

NCCN

NCCN
GUIDELINES
FOR PATIENTS®

2021

Liver Cancer

Hepatobiliary Cancers

Presented with support from:



NATIONAL COMPREHENSIVE CANCER NETWORK
FOUNDATION
Guiding Treatment. Changing Lives.



Available online at [NCCN.org/patients](https://www.NCCN.org/patients)



**It's easy to
get lost in the
cancer world**

 **Let
NCCN Guidelines
for Patients®
be your guide**

- ✓ Step-by-step guides to the cancer care options likely to have the best results
- ✓ Based on treatment guidelines used by health care providers worldwide
- ✓ Designed to help you discuss cancer treatment with your doctors

About



National Comprehensive
Cancer Network®

NCCN Guidelines for Patients® are developed by the National Comprehensive Cancer Network® (NCCN®)



NCCN

- ✓ An alliance of leading cancer centers across the United States devoted to patient care, research, and education

**Cancer centers
that are part of NCCN:**
[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

- ✓ Developed by doctors from NCCN cancer centers using the latest research and years of experience
- ✓ For providers of cancer care all over the world
- ✓ Expert recommendations for cancer screening, diagnosis, and treatment

Free online at
[NCCN.org/guidelines](https://www.nccn.org/guidelines)



NCCN Guidelines for Patients

- ✓ Present information from the NCCN Guidelines in an easy-to-learn format
- ✓ For people with cancer and those who support them
- ✓ Explain the cancer care options likely to have the best results

Free online at
[NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines)



and supported by funding from NCCN Foundation®

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Hepatobiliary Cancers (Version 2.2021, April 16, 2021).

© 2021 National Comprehensive Cancer Network, Inc. All rights reserved. NCCN Guidelines for Patients and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. No one, including doctors or patients, may use the NCCN Guidelines for Patients for any commercial purpose and may not claim, represent, or imply that the NCCN Guidelines for Patients that have been modified in any manner are derived from, based on, related to, or arise out of the NCCN Guidelines for Patients. The NCCN Guidelines are a work in progress that may be redefined as often as new significant data become available. NCCN makes no warranties of any kind whatsoever regarding its content, use, or application and disclaims any responsibility for its application or use in any way.

NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit [NCCN.org/patients](https://www.nccn.org/patients).

National Comprehensive Cancer Network (NCCN) / NCCN Foundation
3025 Chemical Road, Suite 100
Plymouth Meeting, PA 19462
215.690.0300

Supporters

Sponsored by



Global Liver Institute

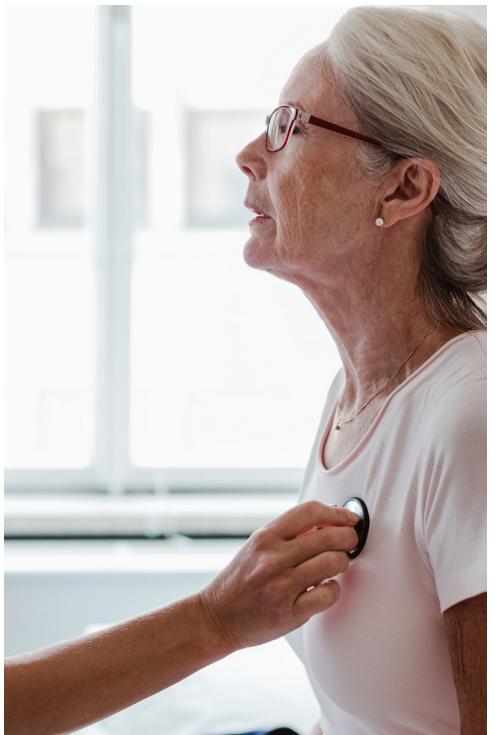
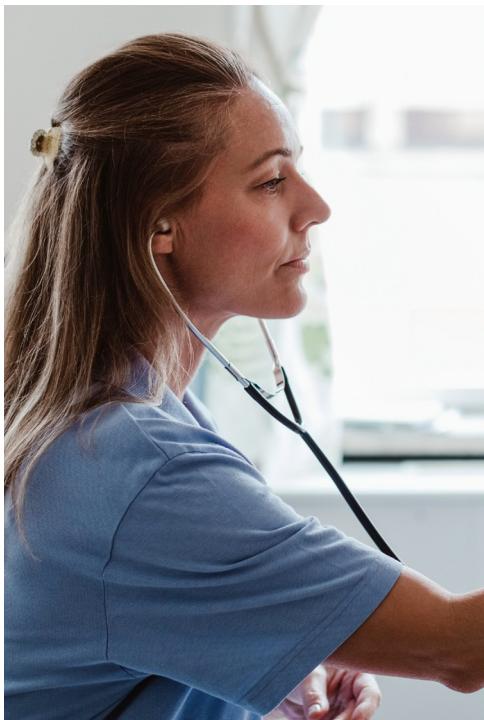
The Global Liver Institute is honored to partner with the NCCN Foundation in our ongoing efforts to empower patients who are at risk for or are facing liver cancer. We hope that liver cancer patients will utilize this resource and that the high-quality information within these guidelines will help you make decisions about your care and ease your journey. globalliver.org.



Cholangiocarcinoma Foundation

The Cholangiocarcinoma Foundation is honored to partner with NCCN to provide this vital resource for bile duct (cholangiocarcinoma), liver, and gallbladder cancer patients. Patients First is a core value of our organization. We believe that the most powerful and positive force in medicine is that of a knowledgeable and self-advocating patient. - Stacie Lindsey, Founder and CEO, Cholangiocarcinoma Foundation. cholangiocarcinoma.org

To make a gift or learn more, please visit NCCNFoundation.org/donate or e-mail PatientGuidelines@NCCN.org.



Contents

- 6 Liver cancer basics
- 17 Diagnosing liver cancer
- 26 Treatment overview
- 41 Resectable
- 44 Unresectable
- 49 Inoperable
- 53 Metastatic
- 56 Making treatment decisions
- 68 Words to know
- 72 NCCN Contributors
- 73 NCCN Cancer Centers
- 74 Index

1

Liver cancer basics

7 The liver

9 Liver cancer

9 How liver cancer spreads

10 Cancer stages

14 Risk factors

16 Screening

16 Key points



The liver is a large organ located on the right side of the body under your rib cage. 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 and makes other important substances called factors that help your body function normally. This chapter will discuss the liver and give an overview of liver cancer.

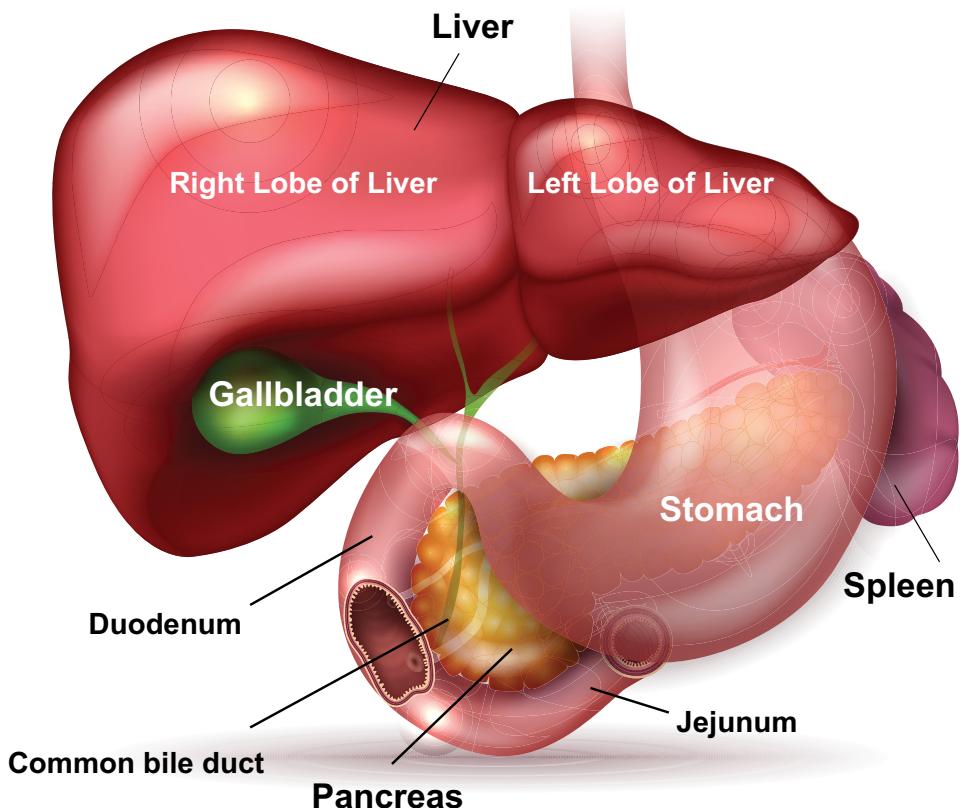
The liver

The liver is a large organ located on the right side of the body under your rib cage. Inside the liver is a network of blood and lymph vessels. The liver filters blood, helps with blood clotting, makes bile, breaks down fats, and helps process sugar for energy. The liver also produces lymph. Lymph gives cells water and food and contains white blood cells that fight germs.

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.

The liver and nearby organs

The gallbladder, stomach, pancreas, spleen, and small intestine are found near the liver.



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

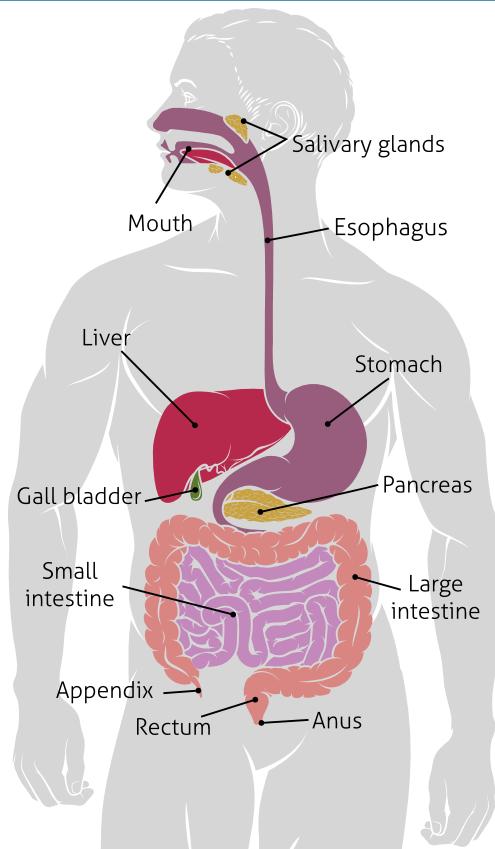
The gallbladder is a small, pear-shaped organ found under the liver. It is sometimes described as sac-like because it holds bile from the liver. Bile is stored in the gallbladder, and when you eat, it then passes through the bile ducts into the small bowel (intestine) to help digest food.

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

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

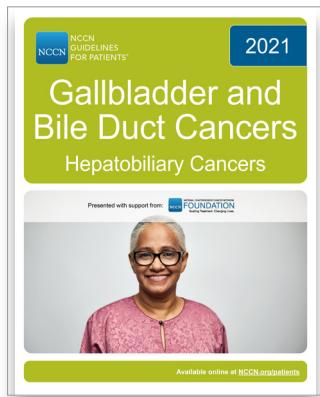


Liver cancer

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 in the liver.

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 very few people and usually occurs at a younger age.

The second most common type of primary liver cancer in adults 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](https://www.NCCN.org/patientguidelines).



Information on sarcomas in the liver can be found in *NCCN Guidelines for Patients: Soft Tissue Sarcoma*, available at [NCCN.org/patientguidelines](https://www.NCCN.org/patientguidelines).

This patient guideline will focus on HCC and its treatment.

How liver cancer spreads

Liver cancer can spread in many ways. It can spread directly through the liver. It can also spread to an area far from the primary tumor called a distant metastasis. Liver cancer most often metastasizes to the lung or bone. This is called metastatic liver cancer.

Inside the liver are blood and lymphatic vessels. Cancer can spread from the liver through the blood and lymphatic system. The lymphatic system is made up of a network of vessels that carry a clear fluid called lymph. Lymph gives cells water and food, and has white blood cells that fight germs. Lymph nodes filter lymph and remove the germs. 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 a staging system 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.

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

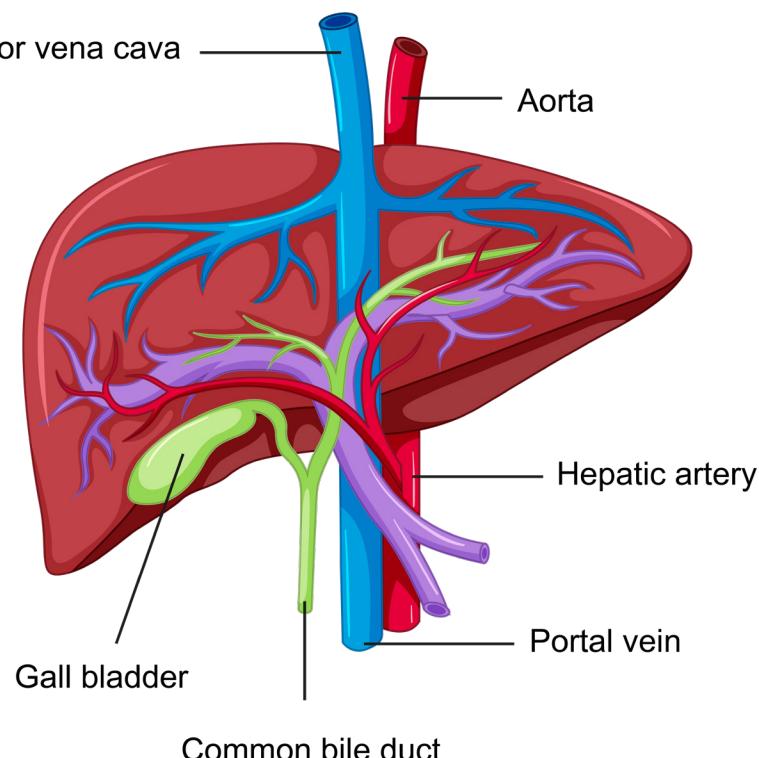
a score or number to each letter. The higher the number, the larger the tumor or the more the cancer has spread. These scores will be combined to assign the cancer a stage. A TNM example might look like this: T1N0M0 or T1, N0, M0.

- **T (tumor)** - Size of the main (primary) tumor
- **N (node)** - If cancer has spread to nearby (regional) lymph nodes
- **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.

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.



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 that has not invaded blood vessels (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

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 uncommon.

- **N0** means no cancer is in regional lymph nodes
- **N1** means cancer in the regional lymph nodes is found

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 is found
- **M1** means distant metastasis is found

G = 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. A stage consists of a TNM score. See Guide 1.

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).

Guide 1

Liver cancer stages

	Stage 1A	• T1a, N0, M0
Stage 1	Stage 1B	• T1b, N0, M0
Stage 2	Stage 2	• T2, N0, M0
	Stage 3A	• T3, N0, M0
Stage 3	Stage 3B	• T4, N0, M0
	Stage 4A	• Any T, N1, M0
Stage 4	Stage 4B	• Any T, Any N, M1

Stage 3

In stage 3a liver cancer, there are multiple tumors. One of these tumor 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).

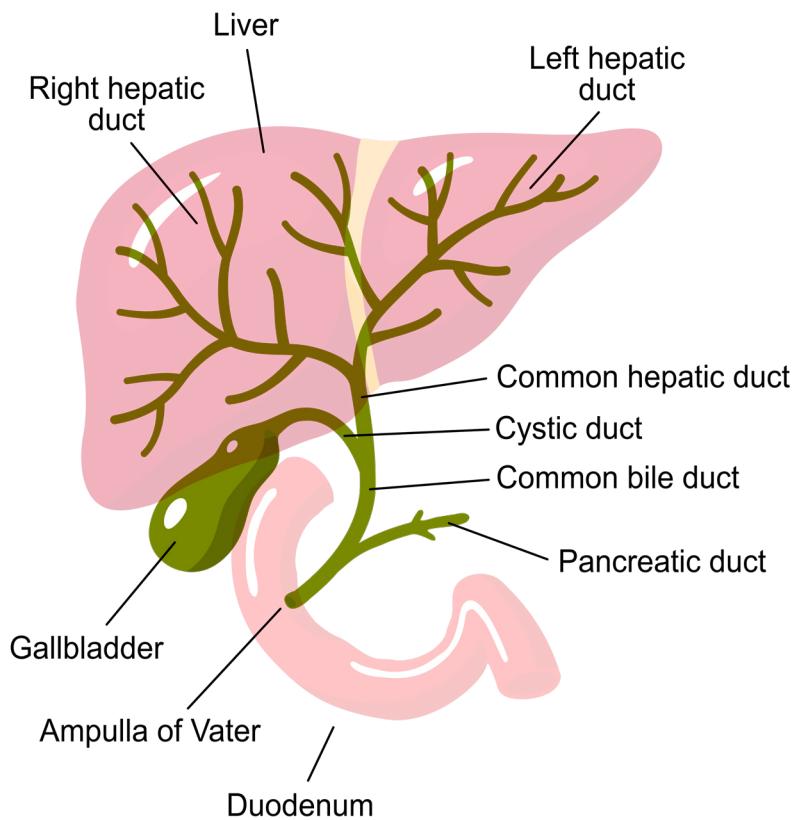
Stage 4

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 called metastatic liver cancer.

Bile duct anatomy

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.



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 2](#).

Risk is based on:

- Those with cirrhosis
- Those without cirrhosis

Guide 2 Risk factors for liver cancer

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

Those without cirrhosis

- 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

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

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

Hepatitis

Hepatitis is a type of liver disease. Viruses called hepatitis A, hepatitis B (HBV), and hepatitis C (HCV) are the most common types 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.

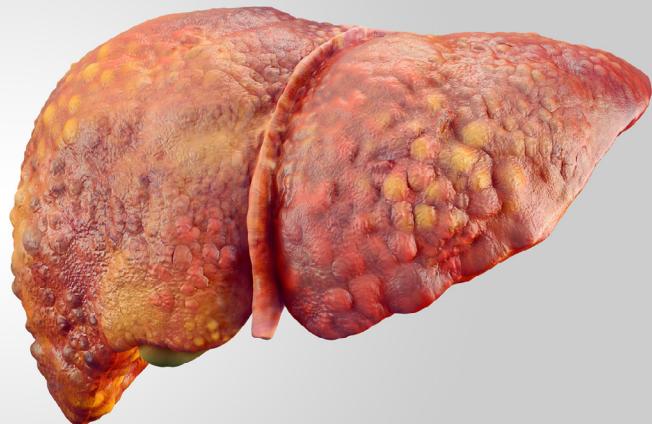
Other risk factors

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 with 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.

Cirrhosis is severe scarring of the liver.



healthy liver



cirrhosis

Screening

Those at risk for liver cancer may have screening tests done on a regular basis to find cancer early. Two tests are recommended every 6 months for those at risk of developing liver cancer.

They include:

- An ultrasound (US)
- An alpha-fetoprotein (AFP) test

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.

Follow-up steps after a screening ultrasound may include:

- If AFP is elevated or an ultrasound finds nodules that are 10 millimeters (mm) or larger, then you will have more tests.
- 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.

Key points

- 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

Diagnosing liver cancer

18 Test results

19 General health tests

20 Blood tests

22 Imaging tests

24 Biopsy

25 Key points



Liver cancer is usually confirmed with imaging tests. More tests will be done to plan treatment. This chapter presents an overview of the tests you might receive and what to expect.



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.

Keep these things in mind:

- Bring someone with you to doctor visits, if possible.
- 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 phone. Hang the list on your fridge or keep it in a place where someone can access it in an emergency.

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!

General health tests

A list of tests can be found in [Guide 3](#).

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, herbals, 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. It is important to ask members from both parents' side of the family about all cancers, not just liver cancer. Ask about other health issues like heart disease and diabetes, at what age they were diagnosed, and if anyone died from their cancer. Share this information and any changes to family history with your health care provider.

Guide 3 Tests for treatment planning

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

Physical exam

During a physical exam, your health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your weight
- 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.

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 (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 is a waste product 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.

One of the LFTs 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. It might cause itchy skin and dark-colored urine.

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 types 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 test positive. A hepatologist is a doctor who specializes in the care of the liver, biliary tract, gallbladder, and pancreas.

Fibrosis score

Fibrosis is mild scarring of liver tissue. Cirrhosis is when this scarring becomes severe. A fibrosis score measures the level of scarring to the liver caused by disease. This scoring system uses a 0 to 6 scale.

- **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 and blood 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 well your liver is working and if surgery is an option.

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 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 enhance and improve the images of several organs and structures in the body. It is used to make the pictures clearer. The contrast is not permanent and will leave the body in your urine immediately after the test.

Tell your doctors if you have had allergic reactions to contrast in the past. This is important. You might be given medicines, such as Benadryl® and prednisone, to avoid the effects of those allergies. 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.

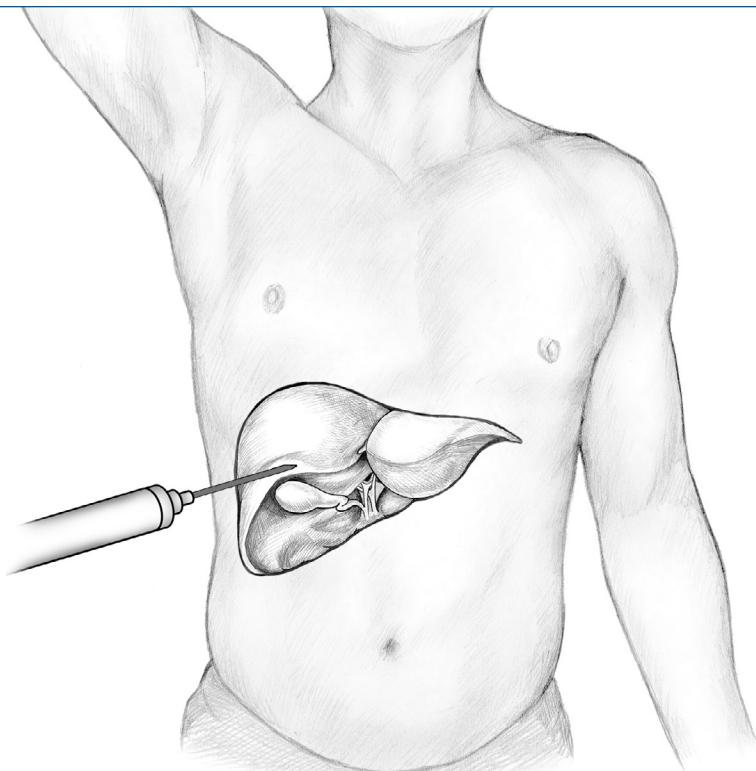
PTC

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.

Liver biopsy

A biopsy uses a needle to remove a sample of tissue or fluid.



Credit: https://commons.wikimedia.org/wiki/File:Human_liver_biopsy.jpg

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** is a minimally invasive surgery that uses a camera 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. 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.

Tumor biomarker tests

Cancer antigen 19-9 (CA 19-9), carcinoembryonic antigen (CEA), and alpha-fetoprotein (AFP) are examples of tumor markers that are occasionally made by tumors and can be detected in the blood. These tumor markers can help with diagnosis, monitoring response to treatment, and surveillance.

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.

Key points

- 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.



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

[NCCN.org/patients/response](https://www.NCCN.org/patients/response)

3

Treatment overview

-
- 27 Treatment team**
 - 28 Surgery**
 - 30 Liver transplant**
 - 32 Ablation**
 - 32 Arterially directed therapy**
 - 34 Radiation therapy**
 - 35 Systemic therapy**
 - 36 Clinical trials**
 - 38 Supportive care**

 - 40 Key points**



There is more than one treatment for liver cancer. This chapter describes treatment options and what to expect. Not everyone will receive the same treatment. Discuss with your doctor which treatment might be best for you.

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. If possible, seek treatment at a hospital or cancer center that specializes in liver cancer.

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.

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:

- **A hepatologist** is an expert in diseases of the liver, gallbladder, bile ducts, and pancreas.
- **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 pathologist** interprets the cells, tissues, and organs removed during a biopsy or surgery.
- **A diagnostic radiologist** interprets 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. Some transplant surgeons and hepatobiliary surgeons also care for patients with liver cancer.
- **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.
- **Palliative care nurses and advanced practice providers** help provide an extra layer of support with your cancer-related symptoms.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects. Sometimes, these experts are called nurse navigators.
- **Nutritionists and dietitians** can provide guidance on what foods 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.
- **Social workers** help people solve and cope with problems in their everyday lives.

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.

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
- Your goals for treatment

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.

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 or extend life)

Liver surgery is not an option for most people with liver cancer. Cancer is often found in multiple places throughout the liver, and removing tumors might not leave enough healthy liver tissue for your liver to function properly. 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.

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.

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.

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.

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

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 or not possible. 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.

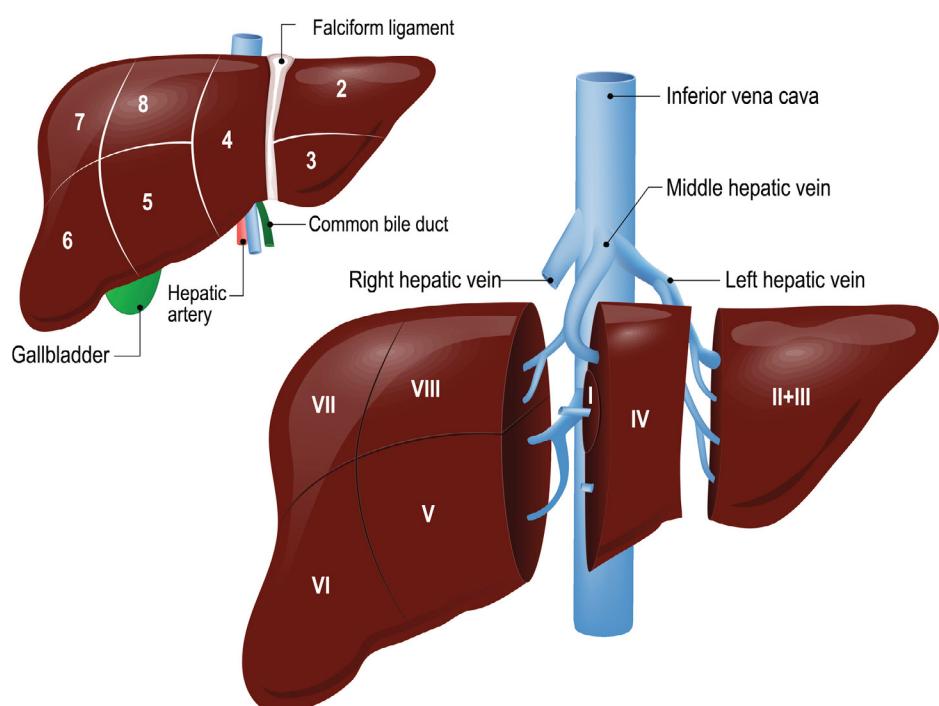
There is still a chance that cancer will return after a liver transplant. It is also possible your body will reject the donor liver. You will be given medicine to prevent rejection.

Bridge therapy

There can be long wait times to receive a liver transplant. Treatments may be given while you wait for a transplant. These treatments are called bridge or bridging therapy and include ablation, embolization, or radiation therapy.

Liver transplant

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



Downstaging therapy

Downstaging therapy is used to reduce the tumor burden in selected patients with more advanced HCC (without distant metastasis) who are beyond the accepted transplant criteria with the goal of future transplant. Treatments include ablation and embolization.

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.

These include:

- 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.



Order of treatments

Most people with liver cancer will receive more than one type of treatment. Next is an overview of the order of treatments and what they do.

- **Noadjuvant (before) treatment** is given to shrink the tumor before primary treatment (surgery).
- **Primary treatment** is the main treatment given to rid the body of cancer. Surgery is usually the main treatment for resectable liver cancer. This is not an option for everyone.
- **Adjuvant (after) treatment** is given after primary treatment to rid the body of any cancer cells left behind from surgery. It is also used when the risk of cancer returning (recurrence) is felt to be high.
- **First-line treatment** is the first set of treatments given.
- **Second-line treatment** is the next set of treatments given after the first treatment has failed.

Talk to your doctor about your treatment plan and what it means for your stage of liver cancer.

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.

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 (Y-90 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 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.

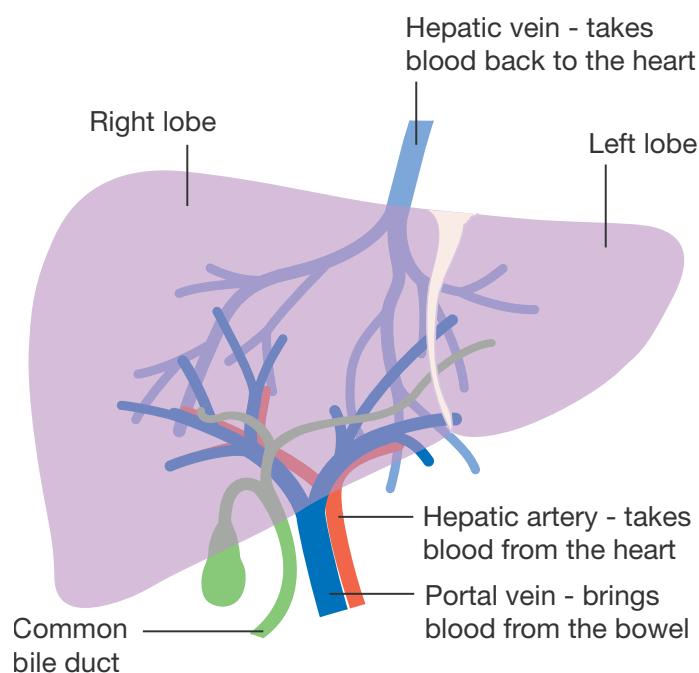
- DEB-TACE (drug-eluting bead transarterial chemoembolization) uses tiny particles loaded with chemotherapy that are injected into the blood vessels feeding the tumor(s). The particles give off small amounts of chemotherapy to the tumor over several days. It might not be used if your bilirubin level 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. This procedure is often referred to as Y-90.

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.

Liver blood supply

Blood enters the liver through the hepatic artery and portal vein. Blood exits the liver through the hepatic vein.

Credit: https://commons.wikimedia.org/wiki/File:Diagram_showing_the_two_lobes_of_the_liver_and_its_blood_supply_CRUK_376.svg



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, 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).

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.
- **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

Systemic therapy works throughout the body. Types include chemotherapy, targeted therapy, and immunotherapy. Systemic therapy might be used alone or with other therapies. Goals of systemic therapy should be discussed before starting treatment. Your wishes about treatment are important.

Chemotherapy

Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells. All chemotherapies affect the instructions (genes) that tell cancer cells how and when to grow and divide. FOLFOX (fluorouracil, leucovorin, and oxaliplatin) is a type of combination chemotherapy that might be used in some cases to treat liver cancer.

Targeted therapy

Targeted therapy 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:

- Bevacizumab (Avastin®)
- Cabozantinib (Cabometyx®)
- Lenvatinib (Lenvima®)
- Ramucirumab (Cyramza®)
- Regorafenib (Stivarga®)
- Sorafenib (Nexavar®)

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.

Targeted therapies may be used to treat tumors that have certain gene mutations such as neurotrophin receptor kinase (*NTRK*) gene fusion. In a tumor with an *NTRK* gene fusion, a piece of the *NTRK* gene and a piece of another gene fuse, or join. This activates the *NTRK* gene in a way that causes uncontrolled cell growth. Larotrectinib (Vitrakvi®) and entrectinib (Rozlytrek™) might be used to target advanced or metastatic cancer that is *NTRK* gene fusion-positive.

Immunotherapy

Immunotherapy is a targeted therapy 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.

The following are types of targeted immunotherapies that might be used to treat liver cancer:

- Atezolizumab (Tecentriq®)
- Ipilimumab (Yervoy®)
- Nivolumab (Opdivo®)
- Pembrolizumab (Keytruda®)



For more information, read the *NCCN Guidelines for Patients: Immunotherapy Side Effects*, available at [NCCN.org/patientguidelines](https://www.NCCN.org/patientguidelines).

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA). Everyone with cancer should carefully consider all treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your treatment team about whether a clinical trial might make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases that build on one another.

- **Phase I trials** study the safety and side effects of an investigational drug or treatment approach.
- **Phase II trials** study how well the drug or approach works against a specific type of cancer.
- **Phase III trials** compare the drug or approach to standard treatment. Therefore, some patients will be treated with the new drug or approach and some patients will receive standard treatment. If the results are good, it may be approved by the FDA.
- **Phase IV trials** study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These rules ensure that participants are alike in specific ways and that the treatment is as safe as possible.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. This information is also described in detail in an informed consent form. Giving informed consent means that you understand the possible benefits and risks and agree to join. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you already began standard treatment, and then decide to join a clinical trial, you may not be eligible. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

[What if I get the placebo?](#)

A placebo is an inactive version of a real medicine. Placebos are almost never used alone in cancer clinical trials. All participants receive commonly used (standard) cancer treatment. You may receive a commonly used treatment, the investigational drug, or both.

[Do I have to pay to be in a clinical trial?](#)

Rarely. It depends on the study, your health insurance, and the state in which you live. Your treatment team and the research team can help determine if you are responsible for any costs.

Supportive care

Supportive care (also called palliative 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

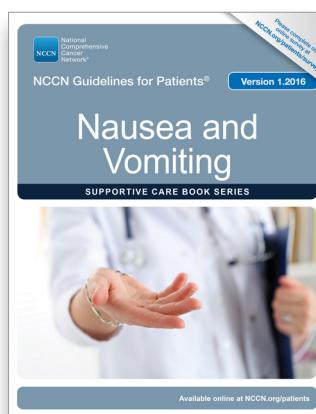
All cancer treatments can cause unwanted health issues. Such health issues are called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant.

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.

It is important to tell your care team about all side effects so they can be managed.

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](https://www.NCCN.org/patientguidelines).

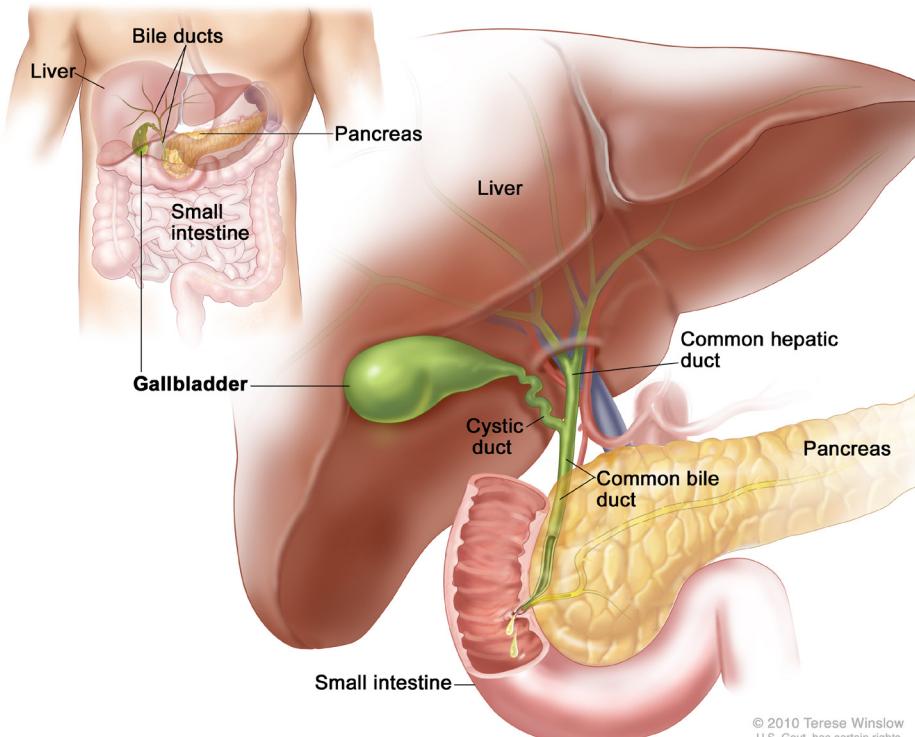
Blocked bile duct

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.

Blocked bile duct

A tumor in the liver may block your bile duct. A stent is a tiny tube that is placed in the bile duct to unblock it or keep it open.



Key points

- Local therapy focuses treatment on a certain area. It includes surgery, radiation therapy, ablation, and arterially directed therapy.
- Surgery is an option for some people with liver cancer.
- 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.

Keep a pain diary

A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:

- The time and dose of all medicines
- When pain starts and ends or lessens
- Where you feel pain
- Describe your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- Does the pain change at different times of day? When?
- Does the pain get worse before or after meals? Does certain food or drink make it better?
- Does the pain get better or worse with activity? What kind of activity?
- Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- Rate your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- Does pain get in the way of doing the things you enjoy?

4

Resectable

42 Overview

43 Transplant

43 Surveillance

43 Key points



A tumor that can be removed with surgery is called resectable. 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 structures such as veins, arteries, or ducts, surgery might not be an option.

Types of surgery:

- Resection removes a tumor. Sometimes, a partial hepatectomy is referred to as resection. A partial hepatectomy removes part of the liver.

- A transplant removes all of your liver and replaces 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. There are many reasons that you may or may not be a good candidate for resection. Ask your health care team about this. For resectable treatment options, [see Guide 4](#).

Guide 4

Resectable treatment options

Surgery to remove tumor (preferred)

Ablation

Arterially directed therapy

External beam radiation therapy (EBRT)

Transplant

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

- AFP levels are 1000 ng/mL or less and tumor is 2 to 5 cm in diameter or 2 to 3 tumors are 1 to 3 cm
- No large veins, arteries, or bile ducts have cancer (no macrovascular involvement)
- No disease outside the liver (extrahepatic)

Transplant is an option

If transplant is an option, then you will:

- Be referred to a liver transplant center that has an experienced transplant team
- Have 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.

Transplant is not an option

If a liver transplant is not an option, then surgery to remove the tumor (resection) is preferred. Other options include ablation, arterially directed therapy, and radiation therapy. [See Guide 4](#).

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.

Surveillance includes:

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

Key points

- 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.

5

Unresectable

45 Overview

45 Transplant

46 Treatment without surgery

48 Key points



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:

- Alpha-fetoprotein (AFP) levels are 1000 ng/mL or less and tumor is 2 to 5 cm in diameter or 2 to 3 tumors are 1 to 3 cm
- No large veins, arteries, or bile ducts have cancer
- No disease outside the liver (extrahepatic)

If transplant is an option, then you:

- Will be referred to a liver transplant center that has an experienced transplant team
- Might have 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.

Surveillance includes:

- Imaging tests every 3 to 6 months for 2 years, then every 6 to 12 months
- 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 5](#).

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.

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. Ask your medical oncologist why one drug might be chosen over another. First-line options are the treatments tried first. For first-line systemic therapy options, [see Guide 6](#).

Guide 5

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 6](#))

Progression

When cancer grows or spreads, it is called disease progression. Progression can happen while on or after systemic therapy. Treatment is based on the type of systemic therapy you had before.

For next-line systemic therapy options, see [Guide 7](#).

Guide 6

First-line systemic therapy options

Preferred options	<ul style="list-style-type: none">Atezolizumab with bevacizumab (Child-Pugh Class A only)
Other recommended	<ul style="list-style-type: none">Sorafenib (Child-Pugh Class A or B7)Lenvatinib (Child-Pugh Class A only)
Useful in some cases	<ul style="list-style-type: none">NivolumabFOLFOX

Guide 7

Next-line systemic therapy options: Disease progression

Options	<ul style="list-style-type: none">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)Larotrectinib and entrectinib are treatment options for HCC that is <i>NTRK</i> gene fusion-positive
Other recommended	<ul style="list-style-type: none">Nivolumab (Child-Pugh Class A or B)Nivolumab with ipilimumab (Child-Pugh Class A only)Pembrolizumab (Child-Pugh Class A only)

Key points

- 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 radiation therapy are preferred.
- Systemic therapy, a clinical trial, or best supportive care are other options for those not undergoing a liver transplant.
- When cancer grows or spreads, it is called disease progression. Progression can happen while on or after systemic therapy. Treatment is based on the type of systemic therapy you had before.



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better:

NCCN.org/patients/feedback

6

Inoperable

50 Treatment options

52 Key points



In inoperable liver cancer, resection and a liver transplant are not options. This chapter discusses the treatment options for inoperable cancer that is confined to the liver. Ablation, arterially directed therapy, and radiation therapy are the preferred treatment options. Sometimes, systemic therapy is used. Together, you and your doctor will choose a treatment plan that is best for you.

Treatment options

Not everyone is healthy enough for surgery. Some people have other serious health issues that prevent surgery. Some people do not want a liver transplant. There are other treatment options. These include locoregional therapy (preferred), clinical trial, best supportive care, or systemic therapy.

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
- External beam radiation therapy (EBRT)

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. Ask your medical oncologist why one drug might be chosen over another.

First-line options are the treatments tried first. The preferred first-line systemic therapy is atezolizumab with bevacizumab. For all first-line systemic therapy options, [see Guide 8](#).

Progression

Cancer that grows or spreads is called disease progression. Progression can happen while on or after systemic therapy. 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 9](#).

Guide 8

First-line systemic therapy options

Preferred options	<ul style="list-style-type: none">Atezolizumab with bevacizumab (Child-Pugh Class A only)
Other recommended	<ul style="list-style-type: none">Sorafenib (Child-Pugh Class A or B7)Lenvatinib (Child-Pugh Class A only)
Useful in some cases	<ul style="list-style-type: none">NivolumabFOLFOX

Guide 9

Next-line systemic therapy options: Disease progression

Options	<ul style="list-style-type: none">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)Larotrectinib and entrectinib are treatment options for HCC that is NTRK gene fusion-positive
Other recommended	<ul style="list-style-type: none">Nivolumab (Child-Pugh Class A or B)Nivolumab with ipilimumab (Child-Pugh Class A only)Pembrolizumab (Child-Pugh Class A only)

Key points

- In inoperable liver cancer, resection and liver transplant are not treatment options.
- Not everyone is healthy enough for surgery. Some people have other serious health issues that prevent surgery. Some people do not want a liver transplant.
- 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.
- When first-line systemic therapy doesn't stop the growth or spread of cancer, then more lines of therapy might be tried.



Finding a clinical trial

In the United States

NCCN Cancer Centers

NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov/

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)

1.800.4.CANCER (1.800.422.6237)

cancer.gov/contact

7

Metastatic

54 Treatment options

55 Progression

55 Key points



Stage 4B liver cancer is metastatic liver cancer. This is cancer that has spread to distant sites in the body. The tumor(s) can be any size and cancer may be found in the lymph nodes. The goal of treatment is to reduce the amount of cancer called cancer burden and to prevent the further spread of cancer. 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. The goal of treatment is to reduce the amount of cancer called cancer burden and to prevent the further spread of cancer. Treatment options include a clinical trial, best supportive care, or systemic therapy.

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 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 first-line systemic therapy is atezolizumab with bevacizumab. For all first-line systemic therapy options, [see Guide 10](#).

Guide 10

First-line systemic therapy options: Metastatic disease

Preferred options	<ul style="list-style-type: none">• Atezolizumab with bevacizumab (Child-Pugh Class A only)
Other recommended	<ul style="list-style-type: none">• Sorafenib (Child-Pugh Class A or B7)• Lenvatinib (Child-Pugh Class A only)
Useful in some cases	<ul style="list-style-type: none">• Nivolumab• FOLFOX

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 11](#).

Key points

- 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.
- First-line options are the treatments tried first. The preferred first-line systemic therapy is atezolizumab with bevacizumab.
- When first-line systemic therapy doesn't stop the growth or spread of cancer, then more lines of therapy might be tried.

Guide 11

Next-line systemic therapy options: Disease progression

Options	<ul style="list-style-type: none">• 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)• Larotrectinib and entrectinib are treatment options for HCC that is <i>NTRK</i> gene fusion-positive
Other recommended	<ul style="list-style-type: none">• Nivolumab (Child-Pugh Class A or B)• Nivolumab with ipilimumab (Child-Pugh Class A only)• Pembrolizumab (Child-Pugh Class A only)

8

Making treatment decisions

57 It's your choice

57 Questions to ask your doctors

66 Resources



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. 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 testing and staging

1. What tests will I have? How often will they be repeated? Will my insurance pay for these tests?
 2. Do I need a biopsy? Will I have more than one? What are the risks?
 3. Will a stent be placed during my biopsy? What else might be done?
 4. How soon will I know the results and who will explain them to me?
 5. Who will talk with me about the next steps? When? Should I see any other specialists?
 6. What will you do to make me comfortable during testing?
 7. What stage is my cancer? Is it resectable, unresectable, inoperable, or metastatic? What does this mean?
 8. Is the cancer in any other areas like my lymph nodes, lungs, or bone?
 9. Where can I learn more information about my cancer?
-
-
-
-
-
-
-
-
-
-
-
-
-

Questions to ask your doctors about their experience

1. What is your experience treating liver cancer?
 2. What is the experience of those on your team?
 3. Do you only treat liver cancer? What else do you treat?
 4. How many patients like me (of the same age, gender, race) have you treated?
 5. Will you be consulting with experts to discuss my care? Who will you consult?
 6. How many procedures like the one you're suggesting have you done?
 7. Is this treatment a major part of your practice?
 8. How many of your patients have had complications? What were the complications?
 9. How many liver cancer surgeries have you done?
 10. Who will manage my day-to-day care?
-
-
-
-
-
-
-
-
-
-
-
-
-

Questions to ask about options

1. What will happen if I do nothing?
 2. How do my age, cancer stage, overall health, and other factors affect my options?
 3. Am I a candidate for a clinical trial?
 4. Which option is proven to work best for my situation?
 5. 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?
 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. Can I stop treatment at any time? What will happen if I stop treatment?
 10. Is there a social worker or someone who can help me decide?
-
-
-
-
-
-
-
-
-
-
-
-

Questions to ask about treatment

1. Does the order of treatment matter?
 2. How long do I have to decide about treatment?
 3. Is there a combination of treatments you recommend and why? In which order will they be given?
 4. 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?
 5. 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?
 6. How much will the treatment hurt? What will you do to make me comfortable?
 7. How much will this treatment cost me? What does my insurance cover? Are there any programs to help me pay for treatment?
 8. Will I miss work or school? Will I be able to drive?
 9. What type of home care will I need? What kind of treatment will I need to do at home?
 10. When will I be able to return to my normal activities?
 11. Which treatment will give me the best quality of life? Which treatment might extend my life? By how long?
 12. Should I get a second opinion? Is there someone you can recommend? Who can help me gather 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?
13. Can my surgery be performed minimally invasively?

Questions to ask your doctors about radiation therapy

1. What type of radiation therapy will I have?
2. What will you target?
3. What is the goal of this radiation treatment?
4. How many treatment sessions will I require? Can you do a shorter course of radiation?
5. Do you offer this type of radiation here? If not, can you refer me to someone who does?
6. What side effects can I expect from radiation?
7. What should I wear?

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 the treatment you are recommending?
2. What are the side effects of liver cancer?
3. How long will these side effects last? Do any side effects lessen or worsen in severity over time?
4. What side effects should I watch for? What side effects are expected and which are life threatening?
5. When should I call the doctor? Can I text? What should I do on weekends and other non-office hours?
6. What emergency department or ER should I go to? Will my treatment team be able to communicate with the ER team?
7. What medicines can I take to prevent or relieve side effects?
8. What can I do to help with pain and other side effects?
9. Will you stop treatment or change treatment if there are side effects? What do you look for?
10. What can I do to lessen or prevent side effects? What will you do?
11. What medicines may worsen side effects of treatment?

Resources

American Association for Clinical Chemistry

labtestsonline.org

American Cancer Society

cancer.org/cancer/liver-cancer.html

cancer.org/content/dam/cancer-org/cancer-control/en/worksheets/pain-diary.pdf

American Liver Foundation

liverfoundation.org

CancerCare

cancercare.org/diagnosis/liver_cancer

Cancer Support Community

cancersupportcommunity.org/quality-life-cancer-patients

Global Liver Institute

globalliver.org/resources

MedlinePlus

medlineplus.gov/livercancer.html

My Survival Story

mysurvivalstory.org

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

OncoLink

oncolink.org

Radiological Society of North America

radiologyinfo.org

The Bili Project Foundation

thebiliproject.org

United Network for Organ Sharing (UNOS)

unos.org

share with us.

Take our [survey](#)

And help make the
NCCN Guidelines for Patients
better for everyone!

NCCN.org/patients/comments



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 abdomen.

bile

A yellowish-brown fluid that is made by the liver and helps to digest food.

bile duct

A small tube-shaped structure that drains digestive fluid (bile) from the liver.

bilirubin

A yellow-brown substance that is part of a digestive fluid called bile.

biopsy

A procedure that removes fluid or tissue samples to be tested for disease.

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.

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.

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.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS <i>Senior Director Patient Information Operations</i>	Laura J. Hanisch, PsyD <i>Medical Writer/Patient Information Specialist</i>	Susan Kidney <i>Graphic Design Specialist</i>	Kim Williams <i>Creative Services Manager</i>
Rachael Clarke <i>Senior Medical Copyeditor</i>	Stephanie Helbling, MPH, MCCHES® <i>Medical Writer</i>	John Murphy <i>Medical Writer</i>	
Tanya Fischer, MEd, MSLIS <i>Medical Writer</i>		Erin Vidic, MA <i>Medical Writer</i>	

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers, Version 2.2021 were developed by the following NCCN Panel Members:

Al B. Benson, III, MD/Chair <i>Robert H. Lurie Comprehensive Cancer Center of Northwestern University</i>	Anne M. Covey, MD <i>Memorial Sloan Kettering Cancer Center</i>	Sanjay Reddy, MD, FACS <i>Fox Chase Cancer Center</i>
Michael I. D'Angelica, MD/Vice-Chair <i>Memorial Sloan Kettering Cancer Center</i>	*Evan S. Glazer, MD, PhD <i>St. Jude Children's Research Hospital/The University of Tennessee Health Science Center</i>	Vaibhav Sahai, MD, MS <i>University of Michigan Rogel Cancer Center</i>
Daniel Abbott, MD <i>University of Wisconsin Carbone Cancer Center</i>	Lipika Goyal, MD <i>Massachusetts General Hospital Cancer Center</i>	Tracey Schefter, MD <i>University of Colorado Cancer Center</i>
Daniel A. Anaya, MD <i>Moffitt Cancer Center</i>	William Hawkins, MD <i>Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine</i>	Gagandeep Singh, MD <i>City of Hope Comprehensive Cancer Center</i>
Robert Anders, MD, PhD <i>The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins</i>	Renuka Iyer, MD <i>Roswell Park Cancer Institute</i>	Stacey Stein, MD <i>Yale Cancer Center/Smilow Cancer Hospital</i>
Chandrakanth Are, MD, MBA <i>Fred & Pamela Buffett Cancer Center</i>	Rojymon Jacob, MD <i>O'Neal Comprehensive Cancer Center at UAB</i>	Jean-Nicolas Vauthey, MD <i>The University of Texas MD Anderson Cancer Center</i>
*Melinda Bachini <i>The Cholangiocarcinoma Foundation</i>	R. Kate Kelley, MD <i>UCSF Helen Diller Family Comprehensive Cancer Center</i>	*Alan P. Venook, MD <i>UCSF Helen Diller Family Comprehensive Cancer Center</i>
Mitesh Borad, MD <i>Mayo Clinic Cancer Center</i>	Robin Kim, MD <i>Huntsman Cancer Institute at the University of Utah</i>	Adam Yopp, MD <i>UT Southwestern Simmons Comprehensive Cancer Center</i>
Daniel Brown, MD <i>Vanderbilt-Ingram Cancer Center</i>	Matthew Levine, MD, PhD <i>Abramson Cancer Center at the University of Pennsylvania</i>	
Adam Burgoyne MD <i>US San Diego Moores Cancer Center</i>	Manisha Palta, MD <i>Duke Cancer Institute</i>	
Prabheen Chahal, MD <i>Case Comprehensive Cancer Center/ University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute</i>	James O. Park, MD <i>Fred Hutchinson Cancer Research Center/ Seattle Cancer Care Alliance</i>	
Daniel T. Chang, MD <i>Stanford Cancer Institute</i>	Steven Raman, MD <i>UCLA Jonsson Comprehensive Cancer Center</i>	
*Jordan Cloyd, MD <i>The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute</i>		

* Reviewed this patient guide. For disclosures, visit [NCCN.org/about/disclosure.aspx](https://www.NCCN.org/about/disclosure.aspx).

NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • pennmedicine.org/cancer

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.org/services/cancer-services
866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/departments/cancer
216.844.8797 • Case CCC
case.edu/cancer

City of Hope National Medical Center
Los Angeles, California
800.826.4673 • cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center |
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
617.732.5500
youhaveus.org
617.726.5130
massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
800.824.2073
huntsmancancer.org

Fred Hutchinson Cancer
Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.606.7222 • seattlecca.org
206.667.5000 • fredhutch.org

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

Robert H. Lurie Comprehensive
Cancer Center of Northwestern
University
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • *Arizona*
904.953.0853 • *Florida*
507.538.3270 • *Minnesota*
mayoclinic.org/cancercenter

Memorial Sloan Kettering
Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

The Ohio State University
Comprehensive Cancer Center -
James Cancer Hospital and
Solove Research Institute
Columbus, Ohio
800.293.5066 • cancer.osu.edu

O'Neal Comprehensive
Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

Roswell Park Comprehensive
Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-
Jewish Hospital and Washington
University School of Medicine
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital/
The University of Tennessee
Health Science Center
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

UC Davis
Comprehensive Cancer Center
Sacramento, California
916.734.5959 | 800.770.9261
health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson
Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family
Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan
Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

The University of Texas
MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

University of Wisconsin
Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/
Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • yalecancercenter.org

Index

- ablation** 32
alpha-fetoprotein (AFP) 16, 24
arterially directed therapy 32–33
best supportive care 36
bile 8, 20, 39
bilirubin 20
biopsy 24
bridging therapy 30
cancer grade 11
cancer stage 10–13
chemotherapy 35
chemoembolization 32–32
Child-Pugh class 21
cirrhosis 15
clinical trials 36–37
computed tomography (CT) 22
downstaging therapy 31
drug-eluting bead transarterial chemoembolization (DEB-TACE) 32–33
dynamic CT scan 22
dynamic MRI scan 22
embolization 32–33
external beam radiation therapy (EBRT) 34
fibrolamellar hepatocellular carcinoma (FLHC) 9
fibrosis 21
hepatitis 15
hepatitis virus B (HVB) 15
hepatitis virus C (HCV) 15
hepatobiliary 8
hepatocellular carcinoma (HCC) 9
immunotherapy 36
jaundice 20, 39
liver 7
liver transplant 30–31
locoregional therapy 46, 50
magnetic resonance imaging (MRI) 22
Model for End-Stage Liver Disease (MELD) 31
multiphasic CT scan 22
mutation 14, 24, 35
non-alcoholic fatty liver disease (NAFLD)
NTRK gene fusion 35
partial hepatectomy 29
percutaneous transhepatic cholangiography (PTC) 23
progression 47
radiation therapy (RT) 34
resectable 29, 41
resection 29
risk factors 14–15
screening 16
supportive care 36
surgery 28–29
surgical margin 29
surveillance 43
systemic therapy 35–36
targeted therapy 35
transarterial bland embolization (TAE) 32–33
transarterial chemoembolization (TACE) 32–33
transarterial radioembolization (TARE) 32–33
tyrosine kinase inhibitor (TKI) 32–33
ultrasound (US) 23
United Network for Organ Sharing (UNOS) 31
unresectable 29, 44





NCCN
GUIDELINES
FOR PATIENTS®

Liver Cancer

Hepatobiliary Cancers

2021

NCCN Foundation gratefully acknowledges our advocacy supporters Global Liver Institute and Cholangiocarcinoma Foundation, and the following corporate supporters for helping to make available these NCCN Guidelines for Patients: Eisai, Inc. and Exelixis, Inc. NCCN independently adapts, updates, and hosts the NCCN Guidelines for Patients. Our corporate supporters do not participate in the development of the NCCN Guidelines for Patients and are not responsible for the content and recommendations contained therein.

To support the NCCN Guidelines for Patients

DONATE NOW

Visit NCCNFoundation.org/Donate



National Comprehensive
Cancer Network®

3025 Chemical Road, Suite 100
Plymouth Meeting, PA 19462
215.690.0300

NCCN.org/patients – For Patients | NCCN.org – For Clinicians