

Dr Shivam Shingla

Consultant Medical Oncologist
MBBS, MD, DNB Medical Oncology
MNAMS MRCP UK (SCE)
Lung Cancer Fellowship From
Zurich Switzerland



www.drshivamshingla.com



+91 98925 96286



drshivamshingla@gmail.com

#Reference From NCCN Guidelines

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

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Liver cancer basics

- 5 The liver
- 7 Liver cancer
- 7 How liver cancer spreads
- 8 Risk factors
- 9 Hepatitis
- 9 Liver cancer screening
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The liver is a large organ located on the right side of the body under the 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.

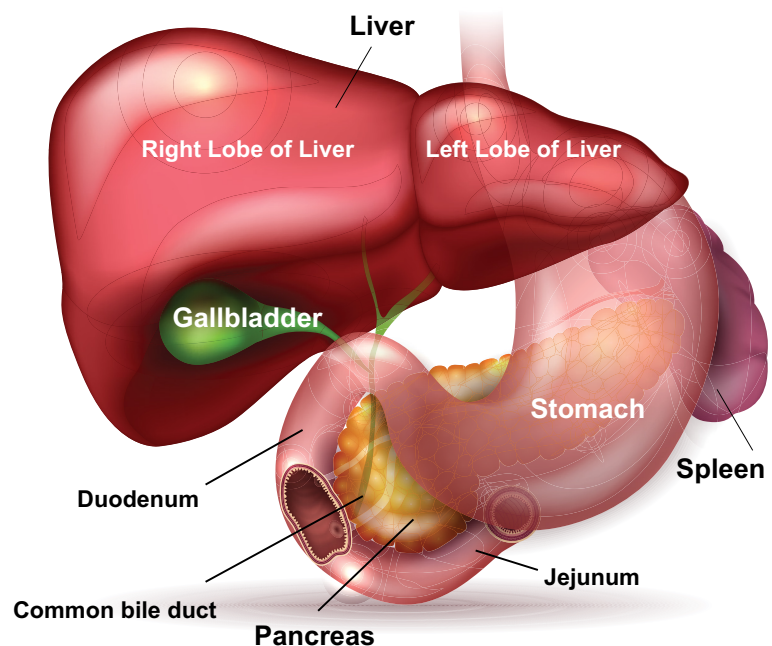
The liver

The liver is a large organ located on the right side of the body under the 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 gallbladder is located near the right side of the liver and close to the first part of the small intestines (duodenum).

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 intestine to help digest food.

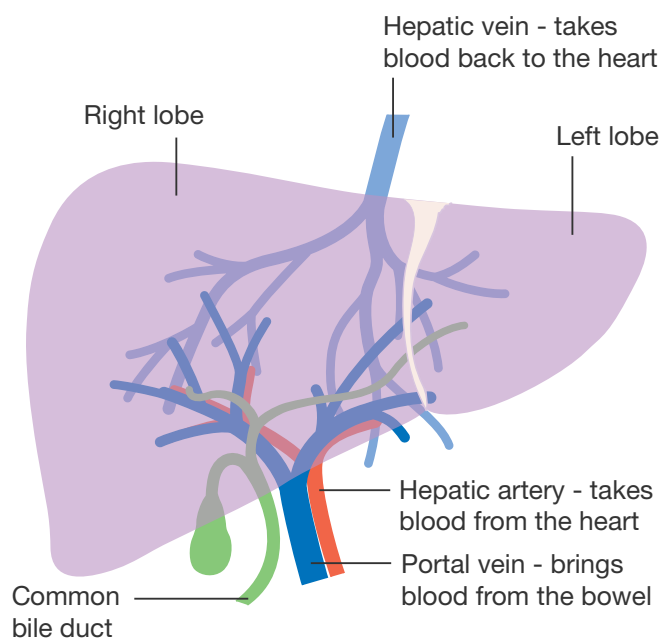
The hepatobiliary system

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, absorbs nutrients, and removes waste from the body. Some doctors consider the pancreas to be a part of this system.

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



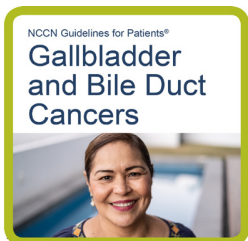
Liver cancer

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 to 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 fibrolamellar hepatocellular carcinoma (FLHC). 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.

More information on gallbladder and bile duct tumors is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



In the following pages, this patient guideline will focus on the most common type of liver cancer, 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 it 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.

Risk factors

Risk is your chance of developing liver cancer. Everyone has some risk for developing liver cancer. However, some people are at increased risk. Risk factors can be activities that people do, things in the environment, or traits passed from biological parents to children through genes. Genes are a set of instructions that tell new cells what to become (for example, heart, liver, and skin) and what to do (make hormones, absorb nutrients, and kill germs).

Risk is based on:

- Those with cirrhosis
- Those without cirrhosis

Known risk factors are listed in **Guide 1**.

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

Guide 1

Risk factors for developing liver cancer

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

Risk factors for those with cirrhosis:

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

Risk factors for those without cirrhosis:

- Hepatitis B virus (HBV) or infection
- Additional risk factors include HBV carrier with family history of liver cancer, Asian male assigned sex at birth 40 years of age or over, Asian female assigned sex at birth 50 years of age or over, and African/North American Black persons with hepatitis B

Hepatitis

Hepatitis is a type of liver disease. Viruses called hepatitis B (HBV) and hepatitis C (HCV) are spread by contact with blood and other bodily fluids. HBV and HCV can cause chronic hepatitis, 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

High alcohol use can cause damage to the liver. Having NAFLD may lead to cirrhosis in those who drink little or no alcohol. NAFLD is seen in those with high weight, diabetes, high cholesterol, or other conditions. Diabetes, high weight, 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.

Liver cancer screening

Screening helps find disease early before symptoms occur, when it is more likely to be cured with treatment. The goal of liver cancer screening is to find liver cancer early in those who are at risk for developing liver cancer. 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. Nodules are small, round areas of tissue. Not all nodules are cancer.
- If an ultrasound finds nodules that are smaller than 10 mm, repeat the ultrasound and AFP in 3 to 6 months.
- If an ultrasound is negative, repeat the ultrasound and AFP in 6 months.

Key points

- The liver filters blood, helps with blood clotting, makes bile, breaks down fats, and helps process sugar for energy. It also produces lymph.
- The liver, gallbladder, and bile ducts are part of the hepatobiliary system.
- Cancer that starts in the liver is called primary liver cancer. Secondary liver cancer is when other cancer types spread to the liver.
- There is more than one type of primary liver cancer in adults. The most common type is hepatocellular carcinoma (HCC). HCC is the focus of this book.
- Anything that increases your chances of developing liver cancer is called a risk factor.
- 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.
- Screening helps find disease early when it is more likely to be cured with treatment. The goal of liver cancer screening is to find liver cancer early in those who are at risk for developing liver cancer.



Although living with liver disease is physically and emotionally challenging, I have been able to live a normal life – traveling, snorkeling, having children. So, do not limit yourself and do not hold back from doing something because you are scared or you are worried about the 'what ifs.' If you live your life with those limitations, you'll have no life at all.”

2

Diagnosing liver cancer

- 12 Test results
- 12 General health tests
- 14 Blood tests
- 16 Imaging tests
- 18 Biopsy
- 19 Performance status
- 20 Key points

Liver cancer is usually confirmed with imaging tests. More tests will be done to plan treatment. Sometimes, a biopsy is needed to confirm cancer. 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 be used to determine your treatment plan. Treatment will be based on these findings. 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:

- Choose a friend, family member, or peer who can drive you to appointments, provide meals, or offer emotional support during diagnosis and treatment.
- 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 help them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.

- 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 refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician (PCP) informed of changes to this list. You are encouraged to keep your PCP in the loop. They are great partners in your care.
- In your contact list, include information on your exact type of cancer, as well as any treatments and the date each treatment started.

A list of tests used for treatment planning can be found in **Guide 2**.

General health tests

Medical history

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter (OTC) medicines, herbals, or supplements you take. Some supplements interact and affect medicines that your care team may prescribe. Tell your care team about any symptoms you have. A medical history, sometimes called a health history, will help determine which treatment is best for you.

Family history

Some cancers and other diseases can run in families. Your health care provider will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer or where the cancer started, if it is in multiple locations, and if they had genetic testing.

Physical exam

During a physical exam, your health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and 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.
- Feel for enlarged lymph nodes in your neck, underarm, and groin.

Guide 2

Tests for treatment planning

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, if not done before or needs updating

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. Some blood tests are described next.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs) in your blood. Red blood cells carry oxygen throughout your body, white blood cells fight infection, and platelets control bleeding.

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) measures 14 different substances in your blood. It is usually done on the plasma part of 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.



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 health.
- ✓ 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, test types (such as blood, imaging, pathology, radiology, and genetics), treatments, and procedures. Organize items in the folder by date.
- ✓ Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- ✓ Add a section for questions and to take notes.

Bring your medical binder to appointments. You never know when you might need it!

One of the chemicals measured by LFTs 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 B (HBV) and hepatitis C (HCV) are the most common types of chronic 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 and the score, as well. You may be referred to a hepatologist if your testing indicates the presence of fibrosis or cirrhosis in your liver.

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

Liver cancer is usually confirmed with imaging tests. Imaging tests take pictures of the inside of your body. Imaging tests show the primary tumor, or where the cancer started, and look for cancer in other parts of the body. A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your health care provider (HCP). It is likely that the report will be sent directly to you through your patient portal or patient access system. You should discuss these results with your HCP.

You will have some but not all the following tests.

Bone scan

Liver cancer can spread to bones. A bone scan uses a radiotracer, a substance that releases small amounts of radiation. Before the pictures are taken, the tracer will be injected into your vein. It can take a few hours for the tracer to enter your bones. However, the test is quick and painless.

A special camera will take pictures of the tracer in your bones as it moves over your body. Areas of bone damage take up more radiotracer than healthy bone and show up as bright spots on the pictures. Bone damage can be caused by cancer, cancer treatment, previous injuries, or other health issues.

Contrast material

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. The types of contrast vary and are different for CT and MRI.

Tell your care team if you have had allergic reactions to contrast in the past. This is important. You might be given medicines to avoid the effects of those allergies. Contrast

CT machine

A CT machine is large and has a tunnel in the middle. During the test, you will lie on the table that moves slowly through the tunnel.



might not be used if you have a serious allergy or if your kidneys aren't working well.

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 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.

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 your care team 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. Because of the very strong magnets used in the MRI machine, tell the technologist if you have any metal in your body. During the test, you will likely be asked to hold your breath for 10 to 20 seconds as

the technician collects the images. Contrast is often used.

A closed MRI has a capsule-like design where the magnet surrounds you. An open MRI has a magnetic top and bottom, which allows for an opening on each end. Closed MRIs are more common than open MRIs, so if you have claustrophobia (a dread or fear of enclosed spaces), be sure to talk to your care team about it.

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.

PET scan

A positron emission tomography (PET) scan uses a radioactive sugar molecule called a tracer. A tracer is a substance injected into a vein to see where cancer spots might be in the body and if they are using sugar produced by the body to grow. Cancer spots show up as bright areas on PET scans. However, not all tumors will appear on a PET scan and not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on the PET scan. Inflammation or infection can also show up as a bright spot. When a PET

scan is combined with CT, it is called a PET/CT scan.

Ultrasound

An ultrasound (US) uses high-energy sound waves to form pictures of the inside of the body. This is similar to a sonogram used for pregnancy. A wand-like probe (transducer) will be held and moved on your skin using a gel. Ultrasound is painless and does not use x-rays, so it can be repeated as needed. Ultrasound is good at showing small areas of cancer that are near the skin. Sometimes, an ultrasound is used to guide a biopsy.

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.

Types of possible biopsies include:

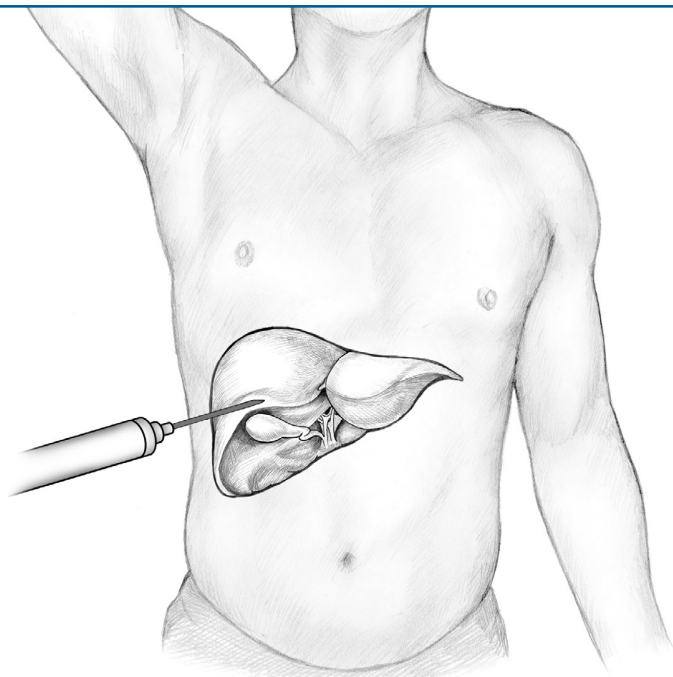
- **Fine-needle aspiration (FNA)** uses a thin needle to remove a sample of tissue or fluid. An ultrasound may guide the FNA biopsy.
- **Core needle biopsy** removes tissue samples with a hollow needle about the same size as a needle used for an intravenous (IV) line. An ultrasound or CT scan may help the radiologist find the area to biopsy.
- **Laparoscopy** is a minimally invasive surgery that uses a camera through a small cut in the abdomen. Sometimes, an ultrasound is performed at the same time. A tool then takes samples of tissue.

The biopsy samples will be sent to a pathologist, an expert in examining cells under

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



a microscope to find disease. A sample 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 tested to see if the cancer cells have any specific mutations. Some mutations, such as *NTRK* and *RET* gene fusions or microsatellite instability-high (MSI-H)/deficient mismatch repair (dMMR) mutations, can be targeted with specific therapies. Tumor mutation testing is separate from genetic testing for mutations that you may have inherited from your biological parents.

Performance status

Performance status (PS) is a person's general level of fitness and ability to perform daily tasks. Your state of general health will be rated using a PS scale called Eastern Cooperative Oncology Group (ECOG) or the Karnofsky Performance Score (KPS).

The ECOG PS scores range from 0 to 5. PS might be referred to as good or poor. Good PS is usually PS 0 or PS 1.

The KPS score ranges from 0 to 100.

PS is one factor taken into consideration when choosing a treatment plan. Your preferences about treatment are always important.

Key points

- Tests are used to find cancer, plan treatment, and check how well treatment is working.
- A medical history and physical exam inform your care team 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. Liver cancer is usually confirmed with imaging tests.
- Fibrosis score and Child-Pugh class are used to see how well the liver is working, help decide if surgery is an option, and plan treatment.
- A biopsy removes a sample of tissue or fluid.
- Performance status (PS) is a person's general level of fitness and ability to perform tasks.
- Online portals are a great way to access your test results.



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

Liver cancer staging

22 How liver cancer is staged

23 TNM scores

25 Key points

Cancer staging is used to reflect prognosis and to guide treatment decisions. It describes the size and location of the tumor(s) and if cancer has spread to lymph nodes, organs, or other parts of the body.

How liver cancer is staged

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. This is called staging.

Based on testing, your cancer will be assigned a stage. Staging helps to predict prognosis and is needed to make treatment decisions. A prognosis is the course your cancer will likely take. AJCC is just one type of staging system. The Barcelona Clinic Liver Cancer (BCLC) Staging System is another type. In BCLC, tumor size and liver function are used.

Information gathered during AJCC staging:

- **The extent (size) of the tumor (T):** How large is the cancer? Has it grown into nearby areas?
- **The spread to nearby lymph nodes (N):** Has the cancer spread to nearby lymph nodes? If so, how many? Where?

- **The spread (metastasis) to distant sites (M):** Has the cancer spread to distant organs such as the lungs or bone?
- **Grade of the cancer (G):** How much do the cancer cells look like normal cells?
- **Biomarker and mutation testing:** Does the cancer have any genes, proteins, markers, or mutations that might suggest treatment?

Staging is based on a combination of information to reach a final numbered stage. Often, not all information is available at the initial evaluation. More information can be gathered as treatment begins. Doctors may explain your cancer stage in different ways than described next.

Staging includes:

- **Anatomic** – based on extent of cancer as defined by tumor size (T), lymph node status (N), and distant metastasis (M).
- **Prognostic** – includes anatomic TNM plus tumor grade and the status of the biomarkers or mutations. The prognostic stage also includes the assumption that you are treated with the standard-of-care approaches.

Prognostic stages are divided into clinical and pathologic. Clinical stage (c) is the rating given before any treatment. It is based on a physical exam, biopsy, and imaging tests. An example might look like cT3. Pathologic stage (p) or surgical stage is determined by examining tissue removed during surgery. An example might be pT3. If you are given drug therapy before surgery, then the stage might look like ypT3. Staging after surgery provides more specific and accurate details about the size of the cancer and lymph node status.

TNM scores

The tumor, node, metastasis (TNM) system is used to stage liver cancer. In this system, the letters T, N, and M describe different areas of cancer growth. Based on cancer test results, a score or number will be given 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: T3N2M0 or T3, N2, 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

TNM scores are not always used to describe liver cancer.

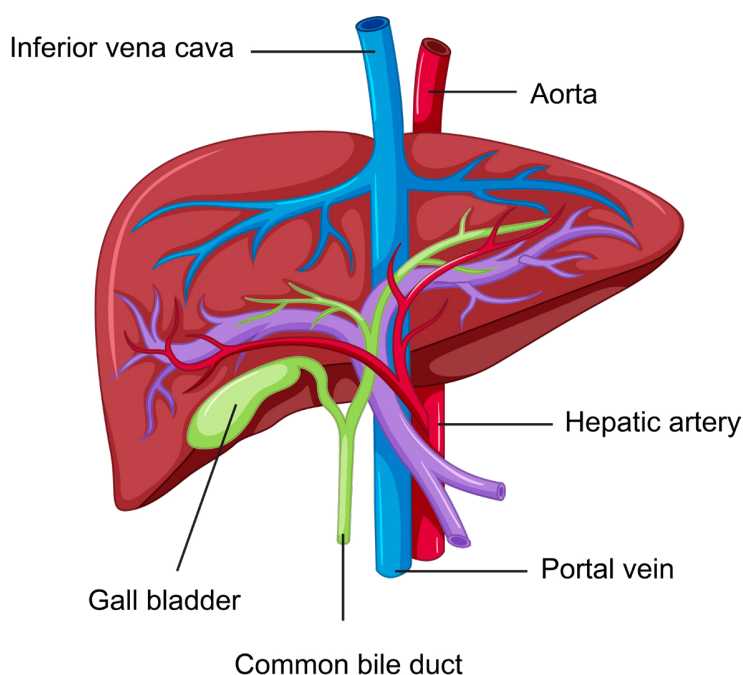
T = Tumor

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)

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.



that involve nearby organs (other than the gallbladder) or have invaded the peritoneum (lining of the abdomen)

N = Regional lymph 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 found 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** – There is no cancer in nearby lymph nodes.
- **N1** – Cancer in regional lymph nodes is found.

M = Metastasis

Cancer that has spread to distant parts of the body is shown as M1. Common sites for metastasis include the lung and bone.

- **M0** – No distant metastasis is found.
- **M1** – Distant metastasis is found.

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

Numbered stages are based on TNM scores. Stages range from stage 0 to stage 4, with 4 being the most advanced. They might be written as stage 0, stage I, stage II, stage III, and stage IV. **See Guide 3.**

Stage 1

In stage 1 liver cancer, there is only one tumor up to 2 cm in size or one tumor larger than 2 cm that does not involve blood vessels found

Guide 3 Liver cancer stages

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

in the liver. It may have grown into veins, arteries, or bile ducts. Cancer has not spread to lymph nodes (N0) or other parts of the body (M0).

Stage 2

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

Stage 3

In stage 3a liver cancer, there are multiple tumors with one tumor 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.

Key points

- Staging helps to predict prognosis and is needed to make treatment decisions. A prognosis is the course your cancer will likely take.
- 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.
- The clinical stage (c) is based on the results of testing before any treatment. It is written as cTNM.
- The pathologic stage (p) is based on the results of tissue examined during surgery. It is written as pTNM.
- Grade describes how abnormal the tumor cells look under a microscope (called histology).
- Regional lymph nodes are found near the liver.
- Cancer that has spread to distant parts of the body is called metastatic cancer.

4

Treating liver cancer

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There is more than one treatment for liver cancer. Often, you will have multiple treatments at different times. This is called multidisciplinary care. This chapter describes treatment options and what to expect. Together, you and your care team will choose a treatment plan that is 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 care team 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. Many factors play a role in how your cancer responds to treatment.

Care team

Treating liver cancer takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of health care and psychosocial care professionals from different professional backgrounds who have knowledge (expertise) and experience in your type of cancer. This team is united in the planning and implementing of your treatment. Ask who will coordinate your care.

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 help 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 diagnostic radiologist** interprets the results of imaging tests.
- **An interventional radiologist** performs needle biopsies, ablations, and arterially directed therapies, and places ports for treatment.
- **A pathologist** analyzes the cells, tissues, and organs removed during a biopsy or surgery and provides cancer diagnosis, staging, and information about biomarker testing.
- **A surgical oncologist** performs operations to remove cancer. Some transplant surgeons and hepatobiliary surgeons also care for those with liver cancer.
- **A medical oncologist** treats cancer in adults using systemic therapy.

- **A radiation oncologist** prescribes and delivers 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.
- **Residents and fellows** are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- **Nurse practitioners (NPs) and physician assistants (PAs)** are health care providers. Some of your clinic visits may be done by a nurse practitioner or physician assistant.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Oncology pharmacists** are experts in knowing how to use medicines to treat cancer and to manage symptoms and side effects.
- **Palliative care nurses, advanced practice providers (APPs), and physicians** help provide an extra layer of support with cancer-related care.
- **Radiation therapists** provide your hands-on delivery of radiotherapy treatments.
- **Nutritionists and dietitians** can provide guidance on what foods are most suitable for your 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 think and feel.
- **Social workers** help people solve and cope with problems in their everyday lives. Clinical social workers also diagnose and treat mental, behavioral, and emotional issues. The anxiety a person feels when diagnosed with cancer might be managed by a social worker in some cancer centers. They, or other designated professionals, can help navigate the complexities of financial and insurance stresses.
- **A research team** helps to collect research data and coordinate care if you are in a clinical trial. Clinical trials help bring new therapies to patients and advance the treatment for everyone. Consider asking your care team about access to clinical trials.

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

- How you feel
- What you need
- What is working and what is not

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

Surgery

Surgery is an operation or procedure to remove cancer from the body. Often, surgery is the main or primary treatment to remove the cancer from the liver. This is only one part of a treatment plan. Surgery can also provide supportive care by easing pain or discomfort. This is called palliative surgery.

When preparing for surgery, seek the opinion of an experienced surgeon. The surgeon should be an expert in performing your type of surgery. Hospitals that perform many surgeries often have better results. You can ask for a referral to a hospital or cancer center that has experience in treating liver cancer.

The removal of the cancer through surgery can be accomplished in different ways depending on the specific circumstances, such as the size and location of the tumor, and if there is cancer in any surrounding organs and tissues. Surgery is based on the safest and best way to remove the cancer.

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

Tumor resection

The removal of the tumor is called tumor resection. Imaging tests will be ordered to see if your cancer is resectable (can be removed completely by surgery) or unresectable (cannot be removed completely by surgery). Sometimes, imaging tests cannot clearly show one way or the other.

Partial hepatectomy (liver resection)

A partial hepatectomy 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 determining if tumor resection is the best option for you. You must also have a working liver and be healthy enough for surgery.

Goal of surgery

The goal of surgery or tumor resection is to remove all of the cancer. To do so, the tumor is removed along with a rim of normal-looking tissue around its edge called the surgical margin. The surgical margin may look normal during surgery, but cancerous cells may be found when viewed under a microscope by a pathologist. A clear or negative margin (R0) is when no cancer cells are found in the tissue around the edge of the tumor. In a positive margin, cancer cells are found in normal-looking tissue around the tumor. If there is a positive margin, you may have another surgery to try to remove the remaining tumor cells. Surgery includes removal of lymph nodes.

Some undergo tumor or liver ablation at the time of surgery. Ablation uses heat to destroy tumors. You and your care team will decide whether resection, ablation, or both is right for you.

Liver transplant

In a liver transplant, the entire 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 those 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 arterially directed therapy (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

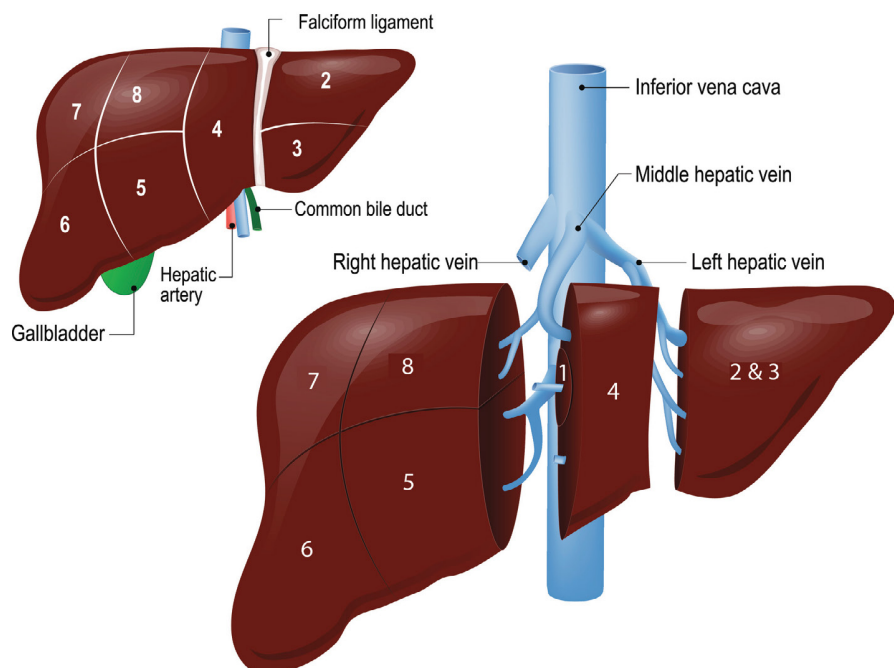
There can be long wait times to receive a liver transplant. Treatments may be given while you wait for a transplant. These treatments are called bridge or bridging therapy and include ablation, arterially directed therapy (embolization), or radiation therapy.

Downstaging therapy

Downstaging therapy is used to reduce the tumor burden in some with more advanced HCC (without distant metastasis) who are

Liver sections

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



beyond the accepted transplant criteria with the goal of future transplant. Treatments include ablation and arterially directed therapy (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:

- AFP level of 1000 ng/mL or less
- One tumor of 5 cm or less, or 2 or 3 tumors of 3 cm or less
- Tumor not in large vein, arteries, or bile ducts (macrovascular involvement)
- Disease confined to liver
- 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.

If you smoke or vape, seek help to quit

A history of smoking or vaping nicotine increases your chances of developing lung and other cancers. Smoking and vaping can limit how well cancer treatment works and prevents wound healing. It also greatly increases your chances of having side effects during and after surgery. Cannabis use might also affect the amount of anesthesia used during surgery.

Nicotine is the chemical in tobacco that makes you want to keep smoking and vaping. Nicotine withdrawal is challenging for most people who smoke or vape. The stress of having cancer may make it even harder to quit. If you smoke or vape, ask your care team about counseling and medicines to help you quit.

For online support, try these websites:

- [SmokeFree.gov](https://www.smokefree.gov)
- [BeTobaccoFree.gov](https://www.betobaccofree.gov)
- [CDC.gov/tobacco](https://www.cdc.gov/tobacco)

Ablation

Ablation is a type of 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 (3 cm or less) with little harm to nearby tissue. Tumors must be in an area that can be reached with ablation and not near other organs, major blood vessels, or bile ducts.

Types of ablation include:

- **Chemical** – Uses percutaneous ethanol injection (PEI) or acetic acid injection to kill cancer cells.
- **Thermal** – Uses radiofrequency ablation (RFA) and microwave ablation (MWA) to kill cancer cells by heating them with high-energy radio waves or microwaves.
- **Cryoablation** – Freezes cancer cells with a very cold substance.

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

Arterially directed therapy

Arterially directed therapy or embolization 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. Arterially directed therapy has risks. It might not be used if your bilirubin level is above a certain level.

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.
- **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).
- **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.

- ▶ **Transarterial radioembolization (TARE or RE)** uses tiny glass or resin beads filled with the radioactive isotope yttrium-90 that are injected directly into the tumor(s). 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.

Radiation therapy

Radiation therapy (RT) uses high-energy radiation from x-rays, photons, protons, electrons, and other sources to kill cancer cells and shrink tumors. RT can be given alone or with other treatments. It might be used as supportive care or palliative care to help ease pain or discomfort caused by cancer, or to control bleeding caused by a tumor. RT may be a treatment for all tumors, regardless of location.

Most types of radiation include short treatment sessions that are given once daily over a few days to weeks. Ask your care team which radiation option(s) are best for you and what side effects to expect.

EBRT

External beam radiation therapy (EBRT) uses a machine outside of the body to aim radiation at the tumor(s) or areas of the body.

Standard of care is the best-known way to treat particular disease based on past clinical trials. There may be more than one treatment regimen that is considered standard of care. Ask your care team what treatment options are available and if a clinical trial might be right for you.



Common types of EBRT that may be used to treat your cancer include the following:

- **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 to match the shape of the tumor. This limits the amount of radiation to normal tissue.
- **Stereotactic body radiation therapy (SBRT)** uses high-energy radiation beams to kill or ablate the tumor.

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. Make your wishes known.

For a list of some systemic therapies, **see Guide 4.**

Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells. It is used in arterially directed therapy.

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 or inhibit the action of molecules that help cancer cells grow and/or survive.

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

Guide 4

Systemic therapy examples

Targeted therapy examples

- | | | |
|--|----------------------------|---------------------------|
| • Bevacizumab (Avastin) or bevacizumab substitutes (biosimilars) such as Vegzelma, Mvasi, Zirabev, and Alymsys | • Cabozantinib (Cabometyx) | • Ramucirumab (Cyramza) |
| | • Entrectinib (Rozlytrek) | • Regorafenib (Stivarga) |
| | • Larotrectinib (Vitrakvi) | • Selpercatinib (Retevmo) |
| | • Lenvatinib (Lenvima) | • Sorafenib (Nexavar) |

Immunotherapy examples

- | | | |
|-------------------------------|----------------------------|------------------------------|
| • Atezolizumab (Tecentriq) | • Ipilimumab (Yervoy) | • Tremelimumab-actl (Imjudo) |
| • Dostarlimab-gxly (Jemperli) | • Nivolumab (Opdivo) | |
| • Durvalumab (Imfinzi) | • Pembrolizumab (Keytruda) | |

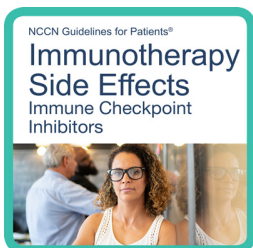
another gene fuse or join. This activates the *NTRK* gene in a way that causes uncontrolled cell growth. Larotrectinib (Vitrakvi) and entrectinib (Rozlytrek) might be used to target cancer that is *NTRK* gene fusion-positive.

A biosimilar or substitute might be used in place of bevacizumab. A biosimilar is an almost identical version of a drug made by another company. It is used in the exact same way and at the same dose as the actual drug. Biosimilars include Vegzelma, Mvasi, Zirabev, and Alymsys.

Immunotherapy

Immunotherapy is a type of systemic treatment that tries to reactivate the immune system against tumor cells. The immune system has many on and off switches. Tumors take advantage of "off switches." Two leading off switches are PD-1 and CTLA-4. Immunotherapy can be given alone or with other types of treatment.

More information on immunotherapy side effects is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Warnings about supplements and drug interactions

You might be asked to stop taking or avoid certain herbal supplements when on a systemic therapy. Some supplements can affect the ability of a drug to do its job. This is called a drug interaction.

It is critical to speak with your care team about any supplements you may be taking. Some examples include:

- Turmeric
- Gingko biloba
- Green tea extract
- St. John's Wort
- Antioxidants

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart or blood pressure medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. Therefore, it is very important to tell your care team about any medicines, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking.

Bring a list with you to every visit.

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of treating 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 of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase I** trials study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase II** trials study how well the drug or approach works against a specific type of cancer.
- **Phase III** trials test the drug or approach against a 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 requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

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. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others whom 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 have already started standard treatment you may not be eligible for certain clinical trials. 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.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

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. In general, procedures, drugs, or tests that are considered standard of care will be billed to you or your insurance, whereas those considered research are covered by the trial sponsor. Your treatment team and the research team can help determine if you are responsible for any costs.

Supportive care

Supportive care will be specific to your needs. Supportive care is health care given to prevent, reduce, and relieve suffering, and to improve quality of life. Supportive care might include pain relief, palliative care, emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects so they can be managed. Best supportive care, supportive care, and palliative care are often used interchangeably.

It is very important to take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized. Strength is needed to sustain you during treatment.

Side effects

All cancer treatments can cause unwanted health issues 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. Treatment can cause several side effects. Some are very serious.

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. You will be monitored closely for side effects.

Late effects

Late effects are side effects that occur months or years after a disease is diagnosed or after treatment has ended. Late effects may be caused by cancer or cancer treatment. They may include physical, mental, and social problems, and second cancers. The sooner late effects are treated the better. Ask your care team about what late effects could occur. This will help you know what to look for.

Survivorship

A person is a cancer survivor from the time of diagnosis until the end of life. When treatment leads to remission (or no evidence of disease), you will need follow-up or survivorship care for late effects. During survivorship care you will still have a care team, but it will look different. Seek out peer support groups, whether online or in person.

Side effects

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

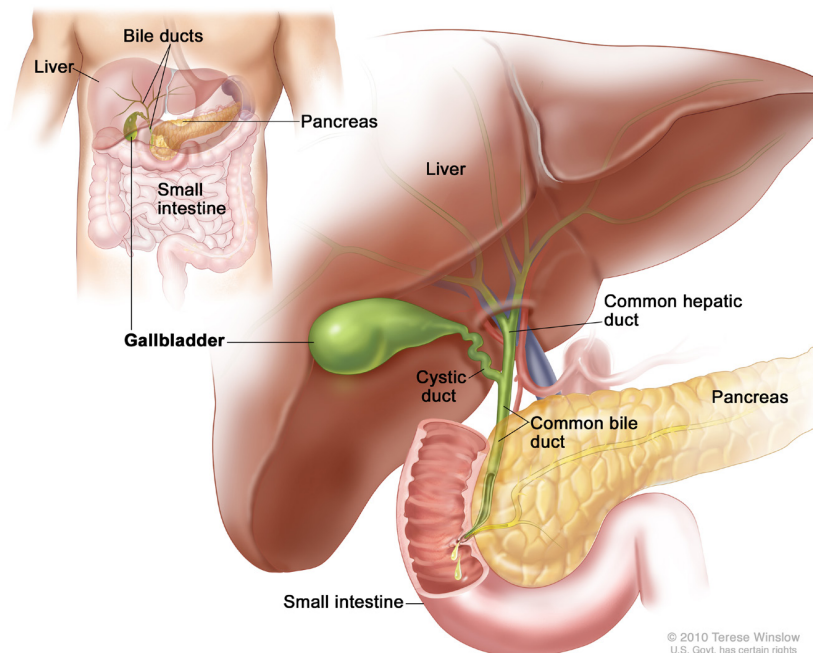
body. You may need a new or second stent during or after cancer treatment if the tumor grows. A biliary bypass is a surgery to re-route the flow of bile from the common bile duct into the small intestine. The result is that the bile flow avoids (bypasses) the blocked part of the duct.

Difficulty eating

Sometimes side effects from surgery, cancer, or its treatment 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 weight.

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.



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Distress

Depression, anxiety, and sleeping issues are common and are a normal part of cancer diagnosis. Talk to your care team and with those whom you feel most comfortable about how you are feeling. There are services, people, and medicine that can help you. Support and counseling services are available.

Fatigue

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, acupuncture, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

Pain

Tell your care team about any pain or discomfort. You might meet with a palliative care specialist or with a pain specialist to manage pain.

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
- ✓ A description of 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?
- ✓ A rating of your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- ✓ Does pain get in the way of you doing the things you enjoy?

Key points

- A resectable tumor can be removed completely with surgery. An unresectable tumor cannot be removed completely with surgery.
 - Surgery is an option for some people with liver cancer.
 - Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.
 - Ablation is a type of 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.
 - Arterially directed therapy or embolization treats tumors by injecting particles, chemotherapy, or radioactive beads directly into the blood vessels that supply the tumor(s).
 - Radiation therapy (RT) uses high-energy radiation from x-rays, protons, photons, and other sources to kill cancer cells and shrink tumors.
 - 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 its treatment and improves quality of life. Supportive care is always given.
 - All cancer treatments can cause unwanted health issues called side effects. It is important for you to tell your care team about all your side effects so they can be managed.
- Get to know your care team and help them get to know you.
- Keeping a pain diary might help you manage pain.
 - A registered dietitian who is an expert in nutrition and food can help if it is hard for you to eat or digest food.
 - If you smoke or vape, it is important to quit for the best treatment results.

5

Resectable

- 42 Resection
- 42 Transplant
- 43 No transplant
- 43 Surveillance
- 44 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 care team will choose a treatment plan that is best for you.

Surgery is not for everyone. The size and location of the tumor(s), how well your liver functions, and if the cancer has spread outside the liver or invaded other structures such as veins, arteries, or ducts will be considered when planning surgery. You may not want surgery. Your preferences about treatment are important.

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.

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 increased pressure in the portal vein (portal hypertension)
- Suitable tumor location
- Adequate liver reserve (the number, type, and health of non-cancerous liver cells)
- 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 why resection might not be the best choice for your situation. Ask your care team about this.

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 cancer in large veins, arteries, or bile ducts (no macrovascular involvement)
- No disease outside the liver (extrahepatic)

If a liver 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.

No transplant

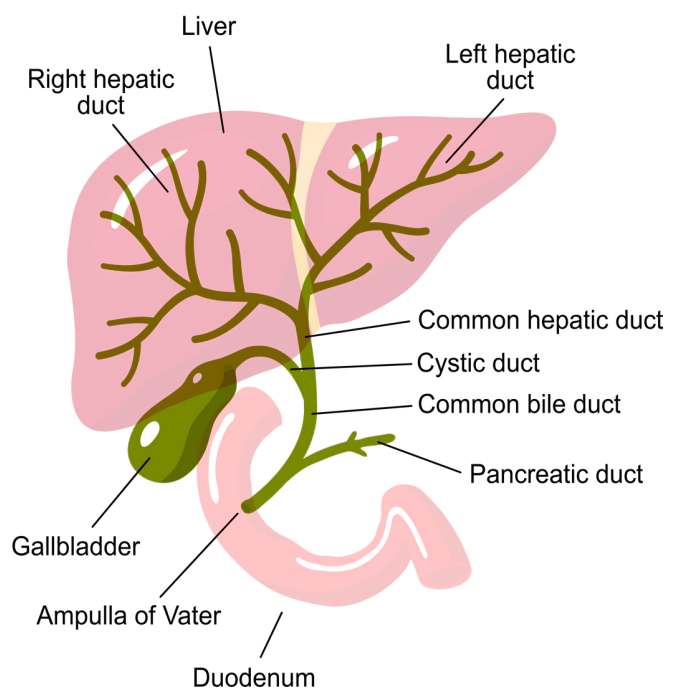
If a liver transplant is not an option, then surgery to remove the tumor (resection) is preferred. Other options include ablation, arterially directed therapy, and radiation therapy.

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. Tests will be done every 3 to 6 months for 2 years, then every 6 months for at least 5 years.

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.



Key points

- A tumor that can be removed completely with surgery is called resectable. 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, arterially directed therapy (embolization), radiation therapy, or systemic therapy.
- Surveillance consists of testing on a regular basis to watch for signs that cancer has returned.



Everything that I went through reflects that I am here for a reason, so giving back is my way of honoring my donor. "

6

Unresectable

- 46 Transplant
- 47 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 care team will choose a treatment plan that is best for you.

Transplant

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

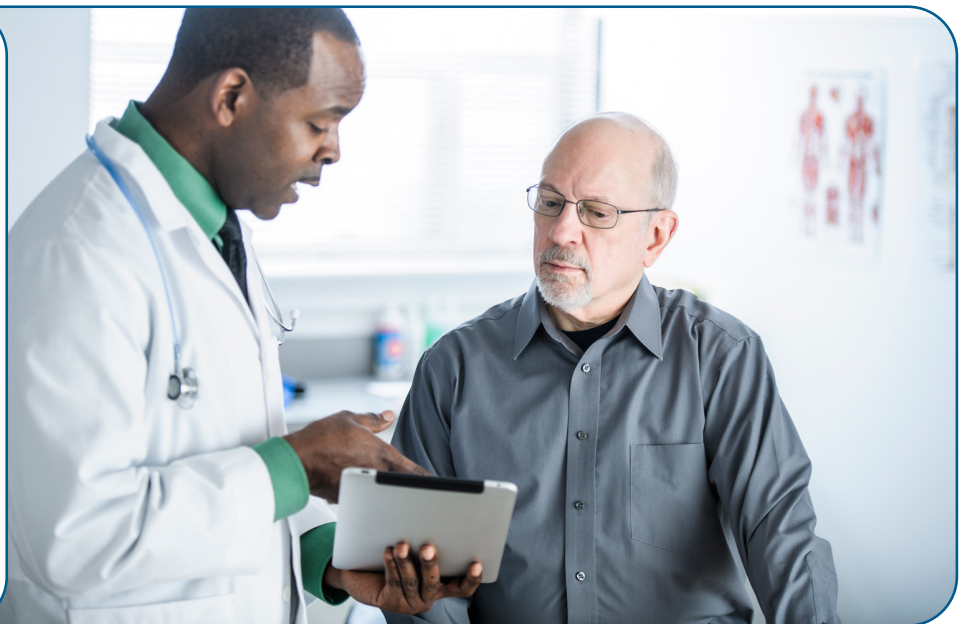
- Alpha-fetoprotein (AFP) levels are 1000 ng/mL or less and tumor is 2 to 5 cm in diameter or 2 to 3 tumors are 1 to 3 cm
- No large veins, arteries, or bile ducts have cancer
- No disease outside the liver (extrahepatic)

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.

Your preferences about treatment are always important. Talk to your care team and make your wishes known.



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. Tests will be done every 3 to 6 months for 2 years, then every 6 months for at least 5 years.

Treatment without surgery

Not everyone is healthy enough for a liver transplant. You may not want a liver transplant. Sometimes, surgery such as resection or partial hepatectomy is not possible because of where the tumor is located or the health of your liver. Treatment options are listed next.

Locoregional therapy

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

Clinical trial

A clinical trial might be an option. Ask your care team for more information.

Systemic therapy

Systemic therapy is drug therapy that works throughout the body. Systemic therapy options are the same used to treat metastatic disease and can be found in the next chapter.



Finding a clinical trial

In the United States

NCCN Cancer Centers
[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

The National Cancer Institute (NCI)
[cancer.gov/about-cancer/treatment/clinical-trials/search](https://www.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](https://www.cancer.gov/contact)

Best supportive care

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

Disease 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.

Systemic therapy options are the same used to treat metastatic disease and can be found in the next chapter.

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.

7

Metastatic disease

- 50 Treatment options
- 51 Disease progression
- 52 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 care team will choose a treatment plan that is best for you.

cancer called cancer burden and to prevent the further spread of cancer. Treatment options include a clinical trial, best supportive care, or systemic therapy.

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 given first. The preferred first-line systemic therapy is atezolizumab with bevacizumab or tremelimumab-actl with durvalumab. A substitute (biosimilar) might be used for bevacizumab. A biosimilar is almost an identical drug made by another company. It is used in the exact same way and at the same dose as bevacizumab. Biosimilars include Vegzelma, Mvasi, Zirabev, and Alymsys.

For all first-line systemic therapy options, **see Guide 5.**

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

Guide 5

First-line systemic therapy options: Metastatic disease

Preferred	<ul style="list-style-type: none"> • Atezolizumab with bevacizumab (Child-Pugh Class A only). A biosimilar might be used for bevacizumab. • Tremelimumab-actl with durvalumab
Other recommended	<ul style="list-style-type: none"> • Sorafenib (Child-Pugh Class A or B7) • Lenvatinib (Child-Pugh Class A only) • Durvalumab • Pembrolizumab
Used in some cases	<ul style="list-style-type: none"> • Nivolumab (Child-Pugh Class B only) • Atezolizumab with bevacizumab (Child-Pugh Class B only) • Nivolumab with ipilimumab for TMB-H tumors

Disease 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 given. Treatment is based on the type of systemic therapy you had before.

For next-line systemic therapy options, **see Guide 6**.

Need help paying for medicine or treatment?

Ask your care team what options are available.

Guide 6

Next-line systemic therapy options: Metastatic disease

Options	<ul style="list-style-type: none"> • Regorafenib (Child-Pugh Class A only) • Cabozantinib (Child-Pugh Class A only) • Lenvatinib (Child-Pugh Class A only) • Sorafenib (Child-Pugh Class A or B7)
Other recommended	<ul style="list-style-type: none"> • Nivolumab with ipilimumab (Child-Pugh Class A only) • Pembrolizumab (Child-Pugh Class A only)
Used in some cases	<ul style="list-style-type: none"> • Ramucirumab (AFP 400 ng/mL or higher and Child-Pugh Class A only) • Nivolumab (Child-Pugh Class B only) • Larotrectinib and entrectinib for <i>NTRK</i> gene fusion-positive tumors • Dostarlimab-gxly for MSI-H/dMMR tumors • Selpercatinib for <i>RET</i> gene fusion-positive tumors • Nivolumab with ipilimumab for TMB-H tumors

Key points

- Stage 4B liver cancer is metastatic liver cancer. It is cancer that has spread to distant sites such as lung or bone.
- 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 given first. The preferred first-line systemic therapy is atezolizumab with bevacizumab or tremelimumab-actl with durvalumab. A substitute (biosimilar) might be used for bevacizumab.
- When first-line systemic therapy doesn't stop the growth or spread of cancer, then more lines of therapy might be given.
- 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.
- Your preferences about treatment are always important.



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**Take our survey,
and help make the
NCCN Guidelines for Patients
better for everyone!**

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

8

Making treatment decisions

- 54 It's your choice
- 54 Questions to ask
- 65 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 care team.

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 care team.

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
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or 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 care

team. If you take the time to build a relationship with your care team, it will help you feel supported when considering options and making treatment decisions.

Second opinion

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

Things you can do to prepare:

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

Support groups

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

Questions to ask

Possible questions to ask 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 about testing and diagnosis

1. What tests will I have? How often will they be repeated?
2. Will my insurance pay for this test?
3. How soon will I know the results and who will explain them to me?
4. What will you do to make me comfortable during testing?
5. How will my biopsy be performed? What else might be done at this time?
6. Is my cancer resectable or unresectable? What does this mean?
7. Is the cancer in any other areas like my lungs or bone?
8. What does the cancer stage mean in terms of length of survival and quality of life?

Questions about options

1. What will happen if I do nothing?
2. How do my age, overall health, and other factors affect the options?
3. Which option is proven to work best for my cancer, age, overall health, and other factors?
4. What are the possible complications and side effects? Are any life-threatening?
5. What can be done to prevent or relieve the side effects of treatment?
6. Am I a candidate for a clinical trial? Can I join a clinical trial at any time?
7. What decisions must be made today?
8. Is there a social worker or someone who can help me decide about treatment?
9. Is there a hospital or treatment center you can recommend for liver cancer treatment?
10. Can I go to one hospital for surgery and a different center for locoregional or radiation therapy?

Questions about treatment

1. Which treatment(s) do you recommend and why?
2. Does the order of treatment matter?
3. When will I start treatment?
4. How long will treatment likely take?
5. What should I expect from treatment?
6. What will you do to make me comfortable during treatment?
7. How much will my insurance pay for treatment?
8. Are there programs to help me pay for treatment?
9. What are the chances my cancer will return after treatment?
10. I would like a second opinion. Is there someone you can recommend?

Questions about food and nutrition

1. What changes will I need to make to my diet after surgery? How can I prepare?
2. What changes should I make to my diet now?
3. Who can help me with meal planning?
4. Should I keep a food diary?
5. I often do not feel well enough to cook or prepare meals. What do you recommend?
6. What can I do if other members of my household cannot prepare my meals? What if they don't eat the same foods?
7. How can you help if I have concerns about paying for food?
8. How can you help if I don't have access to the foods you are suggesting I eat?

Questions about surgery

1. How much of my liver will be removed?
2. What other organs or tissues might be removed during surgery?
3. What are the chances you can remove the whole tumor and I will have a negative margin?
4. What happens if during surgery you find you can't remove the tumor(s)?
5. How long will recovery take and what should I expect?
6. How much pain will I be in? What will be done to manage my pain?
7. When will I be able to return to work or normal activities after surgery?
8. What treatment will I have before, during, or after surgery?

Questions about radiation therapy

1. What type of radiation therapy (RT) will I have?
2. What will you target?
3. What is the goal of this RT?
4. How many treatment sessions will I require? Can you do a shorter course of RT?
5. Do you offer this type of RT here? If not, should I be referred to someone who does?
6. What side effects can I expect from RT?
7. Should I eat or drink before RT?
8. Will I be given medicine to help me relax during RT?
9. What should I wear?

Questions about side effects

1. What are the side effects of this treatment?
2. How are these side effects treated?
3. How long will these side effects last?
4. What side effects should I watch for that could be life-threatening?
5. When should I call my care team?
6. What should I do on weekends and other non-office hours?
7. What emergency department or ER should I go to?
8. Will my treatment team be able to communicate with the ER team?
9. What medicines can I take to prevent or relieve side effects?
10. What can I do to help with pain and other side effects?

Questions about clinical trials

1. What clinical trials are available for my type and stage of liver 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 in the clinical trial?
8. Will I be able to get other treatments if this treatment doesn't work?
9. How will you know the treatment is working?
10. Will the clinical trial cost me anything? If so, how much?

Questions about daily living

Some of the following questions you might ask yourself. Share any concerns with your care team.

1. Do I have transportation to and from appointments?
2. How can I find transportation to and from appointments?
3. Is there a way to combine appointments?
4. How can I find someone to stay with me after surgery?
5. Do I feel safe and secure at home, at work, and/or in my neighborhood?
6. What concerns do I have about stress, money, work, health, and/or relationships?
7. Do I have a support network of family, friends, neighbors, and/or coworkers?
8. How can I build a support system?
9. Do I have concerns about housing and utilities, such as finding housing or paying for utilities?
10. Do I have concerns about food, such as paying for food or finding food that meets my health needs?

Resources

Blue Faery

[Bluefaery.org](https://bluefaery.org)

Cholangiocarcinoma Foundation

[Cholangiocarcinoma.org](https://cholangiocarcinoma.org)

Global Liver Institute

[Globalliver.org](https://globalliver.org)

MedlinePlus

medlineplus.gov/livercancer.html

National Cancer Institute (NCI)

cancer.gov/types/liver

Triage Cancer

[Triagecancer.org](https://trriagecancer.org)



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



Words to know

ablation

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

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).

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 a disease.

biosimilar

An almost identical version of a drug made by another company. It is used in the exact same way and at the same dose as the actual drug.

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 growth and spread of cancer.

carcinoembryonic antigen (CEA)

A protein that is present when some types of cancer form.

catheter

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

chemotherapy

Drugs that kill fast-dividing cells throughout the body, including cancer cells and some normal cells.

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 stage (c)

Rating the extent of a tumor based on tests before treatment.

clinical trial

Research on a test or treatment to assess its safety or how well it works.

Words to know

common bile duct

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

computed tomography (CT)

A test that combines many x-rays to make pictures of the inside 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)

Removal of a tissue sample with a 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 biological parent to child through coded information in cells.

histology

The structure of cells, tissue, and organs as viewed under a microscope.

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.

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.

intravenous (IV)

A method of giving drugs by a needle or tube inserted into a vein.

jaundice

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

laparoscopy

Use of a thin tool inserted through a cut made into the belly area.

lymph

A clear fluid containing white blood cells.

lymph node

A small group of disease-fighting cells located throughout the body.

Words to know

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 oncologist

A doctor who's an expert in cancer drugs.

metastasis

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

microsatellite instability (MSI)

Errors made in small, repeated DNA parts during the copy process because of an abnormal repair system.

microsatellite instability-high (MSI-H)

Mutations in 30% or more microsatellites.

mutation

An abnormal change.

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.

partial hepatectomy

Surgery to remove a portion of the liver.

pathologic stage (p)

A rating of the extent of cancer based on microscopic review after treatment.

pathologist

A doctor who's an expert in examining tissue and cells to find disease.

performance status (PS)

A rating of one's ability to do daily activities.

positron emission tomography (PET)

A test that uses radioactive material to see the shape and function of body parts.

primary treatment

The main treatment used to rid the body of cancer.

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 oncologist

A doctor who's an expert in radiation treatment.

radiation therapy (RT)

A 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.

resectable

Cancer that can be removed with surgery.

risk factor

Something that increases the chance of getting a disease.

side effect

An unhealthy or unpleasant physical or emotional response to treatment.

standard of care

The best-known way to treat a particular disease based on past clinical trials. There may be more than one treatment regimen that is considered standard of care.

Words to know

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 or best supportive care.

surgical margin

The normal-looking tissue around the edge of a tumor removed during surgery.

surgical oncologist

A surgeon who's an expert in performing surgical procedures in cancer patients.

targeted therapy

Drugs that stop the growth process specific to cancer cells.

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.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Hepatobiliary Cancer, Version 1.2023. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS
Senior Director
Patient Information Operations

Tanya Fischer, MEd, MSLIS
Senior Medical Writer

Laura Phillips
Graphic Design Specialist

The NCCN Guidelines[®] for Hepatobiliary Cancer, Version 1.2023 were developed by the following NCCN Panel Members:

Al B. Benson, III, MD/Chair
Robert H. Lurie Comprehensive Cancer
Center of Northwestern University

Michael I. D'Angelica, MD/Vice-Chair
Memorial Sloan Kettering Cancer Center

Thomas Abrams, MD
Dana-Farber/Brigham and Women's
Cancer Center | Massachusetts General
Hospital Cancer Center

Daniel E. Abbott, MD
University of Wisconsin
Carbone Cancer Center

Aijaz Ahmed, MD
Stanford Cancer Institute

Daniel A. Anaya, MD
Moffitt Cancer Center

Robert Anders, MD, PhD
The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins

Chandrakanth Are, MD, MBA
Fred & Pamela Buffett Cancer Center

Melinda Bachini
Cholangiocarcinoma Foundation

David Binder, MD
University of Colorado Cancer Center

Mitesh Borad, MD
Mayo Clinic Comprehensive Cancer Center

Christopher Bowlus, MD
UC Davis Comprehensive Cancer Center

Daniel Brown, MD
Vanderbilt-Ingram Cancer Center

Adam Burgoyne, MD, PhD
UC San Diego Moores Cancer Center

Prabhleen Chahal, MD
Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center
and Cleveland Clinic Taussig Cancer Institute

Jordan Cloyd, MD
The Ohio State University Comprehensive
Cancer Center - James Cancer Hospital/
and Solove Research Institute

Anne M. Covey, MD
Memorial Sloan Kettering Cancer Center

*Evan S. Glazer, MD, PhD
St. Jude Children's Research Hospital/
The University of Tennessee
Health Science Center

William G. Hawkins, MD
Siteman Cancer Center at Barnes-
Jewish Hospital and Washington
University School of Medicine

Renuka Iyer, MD
Roswell Park Comprehensive Cancer Center

Rojmyon Jacob, MD
O'Neal Comprehensive
Cancer Center at UAB

*Lawrence Jennings, MD, PhD
Robert H. Lurie Comprehensive Cancer
Center of Northwestern University

*R. Kate Kelley, MD
UCSF Helen Diller Family
Comprehensive Cancer Center

Robin Kim, MD
Huntsman Cancer Institute
at the University of Utah

Matthew Levine, MD, PhD
Abramson Cancer Center
at the University of Pennsylvania

Manisha Palta, MD
Duke Cancer Institute

James O. Park, MD
Fred Hutchinson Cancer Center

Steven Raman, MD
UCLA Jonsson
Comprehensive Cancer Center

Sanjay Reddy, MD, FACS
Fox Chase Cancer Center

Vaibhav Sahai, MBBS, MS
University of Michigan Rogel Cancer Center

Gagandeep Singh, MD
City of Hope National Medical Center

Stacey Stein, MD
Yale Cancer Center/Smilow Cancer Hospital

*Anita Turk, MD
Indiana University Melvin and Bren Simon
Comprehensive Cancer Center

Jean-Nicolas Vauthey, MD
The University of Texas
MD Anderson Cancer Center

Alan P. Venook, MD
UCSF Helen Diller Family
Comprehensive Cancer Center

Adam Yopp, MD
UT Southwestern Simmons
Comprehensive Cancer Center

NCCN

Cindy Hochstetler, PhD
Oncology Scientist/Medical Writer

Nicole McMillian, MS
Senior Guidelines Coordinator

Ryan Schonfeld, BA
Guidelines Layout Coordinator

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

NCCN Cancer Centers

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

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

City of Hope National Medical Center
Duarte, 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

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

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

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

Indiana University Melvin and Bren Simon
Comprehensive Cancer Center
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive 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

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

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

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

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

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

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

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

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

NCCN Cancer Centers

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

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

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DR SHIVAM SHINGLA

BSES MG Hospital (Andheri):

9 am to 10 am (Monday to Friday)

Nanavati Max Hospital (Vile Parle):

10 am to 12 pm (Monday to Saturday)

S. L. Raheja Hospital (Mahim):

12 pm to 4 pm (Monday to Saturday)

Suvarna Hospital (Borivali):

5 pm to 6 pm (Monday and Friday)

Sushrut Hospital (Chembur):

By appointment

Hinduja Hospital (Khar): By

appointment

Galaxy Healthcare (Borivali): By

appointment



www.drshivamshingla.com



drshivamshingla@gmail.com



+91 98925 96286

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