver transplant are not options. This chapter discusses the treatment options for cancer that is confined to the liver or has spread to just outside of the liver. Ablation, arterially directed therapy, and radiation therapy are the preferred treatment options. Together, you and your doctor will choose a treatment plan that is best for you.

**Overview**

In inoperable liver cancer, a resection and liver transplant are not an option. There are different reasons why a liver transplant is not possible. You might not want a liver transplant. You might not be healthy enough for surgery or you might have other serious health issues that prevent surgery. However, there are treatment options.

**Treatment options**

Not everyone is healthy enough for surgery. You may not want a liver transplant. If this is the case, there are other treatment options. For treatment options, see Guide 11.

**Locoregional therapy**

Locoregional therapy is the preferred treatment for cancer that is confined to the liver. This is called local or regional disease.

Locoregional therapy includes:

- Ablation
- Arterially directed therapy
- Radiation therapy

**Best supportive care**

Best supportive care is used to relieve symptoms caused by cancer or cancer treatment and improve quality of life.

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**Guide 11**

**Inoperable treatment options**

Locoregional therapy (preferred):

- Ablation
- Arterially directed therapy
- External beam radiation therapy (EBRT)

Clinical trial

Best supportive care

Systemic therapy (see Guide 12)
**Clinical trial**
A clinical trial might be an option. Ask your doctor if a clinical trial is right for you.

**Systemic therapy**
Systemic therapy is drug therapy that works throughout the body. Preferred treatment options will be based on your Child-Pugh class. Ask your medical oncologist why one drug might be chosen over another.

First-line options are the treatments tried first. The preferred systemic therapies are sorafenib, lenvatinib, or atezolizumab with bevacizumab. Nivolumab and FOLFOX (fluorouracil, leucovorin, and oxaliplatin) are used in some cases. For first-line systemic therapy options, see Guide 12.

**Progression**
When cancer grows or spreads, it is called disease progression. When first-line systemic therapy doesn’t stop the growth or spread of cancer, then more lines of therapy might be tried. Treatment is based on the type of systemic therapy you had before.

For next-line systemic therapy options, see Guide 13.

---

### Guide 12
**First-line systemic therapy options**

<table>
<thead>
<tr>
<th>Preferred options</th>
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</thead>
<tbody>
<tr>
<td>• Sorafenib (Child-Pugh Class A or B7)</td>
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<tr>
<td>• Lenvatinib (Child-Pugh Class A only)</td>
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<tr>
<td>• Atezolizumab with bevacizumab (Child-Pugh Class A only)</td>
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<td>• Nivolumab (if tyrosine kinase inhibitors [TKIs] or other anti-angiogenic agents are not an option)</td>
</tr>
<tr>
<td>• FOLFOX</td>
</tr>
</tbody>
</table>

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Review

- In inoperable liver cancer, resection and liver transplant are not treatment options.
- The preferred treatment option is locoregional therapy. This includes ablation, arterially directed therapy, or radiation therapy.
- Other options include best supportive care, clinical trial, or systemic therapy.
- Systemic therapy options will be based on your Child-Pugh class.

A preferred treatment option is proven to be more effective.

Guide 13
Next-line systemic therapy options: Disease progression

- Regorafenib (Child-Pugh Class A only)
- Cabozantinib (Child-Pugh Class A only)
- Ramucirumab (only if AFP is 400 ng/mL or more)
- Lenvatinib (Child-Pugh Class A only)
- Sorafenib (Child-Pugh Class A or B7)

For those who have not been previously treated with a checkpoint inhibitor:
- Nivolumab (Child-Pugh Class A or B)
- Nivolumab with ipilimumab (Child-Pugh Class A only)
- Pembrolizumab (Child-Pugh Class A only)

- Larotrectinib and entrectinib are treatment options for HCC that is NTRK gene fusion-positive
7 Metastatic

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51 Treatment options
53 Review
Stage 4B liver cancer is metastatic liver cancer. This is cancer that has spread to distant sites in the body (M1). The tumor(s) can be any size (any T). There may be cancer in the lymph nodes (any N). Together, you and your doctor will choose a treatment plan that is best for you.

Treatment options

Before treatment starts a biopsy is often needed to confirm there are metastases. Treatment options include a clinical trial, best supportive care, or systemic therapy. See Guide 14.

Clinical trial

A clinical trial might be an option. Ask your doctor if a clinical trial is right for you.

Best supportive care

Best supportive care is used to relieve symptoms caused by cancer or cancer treatment and improve quality of life.

Systemic therapy

Systemic therapy is drug therapy that works throughout the body. Preferred treatment options will be based on your Child-Pugh class and other factors. Ask your medical oncologist why one drug might be chosen over another.

First-line options are the treatments tried first. The preferred systemic therapies are sorafenib, lenvatinib, or atezolizumab with bevacizumab. Nivolumab and FOLFOX (fluorouracil, leucovorin, and oxaliplatin) are used in some cases. For first-line systemic therapy options, see Guide 15.

Guide 14
Metastatic treatment options

Clinical trial

Best supportive care

Systemic therapy (see Guide 15)
Progression
When cancer grows or spreads, it is called disease progression. When first-line systemic therapy doesn’t stop the growth or spread of cancer, then more lines of therapy might be tried. Treatment is based on the type of systemic therapy you had before.

For next-line systemic therapy options, see Guide 16.

Guide 15
First-line systemic therapy options

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Guide 16 HCC-F
Next-line systemic therapy options: Disease progression

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• Pembrolizumab (Child-Pugh Class A only)

• Larotrectinib and entrectinib are treatment options for HCC that is NTRK gene fusion-positive
Review

- Stage 4B liver cancer is metastatic liver cancer. It is cancer that has spread to distant sites.
- Treatment options are clinical trial, best supportive care, or systemic therapy.
- The goal of treatment is to reduce the amount of cancer in the body called cancer burden and to prevent the further spread of cancer.

Did you know?

The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same. Chemotherapy, targeted therapy, and immunotherapy are all types of systemic therapy.
Making treatment decisions

- 55 It’s your choice
- 55 Questions to ask your doctors
- 62 Websites
It’s important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

It’s your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can’t be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it’s a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn’t have support groups for people with cancer, check out the websites listed in this book.

Questions to ask your doctors

Possible questions to ask your doctors are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.
Questions to ask about diagnosis and prognosis

1. Where did the cancer start? Is this cancer common?

2. Is this a fast- or slow-growing cancer?

3. How would you describe the cancer stage? Is the tumor small and resectable or large and unresectable? Are there multiple tumors inside my liver? Has cancer spread outside my liver?

4. What tests do you recommend for me?

5. What will you do to make me comfortable during testing?

6. Would you give me a copy of the pathology report and other test results?

7. How soon will I know the results and who will explain them to me?

8. Who will talk with me about the next steps? When?
Questions to ask about options

1. What will happen if I do nothing?
2. How do my age, overall health, and other factors affect my options?
3. Which option is proven to work best?
4. Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
5. What are the possible complications and side effects?
6. Is surgery an option? Why or why not?
7. How do you know if treatment is working? How will I know if treatment is working?
8. What are my options if my treatment stops working?
9. What can be done to prevent or relieve the side effects of treatment?
10. Are there any life-threatening side effects of this treatment? How will I be monitored?
11. Can I stop treatment at any time? What will happen if I stop treatment?
12. Are there any clinical trials I should consider for my condition?
Questions to ask about treatment

1. What are my treatment choices? What are the benefits and risks? How long do I have to decide?

2. Is there a combination of treatments you recommend and why? In which order will they be given?

3. Will I have to go to the hospital or elsewhere for treatment? How often? How long is each visit? Will I have to stay overnight in the hospital or make travel plans?

4. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment? Should I bring someone with me?

5. How much will the treatment hurt? What will you do to make me comfortable?

6. How much will this treatment cost me? What does my insurance cover? Are there any programs to help me pay for treatment?

7. Will I miss work or school? Will I be able to drive?

8. What type of home care will I need? What kind of treatment will I need to do at home?

9. When will I be able to return to my normal activities?

10. Which treatment will give me the best quality of life? Which treatment might extend my life? By how long?

11. I would like a second opinion. Is there someone you can recommend? Who can help me gather all of my records for a second opinion?
Questions to ask about surgery

1. What type of surgery do you recommend? Why?

2. Does my cancer involve any veins or arteries? How might this affect surgery?

3. Is there cancer in any nearby organs such as my gallbladder?

4. Is there cancer in the lymph nodes? Will I have surgery to remove the lymph nodes? Will this be a separate surgery or done at the same time to remove the tumor?

5. Will I have more than one surgery?

6. Will I have surgery to remove the tumor or part of my liver (partial hepatectomy)?

7. What is the difference between my surgery options? What are the risks of each option?

8. Will I have a liver transplant? Is it a partial or whole liver transplant?

9. What do I need to know about a liver transplant?

10. Is there a hospital or treatment center you can recommend for my surgery?

11. What will the recovery from surgery be like?

12. How often will I need check-ups after surgery? What are the chances that the cancer will return?
Questions to ask about clinical trials

1. What clinical trials are available for my type and stage of cancer?

2. What are the treatments used in the clinical trial?

3. What does the treatment do?

4. Has the treatment been used before? Has it been used for other types of cancer?

5. What are the risks and benefits of this treatment?

6. What side effects should I expect? How will the side effects be controlled?

7. How long will I be on the clinical trial?

8. Will I be able to get other treatment if this doesn’t work?

9. How will you know the treatment is working?

10. Will the clinical trial cost me anything? If so, how much?

11. How do I find out about clinical trials that I can participate in? Are there online sources that I can search?
Questions to ask about side effects

1. What are the side effects of treatment?
2. How long will these side effects last?
3. What side effects should I watch for?
4. When should I call the doctor about my side effects? Can I text?
5. What medicines can I take to prevent or relieve side effects?
6. What can I do to help with pain and other side effects?
7. Will you stop treatment or change treatment if I have side effects?
8. What can I do to prevent side effects? What will you do to prevent side effects?
Websites

American Cancer Society
cancer.org/cancer/liver-cancer.html

American Liver Foundation
liverfoundation.org

CancerCare
cancercare.org/diagnosis/liver_cancer

Cancer Support Community
https://www.cancersupportcommunity.org/quality-life-cancer-patients

Global Liver Institute
globalliver.org/resources

MedlinePlus
medlineplus.gov/livercancer.html

National Cancer Institute
cancer.gov/types/liver

National Coalition for Cancer Survivorship
canceradvocacy.org/toolbox/

National Hospice and Palliative Care Organization
nhpco.org/patients-and-caregivers

National Institute of Health
niddk.nih.gov/health-information/liver-disease/liver-transplant

Radiological Society of North America
radiologyinfo.org

The Bili Project Foundation
thebiliproject.org

United Network for Organ Sharing (UNOS)
unos.org
Words to know

**abdomen**
The belly area between the chest and pelvis.

**ablation**
A treatment that destroys very small tumors with heat, cold, lasers, or chemicals. Also called ablative therapy.

**adjuvant therapy**
Treatment that is given after the cancer has been removed to lower the chances of the cancer returning.

**allergic reaction**
An abnormal response by the body to a foreign substance that is harmless.

**alpha-fetoprotein (AFP)**
A protein that can be elevated in those with liver cancer.

**arterially directed therapy**
Treats tumors by injecting particles, chemotherapy, or radioactive beads directly into the blood vessels that supply the tumor(s).

**ascites**
Abnormal buildup of fluid in the belly area.

**blood clot**
A thickened mass of blood. Also called a thrombosis.

**blood vessel**
A tube-shaped structure that carries blood throughout the body.

**bypass**
An operation to re-route the flow of fluid in the body.

**cancer antigen 19-9 (CA 19-9)**
A protein made by certain cancer cells and found in blood.

**cancer grade**
A rating of how much cancer cells look like normal cells.

**cancer stage**
A rating of the outlook of a cancer based on its growth and spread.

**carcinoembryonic antigen (CEA)**
A protein that is present when some types of cancer form.

**carcinoma in situ**
A cancer that has not grown into tissue that would allow it to spread.

**catheter**
A tube-shaped device that is used to give treatment or drain fluid from the body.

**chemoradiation**
Treatment with a combination of chemotherapy and radiation therapy.

**chemotherapy**
Drugs that kill cancer cells by damaging or disrupting the making of the genetic code.

**cholangitis**
An infection of the vessels that drain digestive fluid from the liver (bile ducts).
**cirrhosis**
Scarring of the liver from chronic liver disease that may affect the function of the liver.

**clinical trial**
A type of research that assesses health tests or treatments.

**colon**
The hollow organ in which eaten food turns from a liquid into a solid form.

**common bile duct**
A tube-shaped structure through which digestive fluid (bile) drains into the small intestine.

**computed tomography (CT)**
A test that uses x-rays from many angles to make a picture of the insides of the body.

**contrast**
A substance put into your body to make clearer pictures during imaging tests.

**core needle biopsy**
A procedure that removes tissue samples with a hollow needle. Also called core biopsy.

**donor**
A person who gives their organs, tissues, or cells to another person.

**embolization**
A treatment that blocks blood supply to tumors with beads inserted into an artery.

**external beam radiation therapy (EBRT)**
A cancer treatment with radiation received from a machine outside the body.

**fine-needle aspiration (FNA)**
A procedure that removes tissue samples with a very thin needle.

**gallbladder**
A small organ that holds digestive fluid (bile) from the liver.

**gastroenterologist**
A doctor who is an expert in digestive diseases.

**gene**
Coded instructions in cells for making new cells and controlling how cells behave.

**hepatologist**
A doctor who is an expert in treating diseases of the liver, gallbladder, bile ducts, and pancreas.

**hepatoma**
Another term for hepatocellular carcinoma, primary liver cancer.

**hereditary**
Passed down from parent to child through coded information in cells.

**imaging**
A test that makes pictures (images) of the insides of the body.

**immune system**
The body's natural defense against infection and disease.

**immunotherapy**
a treatment with drugs that help the body find and destroy cancer cells.

**intensity-modulated radiation therapy (IMRT)**
Treatment with radiation that uses small beams of different strengths based on the thickness of the tissue.

**interventional radiologist**
A doctor who is an expert in imaging tests and using image-guided tools to perform minimally invasive techniques to diagnose or treat disease.

**intestine**
The organ that food passes through after leaving the stomach.
Words to know

**jaundice**
Yellow-colored skin or whites of the eyes due to a buildup of bilirubin in the body.

**laparoscopic surgery**
A minimally invasive operation that uses tools through small cuts in the belly area.

**liver**
The largest organ and gland in the body with many vital functions.

**liver function test (LFT)**
A lab test that measures chemicals made or processed by the liver.

**lymph node**
A small, bean-shaped, disease-fighting structure.

**magnetic resonance cholangiopancreatography (MRCP)**
A test that uses radio waves and powerful magnets to make pictures of the pancreas and bile ducts.

**magnetic resonance imaging (MRI)**
A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

**medical history**
A report of all your health events and medications.

**medical oncologist**
A doctor who is an expert in cancer drugs.

**metastasis**
The spread of cancer cells from the first (primary) tumor to a new site.

**minimally invasive procedure**
A procedure that uses small incisions or a tool placed into the opening of the body to reduce damage to body tissue.

**mutation**
An abnormal change.

**neoadjuvant treatment**
A treatment that is given before the main treatment to reduce the cancer. Also called preoperative treatment if given before an operation.

**observation**
A period of testing for changes in cancer status while not receiving treatment.

**oncologist**
A doctor who is an expert in the treatment of cancer.

**palliative care**
Health care that includes symptom relief but not cancer treatment. Also sometimes called supportive care.

**pancreas**
An organ that makes fluids that help digest food and chemicals that control blood sugar.

**partial hepatectomy**
An operation to remove a section of the liver.

**pathologist**
A doctor who is an expert in testing cells and tissue to find disease.

**pelvis**
The body area between the hipbones.

**percutaneous transhepatic cholangiography (PTC)**
A procedure to view the biliary tract with an x-ray and possibly place a catheter to drain fluid from the biliary tract.

**performance status (PS)**
A rating of one's ability to do daily activities.

**physical exam**
A study of the body by a health expert for signs of disease.

**primary treatment**
The main treatment used to rid the body of cancer.
**Words to know**

**primary tumor**
The first mass of cancer cells.

**prognosis**
The likely course and outcome of a disease based on tests.

**progression**
The growth or spread of cancer after being tested or treated.

**radiation therapy (RT)**
A cancer treatment that uses high-energy rays.

**radiologist**
A doctor who is an expert in imaging tests.

**recurrence**
The return of cancer after a cancer-free period.

**stereotactic body radiation therapy (SBRT)**
Treatment with high-dose radiation within one or a few sessions.

**subtype**
A smaller group within a type of cancer that is based on certain cell features.

**supportive care**
Health care that includes symptom relief but not cancer treatment. Also called palliative care.

**surgical margin**
The normal-looking tissue around the edge of a tumor that is removed during surgery to ensure that the cancer is completely removed.

**surveillance**
Testing that is done after treatment ends to check for the return of cancer.

**targeted therapy**
A drug treatment that impedes the growth process specific to cancer cells.

**three-dimensional conformal radiation therapy (3D-CRT)**
A treatment with radiation that uses beams matched to the shape of the tumor.

**tumor marker**
A substance found in body tissue or fluid that may be a sign of cancer.

**ultrasound (US)**
A test that uses sound waves to take pictures of the insides of the body.

**unresectable**
Cancer that can’t be removed by surgery.

**widespread metastatic disease**
The spread of cancer from the first tumor to many new sites in the body.
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