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#Reference From NCCN Guidelines

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# 1

## Gallbladder and bile duct cancer basics

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**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. Together, the gallbladder and bile ducts are known as the biliary tract and are part of the hepatobiliary system.**

## 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.

### The gallbladder

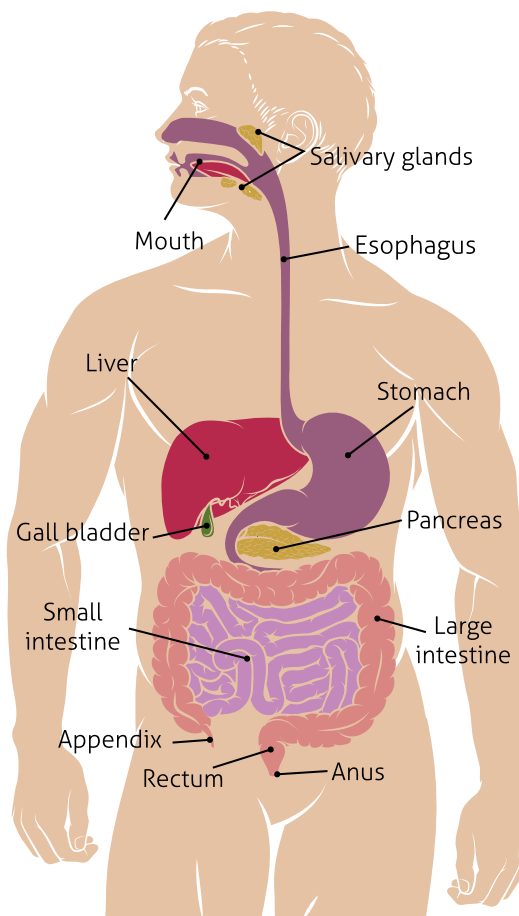
The gallbladder is a small, pear-shaped organ found under the liver. It is sometimes described as sac-like because it holds bile from the liver. Bile is made by the liver and stored in the gallbladder, and when you eat, it then passes through the bile ducts into the small intestine to help digest food. You do not need your gallbladder to eat or live normally.

### Bile ducts and 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. Bile flows into small channels that drain into thin tubes called ducts. These ducts form larger and larger channels that flow into the left and

### The hepatobiliary system

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



right hepatic (liver) ducts. The left and right hepatic ducts join to form the common hepatic bile duct. The common hepatic duct joins with the cystic duct to form the common bile duct. The common bile duct is joined by the pancreatic duct just before it enters the small intestine. The common bile duct carries bile to the first part of the small intestine called the duodenum. In the small intestine, the bile and other fluids break down food to allow your small intestine to absorb nutrients and send waste to your large intestine, also known as the colon.

A more in-depth explanation of how bile travels through the bile ducts is described next.

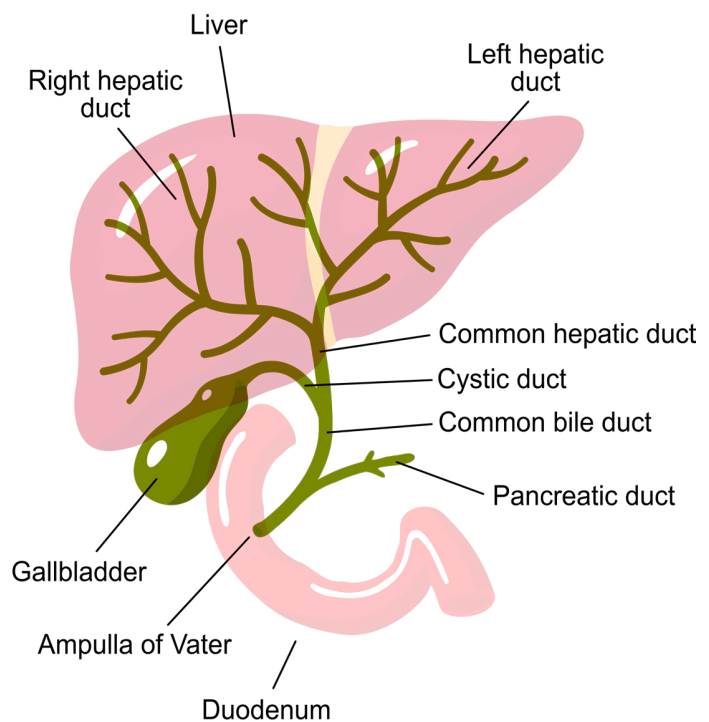
- **Intrahepatic bile ducts** of varying sizes are found inside your liver. Hilar bile ducts are the main bile ducts just

outside the liver. Intrahepatic and hilar bile ducts carry bile between the liver and gallbladder. Bile leaves the liver through the left and right hepatic ducts. These together join to form the common hepatic duct. Bile then travels up the cystic duct and into the gallbladder for temporary storage between meals.

- **The cystic and common bile ducts** carry bile from the gallbladder to the small intestine. Bile leaves the gallbladder through the cystic duct where it connects to the common bile duct. The common bile duct is joined by the pancreatic duct inside the pancreas just before it enters the small intestine.

### 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 to form the common bile duct. The common bile duct is joined by the pancreatic duct just before it enters the small intestine (duodenum).



## Gallbladder cancer

Gallbladder cancer is a rare cancer that can grow and spread quickly. Not all gallbladder cancers are the same. Adenocarcinoma is the most common type of gallbladder cancer. An adenocarcinoma is cancer in the cells that secrete fluids or other substances. Other rare types of cancer can grow in the wall of the gallbladder. Gallbladder adenocarcinoma is the type of cancer described in this book.

### How gallbladder cancer is found

Gallbladder cancer is often found by chance. This is called an incidental finding. For example, a tumor in the gallbladder may be found on an ultrasound being done for other reasons. Since gallbladder cancer doesn't always have symptoms and it spreads quickly, it is usually found in an advanced stage.

Gallbladder cancer can be found in 3 ways:

- During surgery
- During pathology review after removal of the gallbladder for what was thought to be gallstone-related conditions
- On imaging tests

### During surgery

Some gallbladder cancers are found during abdominal (belly) surgery for something other than gallbladder cancer. This could be for treatment for suspected gallstones (cholelithiasis) or inflammation of the gallbladder (cholecystitis). Gallstones are hardened deposits of bile.

### During pathology review

It is common for a pathologist to review all tissue that has been removed during surgery. A pathologist is an expert in examining cells under a microscope to find disease. Often, gallbladder cancers are found during pathology review of a condition that was originally felt to be non-cancerous.

### On imaging tests

A mass or tumor might be found on imaging tests done for other reasons. Cancer is confirmed by biopsy or during surgery.

## Bile duct cancers

The bile ducts carry bile from the liver to the gallbladder and from the gallbladder to the small intestine. Cholangiocarcinoma, also known as bile duct cancer, is a type of adenocarcinoma. An adenocarcinoma is cancer in the cells that secrete fluids or other substances.

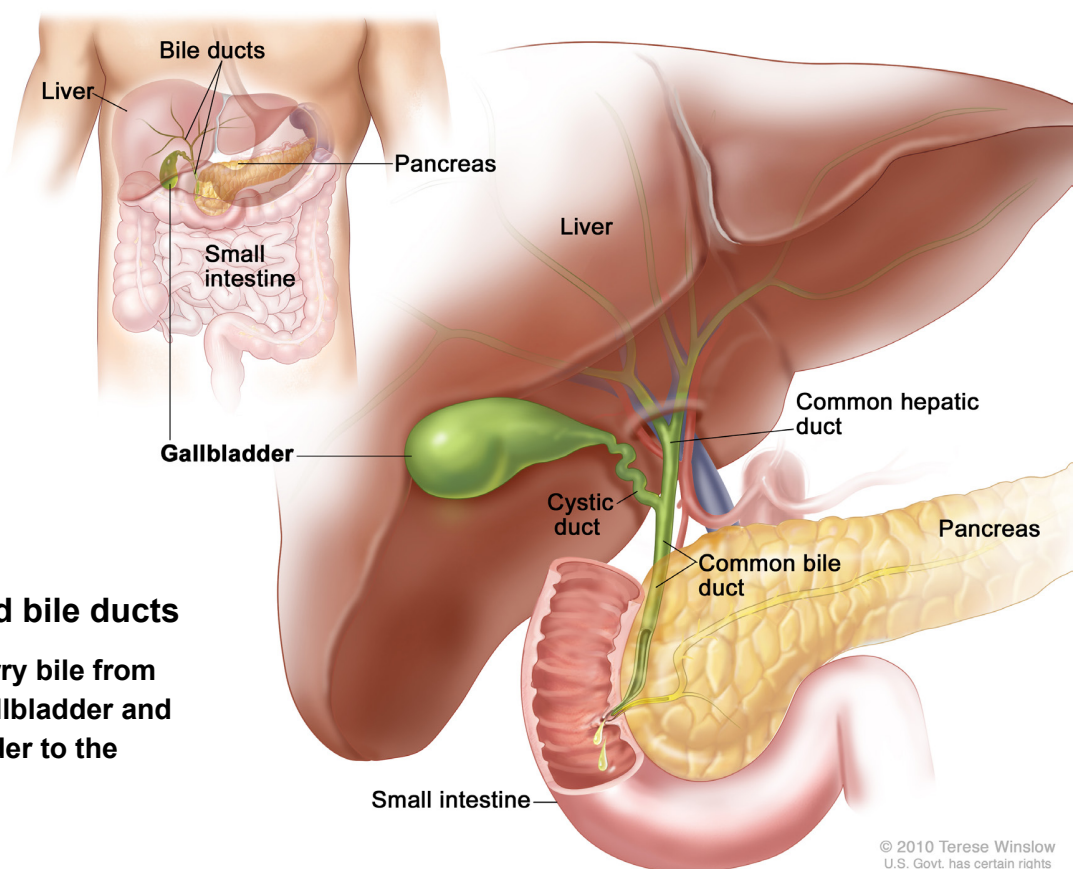
There are 2 types of cholangiocarcinomas:

- **Intrahepatic bile duct cancers** start in the bile ducts found inside the liver.
- **Extrahepatic bile duct cancers** grow in the bile ducts outside the liver.

There are 2 subtypes of extrahepatic bile duct cancer:

- **Hilar bile duct cancer (Klatskin tumors)** is found in the common hepatic duct.
- **Distal bile duct cancer** is found in the common bile duct.

Cancer that forms in the ampulla of Vater (ducts from the liver and pancreas that enter at the small intestine) is not covered in this book.



### Gallbladder and bile ducts

The bile ducts carry bile from the liver to the gallbladder and from the gallbladder to the small intestine.

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## How cancer spreads

Unlike normal cells, cancer cells can spread and form tumors in other parts of the body. Cancer that has spread is called a metastasis.

Cancer can spread 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.

Gallbladder cancer most commonly spreads into nearby lymph nodes or organs, such as the pancreas, bile ducts, or liver.

Bile duct cancers can grow into nearby blood vessels, organs, and other structures. It might also grow into nearby lymphatic or blood vessels, and from there spread to nearby lymph nodes or to other parts of the body.

## Key points

- The liver, gallbladder, and bile ducts are part of the hepatobiliary system.
- The biliary tract includes the gallbladder and bile ducts inside and outside the liver.
- Cancers in the bile ducts or gallbladder are known as biliary tract cancers.
- Gallbladder cancer is the most common type of biliary tract cancer worldwide.
- Adenocarcinoma is the most common type of gallbladder cancer. An adenocarcinoma is cancer in the cells that secrete fluids or other substances.
- The bile ducts carry bile from the liver to the gallbladder and from the gallbladder to the small intestine. Cholangiocarcinoma, also known as bile duct cancer, starts in the bile ducts.
- Cancer can spread to distant parts of the body through the blood or lymphatic system.



Never lose hope, tomorrow could be the day you have been waiting for. "



# 2

## Testing for gallbladder and bile duct cancers

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**Treatment planning starts with testing. 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. Also, include information about any metal stents, foreign body parts or devices, and any wallet-sized ID cards that might be given to you at the time of some procedures.

## 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.

### Liver disease history

You might be asked about conditions that affect the health of the liver such as cirrhosis, hepatitis B or C virus or infection, episodes of jaundice, gallstones, alcohol use, and fatty liver disease.

## 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.

## 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.

One of the LFTs measured is bilirubin, a chemical that gives bile its color. There may be too much bilirubin in the blood if a tumor is blocking a bile duct and preventing the free flow of bile from the liver into the intestines or the liver is not working as well as it should. Too much bilirubin causes a yellowing of the eyes and skin called jaundice. It might cause itchy skin and dark-colored urine.

### **Hepatitis panel**

Hepatitis is a type of liver disease. Viruses called hepatitis B (HBV) and hepatitis C (HCV) are the most common chronic types of hepatitis. A hepatitis panel is a blood test that checks to see if you have a hepatitis infection caused by either 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.

### **Tumor markers in the blood**

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 tests are only one piece of information your treatment team might consider. Not all cancers make these markers and not every person's body makes these markers.

## **Imaging tests**

Imaging tests take pictures of the inside of your body. Images can be made with scanning machines or scoping tools. Imaging tests may show if the tumor involves any veins, arteries, and other organs or if there is a blocked bile duct.

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.

### **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 computed tomography (CT) and magnetic resonance imaging (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 might not be used if you have a serious allergy or if your kidneys aren't working well. Being allergic to one type of contrast does not mean you are allergic to all types of contrast agents or dyes.

## 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 and bile ducts. This allows your care team to see whether 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.

Testing takes time. It might take days or weeks before all test results come in.

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.

## PTC

A percutaneous transhepatic cholangiography (PTC) uses contrast and an x-ray to take pictures of the biliary tract. This procedure is usually performed by an interventional radiologist, doctor who specializes in small procedures using x-rays, ultrasound, or other types of imaging. A needle or small catheter (thin, flexible tube) is placed through the skin (percutaneous) into a bile duct and contrast is injected. Then, x-rays that use small amounts of radiation are taken to make pictures of the bile ducts. If necessary, a catheter can be inserted to drain fluid from the biliary tract into a bag outside the body or into the small intestine. A metal stent may also be placed for an obstruction or blocked bile duct.

For this test, you will be given medicine to help you feel relaxed. Plastic catheters are often placed during the procedure. If so, you and your caregiver will learn how to care for these catheters.

## 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 your 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 the sonogram used for pregnancy. A wand-like probe (transducer) will be held and moved on your skin using gel. Ultrasound is painless and does not use

### 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.**



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.

A contrast-enhanced ultrasound (CEUS) might be used in addition to other tests. Contrast is injected into a vein and another US is performed.

## Scoping procedures

Some imaging tests use a thin, tube-shaped tool called a scope (or endoscope) that is inserted into the body to take pictures. One end of the scope has a small light and camera lens to see inside your body. The image is sent to a television monitor. This will help guide your doctor in a biopsy, stent placement, or other tasks.

The scope is guided into the body through a natural opening, such as the mouth, nose, or anus. It may also be inserted through a small surgical cut.

More than one type of scope may be used for imaging tests. The type of scope often used for gallbladder and bile duct cancer is called an endoscope. An endoscope is often guided into the body through the mouth.

Some scoping procedures are described next.

### Endoscopic ultrasound

An EUS uses an endoscope that has a small ultrasound (US) probe at the end. The endoscope is inserted through your mouth and guided down your throat into your stomach and then the first part of the small intestine (duodenum). The ultrasound probe bounces sound waves off your liver and other organs to make pictures of the inside of your body.

Sometimes, an EUS can detect small lesions in the liver or pancreas that are difficult to see on a CT or MRI scan. It might be used to get a closer look at your bile ducts.

An EUS is done under sedation to keep you comfortable during the procedure. It might be done with an ERCP.

### ERCP

An endoscopic retrograde cholangiopancreatography (ERCP) uses an endoscope and x-rays to take moving pictures of the inside of the body. For this test, the endoscope will be inserted through your mouth and guided down your throat and stomach to the duodenum. Next, a thinner tube called a catheter will be passed through the middle of the endoscope. The catheter will be used to inject a contrast material into the liver and bile ducts. The contrast material allows the ducts to be clearly seen on the x-ray pictures.

An ERCP is used to open a blocked bile duct caused by a tumor in the liver, bile duct, or pancreas. During an ERCP, biopsy samples may be taken from the common bile duct. Samples are removed with a small brush at the end of the endoscope. These samples are called brushings. Brushings are taken before stent placement.

An ERCP is done under sedation to keep you comfortable during the procedure. It might be done with an EUS.

### Upper GI endoscopy or EGD

In an upper gastrointestinal (GI) endoscopy or esophagogastroduodenoscopy (EGD), an endoscope is guided down the throat into the esophagus, stomach, and upper parts of the small intestine (duodenum). An EGD is used to inspect the lining of these organs and to look for

any signs of cancer or other abnormalities such as enlarged blood vessels or ulcers. An EGD can also be referred to as a duodenoscopy.

## Laparoscopy

Laparoscopy (key-hole surgery) is a type of surgical procedure that allows your surgeon to see the inside of your abdomen without using a large incision. It uses a tool like a special endoscope called a laparoscope. For this test, the laparoscope will be inserted through a tiny cut (incision) in your abdomen. Laparoscopy is done under general anesthesia. This is a controlled loss of wakefulness from drugs. A breathing tube is usually used during this operation.

Laparoscopy may only be used in certain cases. It can be used to

- Stage the disease.
- Rule out metastasis by detecting cancer spread inside your abdomen, which may have been missed on imaging scans.
- Obtain biopsy samples.
- Determine if you are a candidate for surgery.

## Colonoscopy

In a colonoscopy, the endoscope is used to examine the inside of the colon. A colonoscope has a light and a lens for viewing and may have a tool to remove tissue. It is guided through the anus, then into the rectum and the colon. A colonoscopy is done under sedation to keep you comfortable during the procedure.

## Biopsy

A biopsy is a procedure that removes samples of fluid or tissue. A biopsy can be negative when cancer is present.

Types of possible biopsies include:

- **Fine-needle aspiration (FNA)** or fine-needle biopsy (FNB) uses a thin needle to remove a sample of tissue or fluid. An ultrasound (US) may guide the FNA biopsy.
- **Brushings** are tumor or cell samples removed with a small brush at the end of the endoscope, usually during an ERCP procedure.
- **Fluid samples** from ascites (fluid in abdominal cavity) can be used to look for cancer cells.
- **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.

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



## Biomarker testing

A sample from a biopsy of your tumor may be tested to look for specific DNA (deoxyribonucleic acid) mutations, protein levels, or other molecular features. It is sometimes called molecular testing or tumor profile testing.

### CA 19-9, CEA, and AFP

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.

### Tumor mutation testing

Tumor mutation testing or molecular profiling uses a sample of your tumor or blood to see if the cancer cells have any specific mutations. Some mutations such as *NTRK* gene fusion, *BRAF* V600E, *FGFR2* fusion or rearrangement, *IDH1*, HER2 (ERBB2) overexpression and/or amplification, and *RET* gene fusion can be targeted with specific therapies. When a tumor has a high number of mutations, it is referred to as tumor mutational burden-high (TMB-H). Tumor mutation testing is different than genetic testing for mutations that you may have inherited from your biological parents.

### MSI-H/dMMR mutation

Microsatellites are short, repeated strings of DNA. When errors or defects occur, they are fixed by mismatch repair (MMR) proteins. Some cancers have DNA mutations for changes that prevent these errors from being fixed. This is called microsatellite instability (MSI) or deficient mismatch repair (dMMR). When cancer cells have more than a normal number of microsatellites, it is called MSI-H

(microsatellite instability-high). This is often due to dMMR genes.

## Genetic risk testing

Depending on your family history or other features of your cancer, your health care provider might refer you for hereditary genetic testing to learn more about your cancer. A genetic counselor or trained provider will speak to you about the results. Tests results may be used to guide treatment planning. The test results may also help guide further testing for your family members.

Genetic testing is done using blood or saliva (spitting into a cup or a cheek swab). The goal is to look for gene mutations inherited from your biological parents called germline mutations. Some mutations can put you at risk for more than one type of cancer. You can pass these genes on to your children. Also, other family members might carry these mutations. Tell your care team if there is a family history of cancer.

### BRCA tests

Everyone has *BRCA* genes. Normal *BRCA* genes help to prevent tumor growth. They help fix damaged cells and help cells grow normally. *BRCA* mutations put you at risk for more than one type of cancer. Mutations in *BRCA1* or *BRCA2* increase the risk of breast, ovarian, prostate, colorectal, pancreatic, and melanoma skin cancers. Mutated *BRCA* genes can also affect how well some treatments work.

## 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. Images can be made with scanning machines or scoping tools.
- A biopsy removes a sample of tissue or fluid. A biopsy of the tumor might be done during surgery or a scoping procedure.
- A sample from a biopsy of your tumor may be tested to look for specific DNA (deoxyribonucleic acid) mutations, protein expression levels, or other molecular features. Some mutations and proteins can be targeted with specific therapies.
- Genetic testing might be done to look for gene mutations inherited from your biological parents called germline mutations.
- Online portals are a great way to access your test results.



### 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!

# 3

## Gallbladder and bile duct cancer staging

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

## How 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.

AJCC staging is used for the following cancers:

- Gallbladder carcinoma
- Intrahepatic bile duct tumors (intrahepatic cholangiocarcinoma)
- Perihilar bile duct tumors (extrahepatic cholangiocarcinoma), also known as Klatskin tumor
- Distal bile duct tumors (extrahepatic cholangiocarcinoma)

Information gathered during 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. Your care team 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 gallbladder and bile duct cancers. 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: T1N0M0 or T1, N0, M0.

- **T (tumor)** – Size of the main (primary) tumor
- **N (node)** – If cancer has spread to nearby (regional) lymph nodes
- **M (metastasis)** – If cancer has spread to distant parts of the body or metastasized

## 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, and G3. Well differentiated means the cancer cells look similar to normal cells. Poorly differentiated means the cancer cells look very different compared to normal cells.

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

## 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.

## Gallbladder cancer stages

Gallbladder cancer is staged by how much the tumor has grown into the layers of the gallbladder wall and if the tumor is on the side nearest to the liver (hepatic) or the small intestine (peritoneal). It can be difficult to determine the exact location of the tumor. Cancer can spread beyond the visible tumor making it difficult to find. Staging for cancer in lymph nodes is based on the number of lymph nodes rather than their location.

For gallbladder cancer stages, **see Guide 1**.

### Guide 1

#### Gallbladder cancer stages

<b>Stage 0</b>	• Tis, N0, M0
<b>Stage 1</b>	• T1, N0, M0
<b>Stage 2A</b>	• T2a, N0, M0
<b>Stage 2B</b>	• T2b, N0, M0
<b>Stage 3A</b>	• T3, N0, M0
<b>Stage 3B</b>	• T1 or T2 or T3, N1, M0
<b>Stage 4A</b>	• T4, N0 or N1, M0
<b>Stage 4B</b>	• Any T, N2, M0 • Any T, Any N, M1

## T = Tumor

Carcinoma in situ (Tis) is the earliest stage of gallbladder cancer. Cancer cells are found inside the lining of the gallbladder wall (epithelium). Cancer has not grown into any other layers of the gallbladder. Gallbladder cancers are rarely found this early.

- **Tis** – Carcinoma in situ (cancer has not grown beyond the innermost epithelial layer)
- **T1a** – Tumor invades lamina propria
- **T1b** – Tumor invades muscle layer
- **T2a** – Tumor invades the perimuscular connective tissue on the peritoneal side, but has not grown into the serosa (visceral peritoneum)
- **T2b** – Tumor invades the perimuscular connective tissue on the hepatic side, but has not grown into the liver
- **T3** – Tumor perforates the serosa and/or invades the liver and/or nearby organs or structures such as the stomach, duodenum, colon, pancreas, and bile ducts outside the liver (extrahepatic)
- **T4** – Tumor invades main portal vein or hepatic artery or invades 2 or more organs or structures outside the liver (extrahepatic)

## N = Node

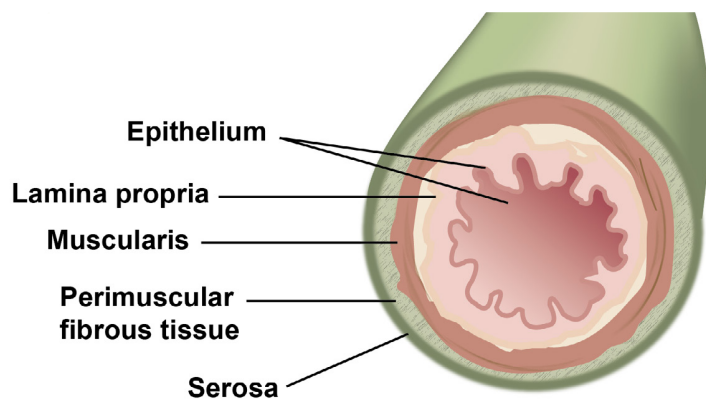
There are hundreds of lymph nodes throughout your body. They work as filters to help fight infection and remove harmful things from your body. Regional lymph nodes are those located near the tumor. The cystic duct lymph node is one example of a regional lymph node.

- **N0** – No cancer in regional lymph node
- **N1** – Cancer is found in 1 to 3 regional lymph nodes
- **N2** – Cancer is found in 4 or more regional lymph nodes

## M = Metastatic

Cancer that has spread to distant parts of the body is shown as M1. The most common site for metastasis is the lining that surrounds the abdominal organs (visceral peritoneum) and the liver.

### 5 layers of the gallbladder and bile duct wall



#### 1. Epithelium

A thin, moist layer of cells that covers the inside of the gallbladder and bile ducts.

#### 2. Lamina propria

A type of connective tissue found under the epithelium.

#### 3. Muscle (muscularis)

A type of soft tissue.

#### 4. Perimuscular fibrous tissue

A type of connective tissue that surrounds muscle.

#### 5. Serosa

An outer membrane that covers the gallbladder and bile ducts. The serosa is also called the serous membrane or visceral peritoneum.

## Bile duct cancer stages

A bile duct is made up of several layers. The inner and outer layers are membranes. A membrane is a very thin layer that covers a surface. In between these membranes are muscle and connective tissue.

Cancer stages for intrahepatic bile duct cancer can be found in **Guide 2**.

### T = Tumor

The primary tumor size can be measured in centimeters (cm) or millimeters (mm). Cancer can grow or spread into nearby blood vessels, the liver, or structures outside the liver.

- **Tis** – Carcinoma in situ (this is an intraductal tumor)

#### Guide 2

#### Bile duct cancer stages: Intrahepatic

<b>Stage 0</b>	• Tis, N0, M0
<b>Stage 1A</b>	• T1a, N0, M0
<b>Stage 1B</b>	• T1b, N0, M0
<b>Stage 2A</b>	• T2, N0, M0
<b>Stage 3A</b>	• T3, N0, M0
<b>Stage 3B</b>	• T4, N0, M0 • Any T, N1, M0
<b>Stage 4</b>	• Any T, Any N, M1

- **T1a** – One tumor that is 5 cm or smaller and has not grown into blood vessels
- **T1b** – One tumor that is larger than 5 cm and has not grown into blood vessels
- **T2** – One tumor that has grown into blood vessels inside the liver (intrahepatic) or multiple tumors that may or may not be in intrahepatic (liver) blood vessels
- **T3** – Tumor perforating the visceral peritoneum
- **T4** – Tumor has grown into nearby structures outside the liver (extrahepatic)

### N = Node

There are hundreds of lymph nodes throughout your body. They work as filters to help fight infection and remove harmful products from your body. Regional lymph nodes are those located near the tumor. These include hilar, cystic duct, common bile duct, hepatic artery, posterior pancreaticoduodenal, and portal vein lymph nodes.

- **N0** – No cancer in regional lymph node
- **N1** – Cancer is found in a regional lymph node

### M = Metastatic

Cancer that has spread to distant parts of the body is shown as M1. The most common site for metastasis is the lung.

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



## Perihilar (Klatskin tumor) cancer stages

Perihilar bile duct (Klatskin) tumors start where the right and left hepatic ducts meet. Staging might be done during laparoscopic surgery to remove the cancer called resection. For perihilar bile duct cancer stages, **see Guide 3.**

### T = Tumor

The primary tumor size might be measured in centimeters (cm) or millimeters (mm). A large pea is about 1 cm (10 mm).

- **Tis** – Carcinoma in situ (cancer is found only in the duct)

#### Guide 3 Bile duct cancer stages: Perihilar

<b>Stage 0</b>	• Tis, N0, M0
<b>Stage 1</b>	• T1, N0, M0
<b>Stage 2</b>	• T2a or T2b, N0, M0
<b>Stage 3A</b>	• T3, N0, M0
<b>Stage 3B</b>	• T4, N0, M0
<b>Stage 3C</b>	• Any T, N1, M0
<b>Stage 4A</b>	• Any T, N2, M0
<b>Stage 4B</b>	• Any T, Any N, M1

- **T1** – Tumor is confined to the duct, but has grown through the muscle layer or the fibrous tissue
- **T2a** – Tumor has grown beyond the wall of the bile duct to surrounding adipose (fat) tissue
- **T2b** – Tumor invades the working part of the liver (parenchyma)
- **T3** – Tumor has invaded branches of the portal vein or hepatic artery
- **T4** – Tumor has invaded the main portal vein or its branches, or the common hepatic artery, or other ducts that join or empty the portal vein or hepatic artery

### N = Node

Lymph nodes are found throughout your body. Regional lymph nodes are those located near the tumor. These include hilar, cystic duct, common bile duct, hepatic artery, posterior pancreaticoduodenal, and portal vein lymph nodes.

- **N0** – No cancer in regional lymph node
- **N1** – Cancer is found in 1 to 3 regional lymph nodes
- **N2** – Cancer is found in 4 or more regional lymph nodes

### M = Metastatic

Cancer that has spread to distant parts of the body is written as M1. Stage 4B is metastatic cancer. The most common site for metastasis is the lining that surrounds the abdominal organs (visceral peritoneum) and the liver.

## Distal cancer stages

Distal bile duct cancer starts in the common bile duct. This is found below where the cystic duct joins the bile duct. Staging might be done during laparoscopic surgery. This would be before surgery to remove the cancer called resection. For distal bile duct cancer stages, **see Guide 4.**

### T = Tumor

The primary tumor size is measured in millimeters (mm). Cancer can grow or spread into nearby ducts, arteries, veins, or organs.

- **Tis** – Carcinoma in situ (cancer has not grown beyond the innermost epithelial layer)
- **T1** – Tumor has grown into the bile duct wall with a depth of less than 5 mm
- **T2** – Tumor has grown into the bile duct wall with a depth of 5 to 12 mm
- **T3** – Tumor has grown into the bile duct wall with a depth of more than 12 mm
- **T4** – Tumor involves the celiac axis, superior mesenteric artery, and/or common hepatic artery

### N = Node

Lymph nodes are found throughout your body. Regional lymph nodes are those located near the tumor. These include hilar, cystic duct, common bile duct, hepatic artery, posterior pancreaticoduodenal, and portal vein lymph nodes.

- **N0** – No cancer in regional lymph node
- **N1** – Cancer is found in 1 to 3 regional lymph nodes
- **N2** – Cancer is found in 4 or more regional lymph nodes

### M = Metastatic

Cancer that has spread to distant parts of the body is written as M1. Stage 4 is metastatic cancer. The most common sites for metastasis are the liver, lungs, the lining that surrounds the abdominal organs (visceral peritoneum), and bones.

#### Guide 4 Bile duct cancer stages: Distal

<b>Stage 0</b>	• Tis, N0, M0
<b>Stage 1</b>	• T1, N0, M0
<b>Stage 2A</b>	• T1, N1, M0 • T2, N0, M0
<b>Stage 2B</b>	• T2, N1, M0 • T3, N0, M0 • T3, N1, M0
<b>Stage 3A</b>	• T1, N2, M0 • T2, N2, M0 • T3, N2, M0
<b>Stage 3B</b>	• T4, N0, M0 • T4, N1, M0 • T4, N2, M0
<b>Stage 4</b>	• Any T, Any N, M1

## 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 tumor size and location and if the tumor(s) involves any nearby lymph nodes or organs.
- TNM scores are not always used to describe gallbladder and bile duct cancers.
- 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).
- The wall of the gallbladder and bile ducts is made up of five layers. Cancer starts inside the gallbladder or bile duct and grows through the layers.

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

# 4

## Treating gallbladder and bile duct cancers

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**There is more than one treatment for gallbladder and bile duct cancers. 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.**

Gallbladder and bile duct cancers are 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 your type of cancer.

There are 2 types of treatment:

- **Local therapy** focuses treatment on a certain area. It includes surgery, arterially directed therapy, 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 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. A multidisciplinary conference is when the MDT gets together to discuss patients, their diagnoses, imaging/laboratory results, and treatment plans. This may also be called a tumor board.

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 gallbladder and bile duct cancers.

- **A medical oncologist** treats cancer 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.
- **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 a primary treatment for gallbladder and bile duct cancers. Primary treatment is the main treatment used to rid the body of cancer. The goal of surgery is to remove all of the cancer, or to remove as much as possible so other treatments may be given. Surgery can also provide supportive care by easing pain or discomfort or to extend life. 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 your type of 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.

### 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 require another surgery to try to remove the remaining tumor cells. Surgery includes removal of lymph nodes.

### Open surgery

Open surgery or laparotomy removes tissue through one large surgical cut below your ribs. The large cut lets the surgeon directly view and access the tumor to remove it. Open surgery may take several hours or longer. After the surgery, you will need to stay in the hospital to recover.

### Minimally invasive surgery

Minimally invasive surgery (or key-hole surgery) uses several small incisions or cuts. Small tools are inserted through each incision to perform the surgery. One of the tools, called a laparoscope, is a long tube with a video camera at the end. The camera lets your surgeon see your gallbladder and other tissues inside your abdomen. Other tools are used to remove the tumor. Laparoscopic surgery can also be done using robotic arms to control the surgical tools. This is called robot-assisted laparoscopic surgery.

### Cholecystectomy

A cholecystectomy removes the gallbladder and some tissue around it. The goal is to have negative surgical margins, which means there is no cancer in the remaining area.

During a cholecystectomy, some people will also have a hepatic resection (parts of liver removed), lymphadenectomy (nearby lymph nodes removed), and bile duct removal. The tumor size and location will help your surgeon decide on the extent of surgery. Ask what might be removed during surgery, how

this might affect recovery, and what further treatment might be needed.

### Tumor resection

The removal of the tumor is called tumor resection. Imaging tests will be used 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.

### Liver resection (partial hepatectomy)

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.

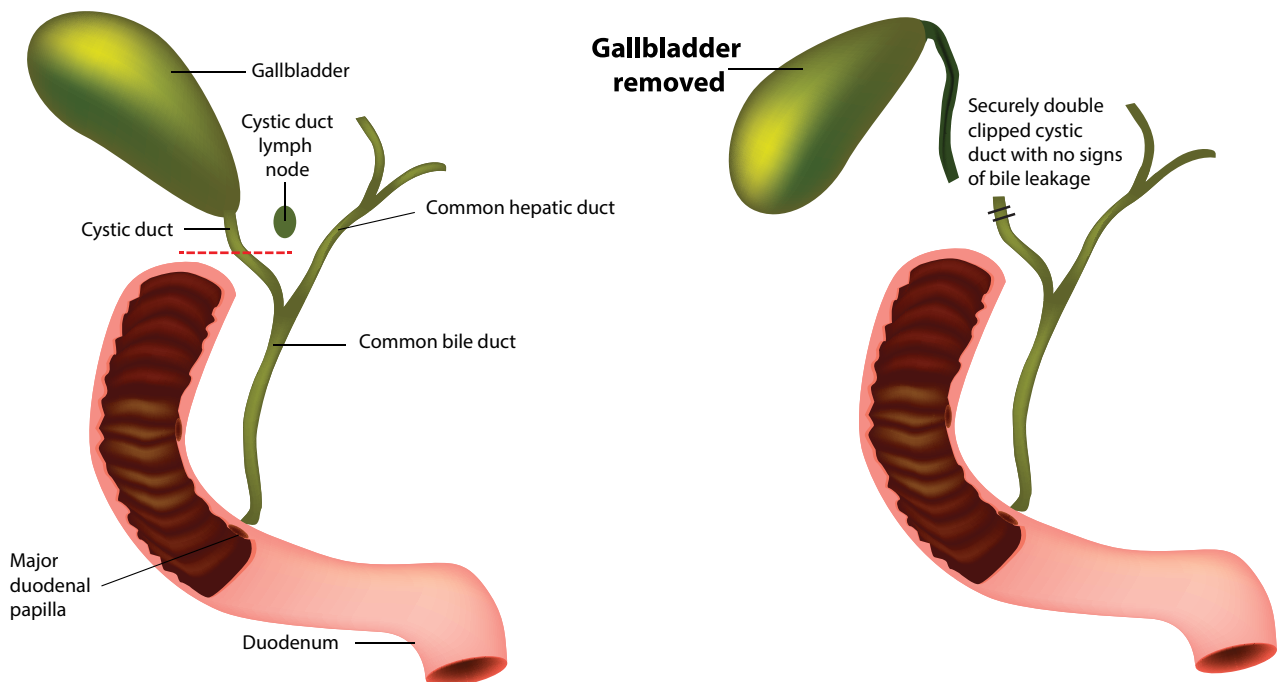
### Liver transplant

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 tumor 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

## Cholecystectomy

In a cholecystectomy, the gallbladder and part of the cystic duct are removed.





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.

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.

### Lymphadenectomy

During a lymphadenectomy, the lymph nodes are removed and a sample of tissue is checked under a microscope for signs of cancer. A lymphadenectomy is sometimes called lymph node dissection.

- **In a regional lymphadenectomy,** some of the lymph nodes in the tumor area are removed.
- **In a radical lymphadenectomy,** most or all of the lymph nodes in the tumor area are removed.

### Pancreaticoduodenectomy

A pancreaticoduodenectomy or Whipple procedure is surgery that removes the head of the pancreas, gallbladder, duodenum (first part of the small intestine), part of the bile duct, and nearby lymph nodes. This surgery is often used for tumors located in the mid and lower part of the common bile duct.

### Roux-en-Y hepaticojejunostomy

A Roux-en-Y hepaticojejunostomy is a procedure that bypasses the bile duct to allow digestive juices to drain from the liver directly into the small intestine.

#### 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)

## 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.

- Systemic therapy given before surgery is called **neoadjuvant or preoperative therapy**.
- Systemic therapy given after surgery is called **adjuvant or postoperative therapy**.
- Systemic therapy is given for advanced disease may be called **palliative therapy**.

For a list of some systemic therapies, **see Guide 5**.

### Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells. Often, chemotherapies are combined. This is called multiagent chemotherapy. Examples include FOLFOX and FOLFIRI. FOLFOX is a combination of 5-fluorouracil (5-FU), leucovorin, and oxaliplatin. FOLFIRI is a combination of 5-FU with leucovorin and irinotecan. Chemotherapy is also used in arterially directed therapy.

#### Guide 5 Systemic therapy examples

<b>Chemotherapy examples</b>	<ul style="list-style-type: none"> <li>• Capecitabine (Xeloda)</li> <li>• Cisplatin (Platinol)</li> <li>• 5-Fluorouracil (5-FU)</li> <li>• FOLFIRI</li> <li>• FOLFOX</li> </ul>	<ul style="list-style-type: none"> <li>• Gemcitabine (Gemzar, Infugem)</li> <li>• Methotrexate</li> <li>• Oxilaplatin (Eloxatin)</li> <li>• Paclitaxel (Taxol, Abraxane)</li> </ul>
<b>Targeted therapy examples</b>	<ul style="list-style-type: none"> <li>• Dabrafenib (Tafinlar)</li> <li>• Entrectinib (Rozlytrek)</li> <li>• Futibatinib (Lytgobi)</li> <li>• Ivosidenib (Tibsovo)</li> <li>• Larotrectinib (Vitrakvi)</li> <li>• Lenvatinib (Lenvima)</li> <li>• Pemigatinib (Pemazyre)</li> <li>• Pertuzumab (Perjeta)</li> </ul>	<ul style="list-style-type: none"> <li>• Pralsetinib (Gavreto)</li> <li>• Regorafenib (Stivarga)</li> <li>• Selpercatinib (Retevmo)</li> <li>• Trametinib (Mekinist)</li> <li>• Trastuzumab (Herceptin) or trastuzumab substitutes (biosimilars) such as Kanjinti, Ogivri, Herzuma, Ontruzant, and Trazimera</li> </ul>
<b>Immunotherapy examples</b>	<ul style="list-style-type: none"> <li>• Dostarlimab-gxly (Jemperli)</li> <li>• Durvalumab (Imfinzi)</li> <li>• Ipilimumab (Yervoy)</li> </ul>	<ul style="list-style-type: none"> <li>• Nivolumab (Opdivo)</li> <li>• Pembrolizumab (Keytruda)</li> </ul>

## Chemoradiation

Treatment that combines chemotherapy with radiation therapy is called chemoradiation. Chemotherapy may improve how well radiation works, and that is why they are sometimes used together. Fluoropyrimidine-based chemotherapies such as 5-fluorouracil (5-FU) and capecitabine (Xeloda) are used with radiation to treat gallbladder and bile duct cancers. Chemoradiation may be used to control symptoms caused by a tumor.

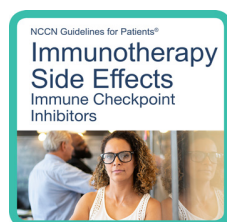
## Targeted therapy

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. If your tumor has certain mutations, targeted therapy might be used. If your tumor has a high number of mutations, immunotherapy might be given.

## 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 programmed death-1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (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
- Ginkgo 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 or supportive care medicines given during 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.**

## 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.

The type of arterially directed therapy recommended will depend on the size, number, and location of tumors as well as your

**Your preferences about treatment are always important. How much time you want to spend in treatment is also important. Talk to your care team and make your wishes known.**



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 the body to aim radiation at the tumor(s) or areas of the body.

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.

## 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 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.

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

### 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

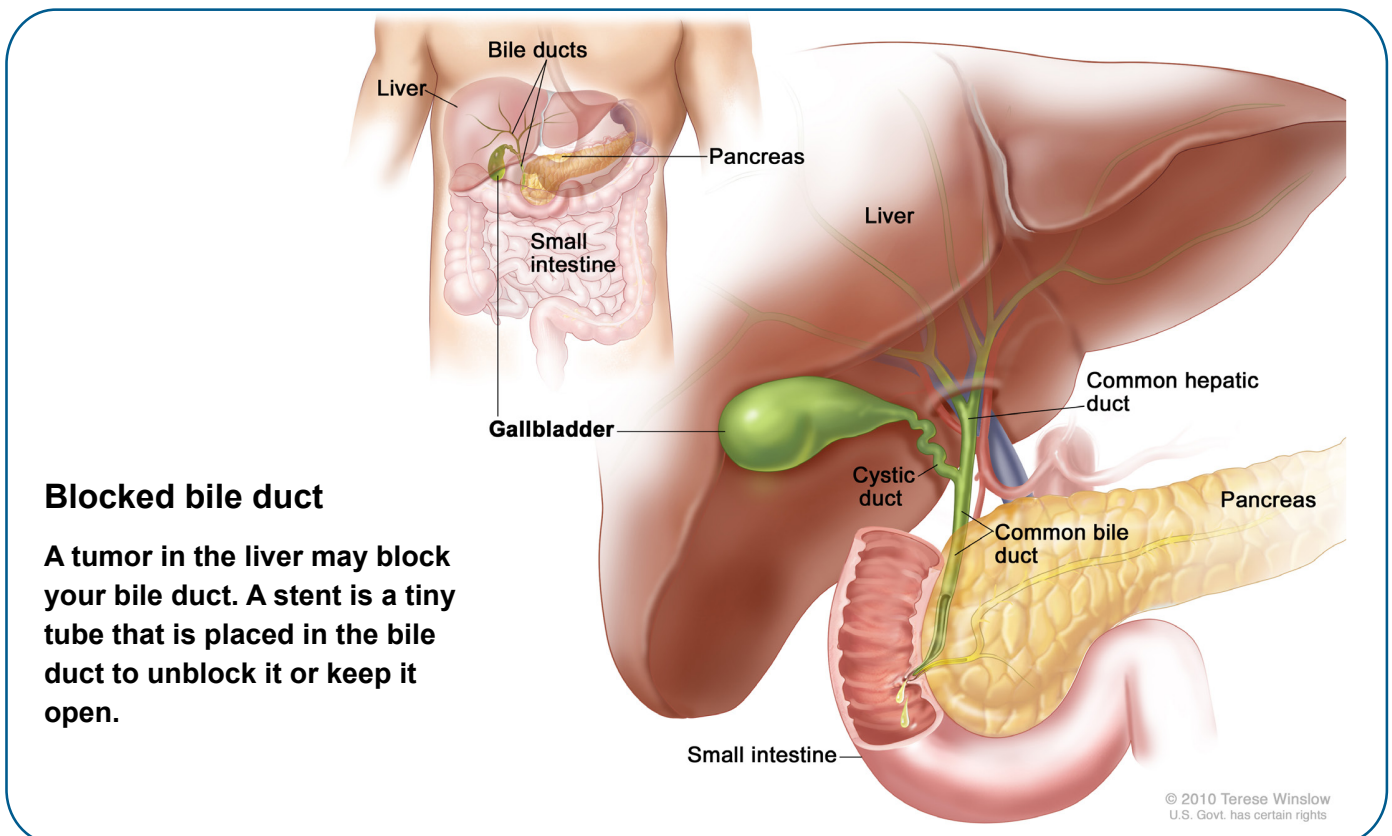
A tumor in the liver may grow large enough to block your bile duct. A bile duct is a small tube that drains digestive fluid (bile) from the liver. The common bile duct carries bile from the liver through the pancreas and into the first part of the small intestine (duodenum). A blocked duct causes bile 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.

### When biliary drainage is an option

Biliary drainage before surgery may help improve your health and recovery after surgery. Biliary drainage may be an option even if you cannot have surgery. It may also be recommended if you have metastatic disease, to improve your liver function and nutrition, and to reduce the risk of infection.





Biliary drainage requires careful planning. Your treatment team should discuss and decide if this is a safe procedure for you.

If it is an option, you may have biliary drainage using one of the following methods.

- **Surgical bypass** involves attaching the gallbladder or bile duct directly to the small intestine to drain the fluid. However, this way of draining fluid is rarely used. It carries the same risks as major surgery.
- **Endoscopic retrograde cholangiopancreatography (ERCP)** uses an endoscope to reach the bile ducts and drain the fluid. Your doctor may insert a plastic or metal stent so the fluid drains directly into the small intestine. This is usually an outpatient procedure performed by a gastroenterologist that does not require you to stay in the hospital. A wallet-sized ID card may be given to you at the time of the stent placement. Biliary stents may block over time and may need to be replaced.
- **Percutaneous transhepatic cholangiography (PTC)** places a stent through the skin to drain the fluid. This approach may be used when the endoscope cannot reach the blocked bile duct. This is usually an outpatient procedure performed by an interventional radiologist that does not require you to stay in the hospital.

## 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.

## 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.

## 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 most people with gallbladder and bile duct cancers.
  - Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.
  - 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.
  - 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.



### **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](https://www.nccn.org/patients/feedback)**

# 5

## Gallbladder cancer

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**Gallbladder cancer starts in the innermost layer and grows outward through the layers of the gallbladder wall. Cancer can spread to nearby veins, arteries, bile ducts, and organs such as the liver. Together, you and your care team will choose a treatment plan that is best for you.**

## Overview

The gallbladder is a pear-shaped organ found under the liver. It is made up of several layers of tissue. The inner and outer layers are membranes. A membrane is a very thin layer that covers a surface. In between these membranes are layers of muscle and connective tissue.

Gallbladder cancer starts in the innermost layer and grows outward through the layers of the gallbladder wall. Cancer can spread to nearby veins, arteries, bile ducts, and organs such as the liver.

Gallbladder cancer is often found by chance. This is called an incidental finding. Treatment is based on how the cancer was found, if the cancer has spread, and if there is cancer in any nearby organs and blood vessels. Tests will determine if the tumor can be removed with surgery.

Before starting treatment, you might have the following:

- Multiphasic CT and MRI of the abdomen and pelvis with contrast
- Chest CT with or without contrast
- Staging laparoscopy
- Biomarker or genetic risk testing

A CT and MRI are used to learn more about the cancer and if it involves any nearby veins, arteries, or ducts. A chest CT is used to see if the cancer has spread (metastasized) to the lungs.

Treatment will be based on if the cancer is resectable or unresectable. Ask questions about the tests and procedures you might have. You might meet with a surgeon during this time. Treatment will be based on if the tumor is resectable or unresectable. More information can be found on the following pages.

## Found during surgery

Gallbladder cancer might be found by chance during surgery for something other than gallbladder cancer. This could be for treatment for suspected gallstones or inflammation of the gallbladder known as cholecystitis. A sample of the tumor might be taken and tested for cancer. Also, if any lymph nodes look like they might have cancer, they will be biopsied and tested.

## Found at pathology

Gallbladder cancer can be found during pathology review following a cholecystectomy for cholelithiasis (gallstones) or of a condition that was originally felt to be non-cancerous. An expert hepatobiliary pathologist should review your pathology results. Your care team will check the pathology report for details on the tumor size and location, and if there were signs of disease in the cystic duct, other ducts, or nearby areas. The location of the tumor or abnormal cells is very important in guiding therapy, especially with surgery.

### T1a tumor

A T1a tumor has grown through the innermost layer (epithelium) into the lamina propria. If the tumor is small with negative margins, then observation will be considered. You might hear this called watch-and-wait. During observation, you might have imaging and blood tests to monitor tumor growth.

### Cystic duct node-positive

The cystic duct lymph node is found near the cystic duct. Cancer found outside the gallbladder and in the nearby cystic duct lymph node is called cystic duct node-positive.

Treatment is often surgery. This would remove part of the liver (hepatic resection), nearby lymph nodes (lymphadenectomy), and possibly the bile duct. If there is cancer in the cystic duct lymph node, then you might have treatment before surgery called neoadjuvant therapy. Neoadjuvant therapy aims to reduce the amount of cancer or to shrink the tumor in order to make surgery easier. However, if there is a large tumor invading the liver and/or cancer is near the lymph nodes, then neoadjuvant chemotherapy might be given to

see if your cancer is fast-growing. If this is the case, then surgery would not be used.

A clinical trial is also an option for cancer found in the cystic duct lymph node.

### T1b or larger

A T1b tumor has invaded the muscle layer of the gallbladder wall. For a tumor that is T1b or greater, surgery might be possible. This would remove part of the liver (hepatic resection), nearby lymph nodes (lymphadenectomy), and possibly the bile duct.

## Found on imaging

Sometimes, a tumor or mass may be found on an imaging test being done for other medical reasons. If there is concern for gallbladder cancer, more tests will be ordered. It can be difficult to see exactly how much cancer there is and where it might have spread using imaging tests alone. As a result, a laparoscopy can be helpful to stage your cancer. If you have jaundice, biliary drainage might be done to see if it can relieve any bile duct blockage.

## Jaundice with cancer

Bile is made by the liver. It contains bilirubin, the yellow-brown substance that gives bile its color. Jaundice is a yellowing of the skin and whites of the eyes due to a buildup of bilirubin in the body. Sometimes, a tumor can block the flow of bile, leading to increased bilirubin levels in the blood, as well as jaundice. You may have itching and dark-colored urine. If the common bile duct or the common hepatic duct is blocked, your stool (poop) may turn white.

### Tests

If you have jaundice with gallbladder cancer, you will have blood and imaging tests. Tests include an x-ray of the bile ducts called a cholangiography. Magnetic resonance cholangiopancreatography (MRCP) is the preferred type of cholangiography.

### Treatment

You might meet with a surgeon to learn about treating your jaundice and cancer. You might have a staging laparoscopy to find out the extent of disease and why there is a blockage causing the jaundice.

If you have a blocked bile duct or jaundice, then biliary drainage will be done before surgery or treatment with systemic therapy. Endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC) are used to treat jaundice.

**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.**



## Resectable

A resectable tumor can be removed with surgery. You will have surgery to remove the gallbladder (cholecystectomy), part of the liver (en bloc hepatic resection), some lymph nodes (lymphadenectomy), and possibly the bile duct.

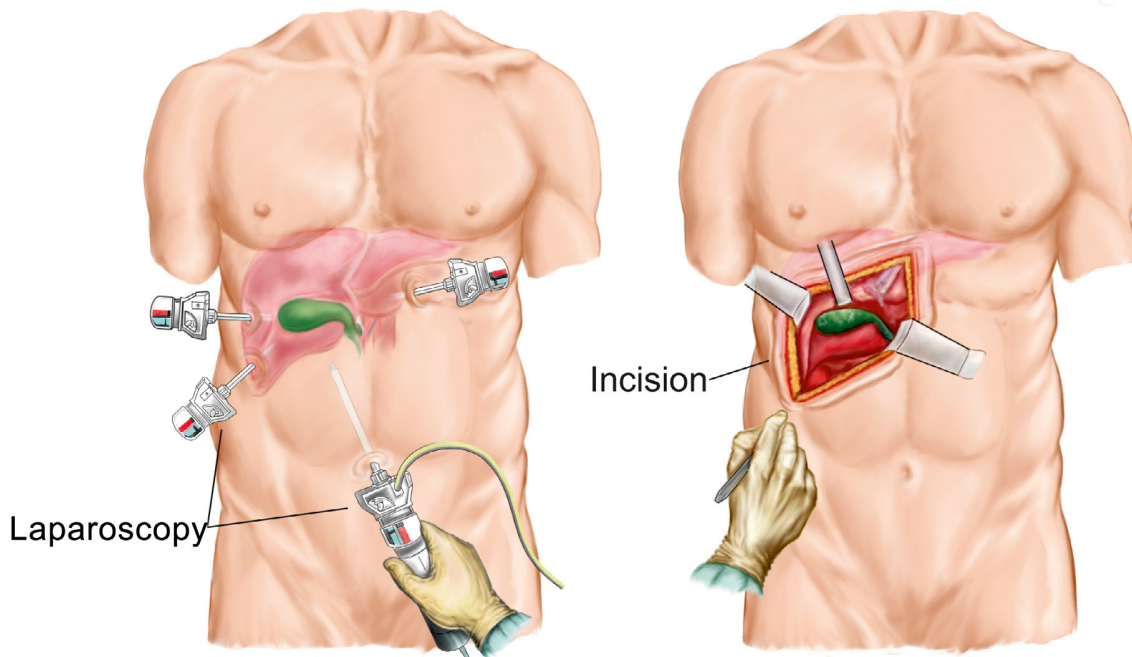
A gallbladder cancer operation requires a skilled surgeon. Sometimes, a resectable tumor cannot be removed during surgery. This might be due to the tumor being wrapped around major veins or arteries. If cancer has spread to lymph nodes, bile ducts, or organs, it may not be possible to remove all of the cancer.

Need help paying for medicine or treatment?

Ask your care team what options are available.

### Cholecystectomy

A cholecystectomy is the removal of the gallbladder. Surgery can be open or minimally invasive (laparoscopic).



Laparoscopic cholecystectomy procedure

Open cholecystectomy procedure

Sometimes, systemic therapy is given before surgery. This is called neoadjuvant therapy. The goal is to reduce the amount of cancer. For neoadjuvant systemic therapy options, **see Guide 6.**

### Treatment after surgery

Treatment after surgery is called adjuvant therapy. It is not always possible to remove all of the cancer during surgery. Adjuvant therapy is given to kill any cancer cells that might have been left behind. It also helps prevent the return of cancer called recurrence.

Adjuvant therapy options include:

- Systemic therapy (preferred)
- Clinical trial (preferred)
- Chemoradiation
- Chemotherapy might be given before or after chemoradiation

A preferred treatment is one proven to have a better result. Observation (or watch-and-wait) might be an option in some cases. If

you will have systemic therapy after surgery, then capecitabine is the preferred option. For adjuvant systemic therapy options, **see Guide 6.**

### Surveillance

After completing treatment for resectable disease, you will enter surveillance. Surveillance is a period of testing to watch for signs that cancer has returned. It includes tests for CA 19-9, CEA, as well as imaging every 3 to 6 months for 2 years, then every 6 to 12 months for up to 5 years, or as needed.

#### Guide 6

#### Neoadjuvant and adjuvant systemic therapy options

<b>Neoadjuvant</b>	<ul style="list-style-type: none"> <li>• FOLFOX</li> <li>• Capecitabine with oxaliplatin</li> <li>• Gemcitabine with capecitabine</li> <li>• Gemcitabine with cisplatin</li> </ul>	<ul style="list-style-type: none"> <li>• Durvalumab with gemcitabine and cisplatin</li> <li>• Gemcitabine with cisplatin and paclitaxel</li> </ul>
<b>Adjuvant</b>	<ul style="list-style-type: none"> <li>• Capecitabine (preferred)</li> <li>• FOLFOX</li> <li>• Capecitabine with oxaliplatin</li> <li>• Gemcitabine with capecitabine</li> </ul>	<ul style="list-style-type: none"> <li>• Gemcitabine with cisplatin</li> <li>• 5-fluorouracil (5-FU)</li> <li>• Gemcitabine</li> </ul>



## Unresectable

An unresectable tumor cannot be removed with surgery. Before treatment begins, biomarker and genetic tests might be done to learn more about your cancer. If you have MSI/dMMR or a family history of *BRCA1* or *BRCA2* mutations, then you might be referred to a genetic counselor.

### Treatment options

Treatment options depend on size, spread, and location of cancer and what is available at your hospital or treatment center. Seek treatment at an experienced center.

Unresectable treatment options include:

- Systemic therapy (preferred)
- Clinical trial (preferred)
- Palliative radiation therapy
- Best supportive care

Systemic therapy or a clinical trial are the preferred treatment options for unresectable tumors. A preferred treatment is one proven to have the best result. Other options include palliative radiation therapy and best supportive care. When radiation is used to reduce symptoms caused by the cancer or to extend life, it is called palliative radiation. Best supportive care is treatment to relieve the side effects of cancer and its treatment.

For systemic therapy options, **see Guide 7.**

### Guide 7

#### Systemic therapy options: Unresectable and metastatic disease

<b>Preferred</b>	<ul style="list-style-type: none"> <li>• Durvalumab with gemcitabine and cisplatin</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• Gemcitabine with cisplatin</li> <li>• FOLFOX</li> <li>• Capecitabine with oxaliplatin</li> <li>• Gemcitabine with paclitaxel</li> <li>• Gemcitabine with capecitabine</li> <li>• Gemcitabine with oxaliplatin</li> <li>• Gemcitabine with cisplatin and paclitaxel</li> <li>• 5-fluorouracil (5-FU)</li> <li>• Capecitabine</li> <li>• Gemcitabine</li> </ul>
<b>Used in some cases</b>	<ul style="list-style-type: none"> <li>• Targeted therapy</li> </ul>

## Metastatic disease

Metastatic cancer is cancer that has spread to distant sites in the body. A biopsy and biomarker testing will be done before starting treatment. Treatment options are based on the size and location of the cancer.

Treatment options for metastatic gallbladder cancer include:

- Systemic therapy (preferred)
- Clinical trial (preferred)
- Best supportive care

Systemic therapy or a clinical trial are the preferred choices. Best supportive care is used with other treatments to improve quality of life. For systemic therapy options, **see Guide 8.**

## Disease progression

When unresectable cancer progresses during or after systemic therapy, then your medical oncologists might try a different systemic therapy.

For disease progression, the preferred option is FOLFOX. FOLFOX is a combination of chemotherapy drugs that includes 5-fluorouracil (5-FU), leucovorin, and oxaliplatin. If your tumor has a specific gene mutation, then you might receive drug therapy that targets the mutation. For next-line systemic therapy options, **see Guide 8.**

**FOLFOX is a combination of 5-fluorouracil (5-FU), leucovorin, and oxaliplatin.**

**FOLFIRI is a combination of 5-FU, leucovorin, and irinotecan.**

### Guide 8

#### Next-line systemic therapy options: Disease progression

<b>Preferred</b>	<ul style="list-style-type: none"> <li>• FOLFOX</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• FOLFIRI</li> <li>• Irinotecan with fluorouracil and leucovorin</li> </ul>
<b>Used in some cases</b>	<ul style="list-style-type: none"> <li>• Targeted therapy</li> <li>• Nivolumab</li> <li>• Lenvatinib with pembrolizumab</li> </ul>

## Key points

- Cancer starts inside the gallbladder and grows through the layers of the gallbladder wall.
- Gallbladder cancer is found by chance during surgery, during pathology review, or on an imaging test.
- When a tumor blocks fluid from draining from the bile ducts, it can cause jaundice.
- Treatment for gallbladder cancer is based on if the cancer can be removed with surgery (resectable), cannot be removed with surgery (unresectable), has spread to other parts of the body (metastatic), and the risk of recurrence.
- Treatment options for gallbladder cancer may include surgery, systemic therapy, clinical trial, chemoradiation, palliative radiation therapy, and best supportive care.
- Systemic therapy or a clinical trial are the preferred treatment options for unresectable or metastatic gallbladder cancer.
- If your tumor has a high number of mutations (TMB-H) or a specific gene mutation such as *NTRK*, MSI-H/dMMR, *FGFR2*, *IDH1*, or *BRAF* V600E, then you might receive drug therapy that targets the mutation.
- Best supportive care may offer symptom relief.



### 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/](https://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)

# 6

## Intrahepatic bile duct cancer

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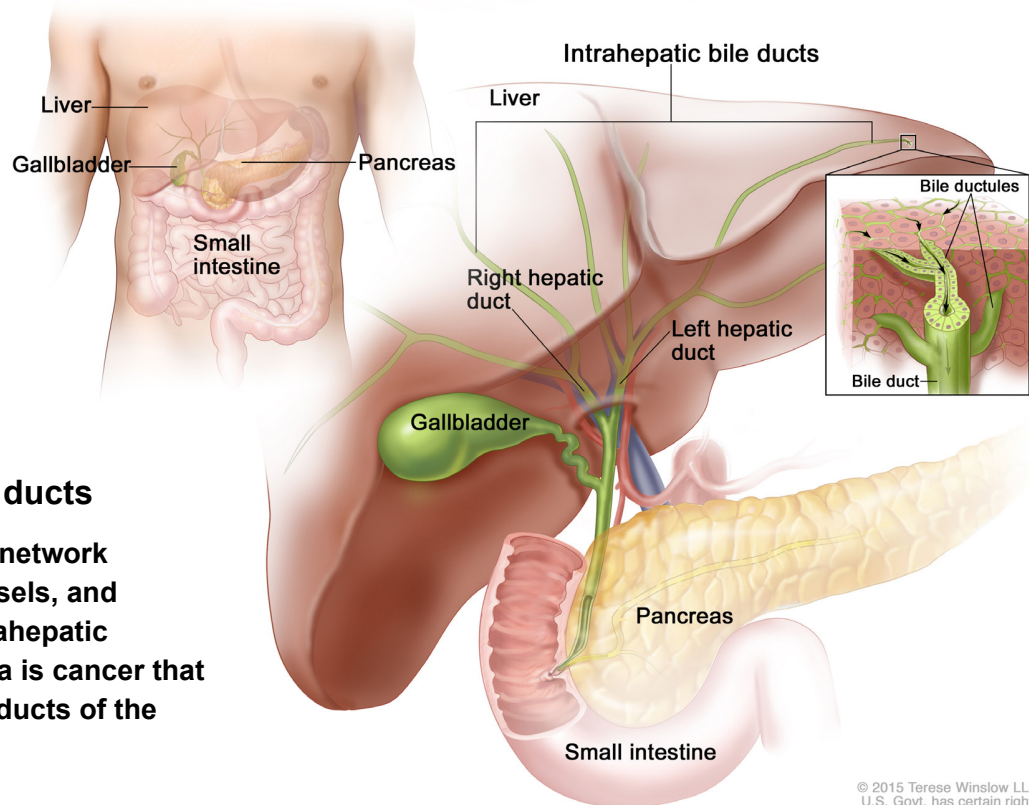
**Cholangiocarcinoma (CCA)** is a cancer of the bile duct. **Intrahepatic cholangiocarcinoma (ICC)** or **intrahepatic bile duct cancer** is found in the bile ducts of the liver. Together, you and your care team will choose a treatment plan that is best for you.

## Overview

A cholangiocarcinoma (CCA) is a rare cancer that forms in the bile ducts.

- **Intrahepatic cholangiocarcinoma (ICC)** is found in bile ducts inside the liver.
- **Extrahepatic cholangiocarcinoma (ECC)** is found in bile ducts outside the liver.

Bile is produced and secreted by cells (hepatocytes) in the liver. It travels from the liver to the gut through bile ducts. Epithelial cells (cholangiocytes) line the bile ducts. Abnormal growth of these cells can cause a blockage in the bile duct. Cholangiocarcinomas are tumors that start in the lining of the



### Intrahepatic bile ducts

Inside the liver is a network of ducts, blood vessels, and lymph vessels. Intrahepatic cholangiocarcinoma is cancer that is found in the bile ducts of the liver.

bile duct. Most cholangiocarcinomas are adenocarcinomas. Adenocarcinomas start in cells that secrete fluids.

Inside the liver is a network of ducts, blood vessels, and lymph vessels. Intrahepatic bile ducts are a network of small tubes that carry bile inside the liver. The smallest ducts (ductules) join to form the right hepatic bile duct and the left hepatic bile duct. The right and left hepatic duct drain bile from the liver. Cancer that starts inside these ducts is intrahepatic bile duct cancer. It is not liver cancer, which arises from liver cells called hepatocytes.

There can be more than one tumor and it can be found in the small ductules or in the larger hepatic ducts. Treatment aims to prevent or slow the spread of cancer.

## Testing

Once it is confirmed that the isolated tumor found on imaging is not liver cancer (hepatocellular carcinoma), then you will have imaging scans, blood tests, and scoping procedures.

Blood tests will measure CEA, CA 19-9, AFP, and liver function, and will check for a past or current viral hepatitis infection. Hepatitis is a risk factor for bile duct cancer. Some cancer treatments can wake up (or reactivate) the virus. If this happens, it can cause harm to the liver.

You will meet with a surgeon to discuss if:

- You will have a biopsy
- You are healthy enough for surgery or a liver transplant
- The cancer can be removed with surgery

Imaging tests may include a CT of the chest, a multiphase CT of the abdomen and pelvis, and a multiphase MRI of the abdomen and pelvis. Imaging of this area shows the size of the cancer, if it spread to the liver, or if it invaded the lymph nodes or blood vessels.

Sometimes, intrahepatic bile duct cancers can be confused with stomach, small intestine, or colon tumors that spread to the liver. An esophagogastroduodenoscopy (EGD) and colonoscopy may be done to check if cancer has spread to the liver rather than occurring in the bile ducts. You might be referred to a hepatologist. A hepatologist specializes in the care of the liver, biliary tract, gallbladder, and pancreas.

## Treatment

Treatment is based on if the tumor is:

- **Resectable** – can be removed with surgery
- **Unresectable** – cannot be removed with surgery
- **Metastatic** – cancer has spread to other parts of the body

If the cancer is unresectable or metastatic, then MSI/MMR testing and other biomarker testing will be done. For those with dMMR/MSI-H tumors or a family history that suggests *BRCA1* or *BRCA2* mutations, then you might have genetic testing and be referred to a genetic counselor.

## Resectable

A resectable tumor is one that can be removed with surgery. Surgery to remove the tumor is called liver resection (or partial hepatectomy). During resection, some lymph nodes might be removed in a lymphadenectomy. A lymphadenectomy is done to check for cancer. Also, your surgeon will look for cancer in nearby veins, arteries, and tissues.

For intrahepatic bile duct cancers, resection with cancer-free or negative margins (R0) is the goal. Because this type of cancer occurs in the bile ducts inside the liver, surgery may include the removal of a section or piece of the liver. The extent of surgery will depend on the tumor size and location. If cancer has spread beyond the nearby lymph nodes or to distant sites, treatment other than surgery may be offered.

## Treatment after surgery

Treatment after surgery is called adjuvant therapy. It is determined by the risk of the tumor returning and/or if not all tumor could be removed during surgery.

- In a clear or negative margin (R0), no cancerous cells are found.
- In an R1 positive margin, there is higher risk that very small (microscopic) cancer cells remain.
- In an R2 positive margin, cancer that can be seen without a microscope remains.

Adjuvant systemic therapies can be found in **Guide 9**.

### Guide 9

#### Adjuvant systemic therapy options

##### Preferred

- Capecitabine

##### Other recommended

- FOLFOX
- Capecitabine with oxaliplatin
- Gemcitabine with capecitabine
- Gemcitabine with cisplatin
- 5-fluorouracil (5-FU)
- Gemcitabine

## No cancer remains

If no cancer remains (R0), the preferred adjuvant treatment options are systemic therapy or a clinical trial. A preferred treatment is one proven to have a better result. Observation might be considered. This is sometimes called watch-and-wait. After treatment, you will enter surveillance.

## Microscopic cancer remains

If there is a higher risk that microscopic cancer cells remain (R1) or cancer is found in nearby lymph nodes, then treatment options include systemic therapy (preferred), clinical trial (preferred), or chemoradiation. Chemotherapy might be given before or after chemoradiation.

## Visible cancer remains

If visible cancer remains, then treatment will be for unresectable disease.

## Surveillance

After treatment is finished, you will enter surveillance. This is a period of testing to watch for cancer recurrence. During this time you might have multiphasic CT and MRI scans and a chest CT every 3 to 6 months for 2 years, then every 6 to 12 months for up to 5 years, or as needed. It is important to keep any follow-up doctor visits and imaging test appointments.

## Unresectable

An unresectable tumor cannot be removed with surgery.

Treatment options include the following:

- Systemic therapy
- Clinical trial
- Chemoradiation (EBRT with fluoropyrimidine)
- Locoregional therapy such as radiation therapy or arterially directed therapy
- Best supportive care

Treatment options will be based on your preferences and your care team's recommendations. Best supportive care is always given. Locoregional therapy focuses on a specific area of the body. You may choose to enroll in a clinical trial. Chemoradiation and systemic therapy are also options. For systemic therapy options, **see Guide 10.**

## Metastatic

Metastatic cancer is cancer that has spread to other parts of the body.

Treatment options include the following:

- Systemic therapy (preferred)
- Clinical trial (preferred)
- Locoregional therapy such as radiation therapy or arterially directed therapy
- Best supportive care

For systemic therapy options, **see Guide 10.**



## Disease progression

If unresectable or metastatic intrahepatic bile duct cancer progresses during or after systemic therapy, then FOLFOX is the preferred option. If your tumor has a high number of mutations (TMB-H) or a specific gene mutation such as *NTRK*, MSI-H/dMMR,

*FGFR2*, *IDH1*, or *BRAF* V600E, then you might receive drug therapy that targets the mutation. A clinical trial is always an option. For next-line systemic therapy options, **see Guide 11.**

### Guide 10

#### Systemic therapy options: Unresectable and metastatic disease

##### Preferred

- Durvalumab with gemcitabine and cisplatin

##### Other recommended

- Gemcitabine with cisplatin
- FOLFOX
- Capecitabine with oxaliplatin
- Gemcitabine with paclitaxel
- Gemcitabine with capecitabine
- Gemcitabine with oxaliplatin
- Gemcitabine with cisplatin and paclitaxel
- 5-fluorouracil (5-FU)
- Capecitabine
- Gemcitabine

##### Used in some cases

- Targeted therapy

### Guide 11

#### Next-line systemic therapy options: Disease progression

##### Preferred

- FOLFOX

##### Other recommended

- FOLFIRI
- Irinotecan with fluorouracil and leucovorin

##### Used in some cases

- Targeted therapy
- Nivolumab
- Lenvatinib with pembrolizumab

## Key points

- Not all bile duct cancers are the same.
- A cholangiocarcinoma (CCA) is a rare cancer that forms in the bile ducts. Intrahepatic cholangiocarcinoma (ICC) is found in bile ducts inside the liver. It is also called intrahepatic bile duct cancer.
- Treatment is based on if the cancer can be removed with surgery (resectable), cannot be removed with surgery (unresectable), has spread to other parts of the body (metastatic), and the risk of recurrence.
- Treatment before surgery is called neoadjuvant. Treatment after surgery is called adjuvant.
- ICC can spread to blood vessels inside the liver. From here it can spread throughout the liver and structures outside the liver such as the lining that surrounds the abdominal organs (visceral peritoneum).
- If your tumor has a high number of mutations (TMB-H) or specific gene mutation such as *NTRK*, MSI-H/dMMR, *FGFR2*, *IDH1*, or *BRAF V600E*, then you might receive drug therapy that targets the mutation.
- Best supportive care may offer symptom relief.



While it's true that cholangiocarcinoma can be a cunning and devastating cancer, there are many of us living with cholangiocarcinoma like it's a chronic disease, playing 'whack-a-mole' with anything that pops up. Use this diagnosis as a catalyst to start cure-ating your life every day! Stay in the Here and Now, but also keep dreaming about and planning for your future."

# 7

## Extrahepatic bile duct cancer

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- 65 Disease progression
- 67 Key points

**Extrahepatic bile ducts are small tubes that carry bile outside the liver. In perihilar extrahepatic bile duct cancer, cancer is found in the common hepatic duct. In distal extrahepatic bile duct cancer, cancer is found in the common bile duct. Together, you and your care team will choose a treatment plan that is best for you.**

## Overview

A cholangiocarcinoma (CCA) is a rare cancer that forms in the bile ducts.

- **Intrahepatic cholangiocarcinoma (ICC)** is found in bile ducts inside the liver.
- **Extrahepatic cholangiocarcinoma (ECC)** is found in bile ducts outside the liver.

Extrahepatic bile ducts are small tubes that carry bile outside the liver. These include the common hepatic duct (hilar/hilum section) and the common bile duct (distal section). The name differs depending on the part of the bile duct. This is based on location.

- **Common hepatic duct** – The section above the cystic duct that connects to the liver.
- **Distal common bile duct** – The section below the cystic duct that

connects to the small intestine (duodenum).

**The perihilar bile duct** starts where the right and left hepatic ducts join outside the liver and form the common hepatic duct. It ends where the cystic duct from the gallbladder joins to form the common bile duct.

**The distal bile duct** starts where the cystic duct connects and forms the common bile duct.

## Testing

Extrahepatic cholangiocarcinoma might be suspected if you have pain, jaundice, abnormal liver function test results, or a blockage or tumor found on images tests. You will have imaging and blood tests.

### Imaging tests

Imaging tests may include a CT of the chest, along with a CT or MRI of the abdomen and pelvis. Imaging this area allows your care team to see the size of the cancer, if it spread to the liver, or if it invaded the lymph nodes or blood vessels.

You may have a test called a cholangiography to see if the bile ducts are blocked. Endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) are types of cholangiography. MRCP is preferred.

### Blood tests

You might have blood tests to measure CEA, CA 19-9, AFP, liver function, and serum IgG4. Serum IgG4 is used to rule out autoimmune cholangitis or other IgG4-related disease. Cholangitis is an inflammation of the bile duct.

This disease of the immune system may be chronic and affect the liver and biliary tract.

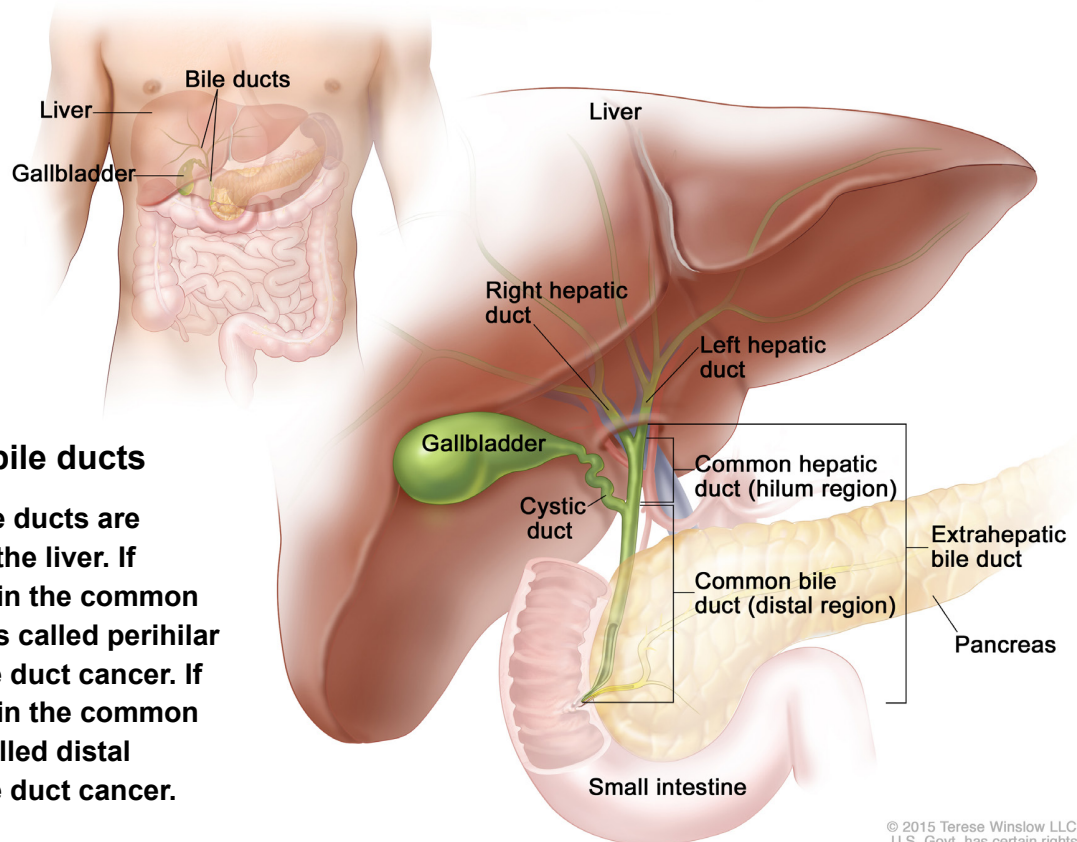
### Other procedures

Sometimes, an endoscopic ultrasound (EUS) is done to get a closer look at the bile ducts.

## Treatment

Treatment is based on if the tumor is:

- **Resectable** – can be removed with surgery
- **Unresectable** – cannot be removed with surgery
- **Metastatic** – cancer has spread to other parts of the body



### Extrahepatic bile ducts

Extrahepatic bile ducts are located outside the liver. If cancer is found in the common hepatic duct, it is called perihilar extrahepatic bile duct cancer. If cancer is found in the common bile duct, it is called distal extrahepatic bile duct cancer.

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## Resectable

Before surgery you might have biliary drainage. Extrahepatic cancers can spread to the liver, gallbladder, pancreas, and various arteries and veins. Therefore, you might have a staging laparoscopy or exploratory surgery to gain knowledge about the amount and location of your cancer.

Your treatment team of experts will discuss if surgery is safe for you and whether the cancer can be removed. This is called multidisciplinary review.

You may have biliary drainage to drain fluid from the biliary tract before surgery. During surgery, the bile duct and nearby lymph nodes are removed.

### Distal tumors

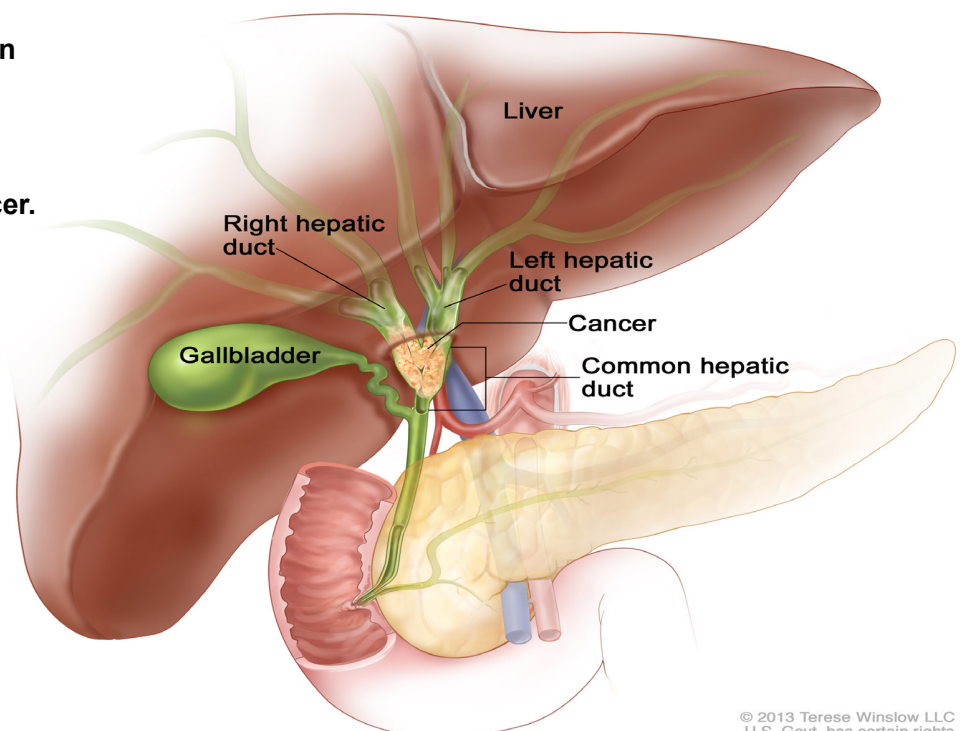
Distal tumors are in the common bile duct that passes through the pancreas. If the tumor has invaded the pancreas, then a Whipple procedure (pancreaticoduodenectomy) might be needed. A Whipple procedure is surgery that removes the head of the pancreas, the gallbladder, duodenum (first part of the small intestine), part of the bile duct, and often part of the stomach.

### Hilar or perihilar tumors (Klatskin tumors)

Hilar tumors are in the upper part of the common bile duct that is closest to the liver. Surgery to remove part of the liver (hepatic resection) is likely for tumors in the hilar area.

#### Klatskin tumor

A Klatskin tumor is found in the common hepatic duct/ right or left hepatic ducts. It is a proximal (perihilar) extrahepatic bile duct cancer.



## Treatment after surgery

Treatment after surgery is called adjuvant therapy. It is determined by the risk of the tumor returning and/or if not all tumor could be resected (removed). The goal is to kill any remaining microscopic cancer cells.

Adjuvant therapy options include:

- Systemic therapy (preferred)
- Clinical trial (preferred)
- Chemoradiation (chemotherapy might be given before or after chemoradiation)
- Observation

For adjuvant systemic therapy options, **see Guide 12.**

## No cancer remains

In a clear or negative surgical margin (R0), no cancerous cells are found. If no cancer remains (R0) and no cancer is found in the regional lymph nodes or cancer is found in situ, then options include systemic therapy (preferred), clinical trial (preferred), fluoropyrimidine-based (5-FU or capecitabine) chemoradiation, or observation. Observation

is sometimes called watch-and-wait. After treatment, you will enter surveillance.

## Microscopic cancer remains

If there is a higher risk that very small (microscopic) cancer cells remain (R1) or cancer is found in nearby lymph nodes, then treatment options include systemic therapy (preferred), clinical trial (preferred), or chemoradiation. Chemotherapy might be given before or after chemoradiation. After treatment, you will enter surveillance.

## Visible cancer remains

In an R2 positive surgical margin, cancer that can be seen without a microscope remains. If visible cancer remains, then treatment will be for unresectable disease.

## Surveillance

Surveillance is a period of testing to monitor for the return of cancer. During this time you will have imaging tests every 3 to 6 months for 2 years, then every 6 to 12 months for up to 5 years, or as needed. It is important to keep any follow-up doctor visits and imaging test appointments.

### Guide 12

#### Adjuvant systemic therapy options

##### Preferred

- Capecitabine

##### Other recommended

- FOLFOX
- Capecitabine with oxaliplatin
- Gemcitabine with capecitabine
- Gemcitabine with cisplatin
- 5-fluorouracil (5-FU)
- Gemcitabine

## Unresectable

Before treatment, you will be evaluated to see if resection might be an option or if you are a candidate for a liver transplant. If a liver transplant is an option, then you will be referred to a specialized transplant center before a biopsy is done.

### Liver transplant

A liver transplant is only for hilar tumors, but not everyone is eligible for this treatment. It requires an early visit to a specialized center. You will have treatment and operative staging before the actual 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.

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 duct are reconnected to the new liver. Other treatments may be given if you are waiting for a transplant. These treatments are called bridge or bridging therapy.

### Treatment

Treatment options include the following:

- Systemic therapy
- Clinical trial
- Chemoradiation (EBRT with fluoropyrimidine)
- Palliative radiation therapy (EBRT)
- Best supportive care

There are a variety of treatment options for unresectable extrahepatic bile duct cancers. Best supportive care is always given. You may consider joining a clinical trial. Systemic therapy, chemoradiation, and palliative radiation are all options. Ask your care team why one treatment might work better in your situation and what to expect from treatment.

### Systemic therapy

If you have jaundice, biliary drainage might be done before starting systemic therapy. The preferred systemic therapy is durvalumab with gemcitabine and cisplatin. There are many recommended options. For all systemic therapy options, **see Guide 13.**

## Metastatic

Metastatic cancer is cancer that has spread to other parts of the body. Fluid may block the bile ducts, causing jaundice. If you have jaundice, blocked bile duct will be treated and drained. A biopsy may be done of the metastasis to confirm that the cancer is bile duct cancer (and not another type of cancer).

Options include systemic therapy, clinical trial, and best supportive care. Best supportive care is always given. You may consider joining a clinical trial. For systemic therapy options, **see Guide 13.**

## Disease progression

If unresectable or metastatic extrahepatic bile duct cancer progresses during or after systemic therapy, then FOLFOX is the preferred option. FOLFOX is a combination of chemotherapy drugs that includes 5-fluorouracil (5-FU), leucovorin, and



oxaliplatin. If your tumor has a high number of mutations (TMB-H) or a specific gene mutation such as *NTRK*, MSI-H/dMMR, *FGFR2*, *IDH1*, or *BRAF* V600E, then you might receive drug therapy that targets the mutation. A clinical trial is always an option. For next-line systemic therapy options, **see Guide 14.**



Inside your mind is the greatest battle for your success.”

### Guide 13 Systemic therapy options: Unresectable and metastatic disease

<b>Preferred</b>	<ul style="list-style-type: none"> <li>• Durvalumab with gemcitabine and cisplatin</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• Gemcitabine with cisplatin</li> <li>• FOLFOX</li> <li>• Capecitabine with oxaliplatin</li> <li>• Gemcitabine with paclitaxel</li> <li>• Gemcitabine with capecitabine</li> <li>• Gemcitabine with oxaliplatin</li> <li>• Gemcitabine with cisplatin and paclitaxel</li> <li>• 5-fluorouracil (5-FU)</li> <li>• Capecitabine</li> <li>• Gemcitabine</li> </ul>
<b>Used in some cases</b>	<ul style="list-style-type: none"> <li>• Targeted therapy</li> </ul>

### Guide 14 Next-line systemic therapy options: Disease progression

<b>Preferred</b>	<ul style="list-style-type: none"> <li>• FOLFOX</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• FOLFIRI</li> <li>• Irinotecan with fluorouracil and leucovorin</li> </ul>
<b>Used in some cases</b>	<ul style="list-style-type: none"> <li>• Targeted therapy</li> <li>• Nivolumab</li> <li>• Lenvatinib with pembrolizumab</li> </ul>

## Key points

- Not all bile duct cancers are the same.
- Extrahepatic bile ducts are small tubes that carry bile outside the liver. They include the common hepatic duct and the common bile duct.
- A cholangiocarcinoma (CCA) is a rare cancer that forms in the bile ducts. Extrahepatic cholangiocarcinoma (ECC) is found in bile ducts outside the liver. It is also called extrahepatic bile duct cancer.
- There are 2 types of extrahepatic bile duct cancers: perihilar and distal types.
- Treatment is based on if the cancer can be removed with surgery (resectable), cannot be removed with surgery (unresectable), has spread to other parts of the body (metastatic), and the risk of recurrence.
- Treatment before surgery is called neoadjuvant. Treatment after surgery is called adjuvant.
- If your tumor has a high number of mutations (TMB-H) or a specific gene mutation such as *NTRK*, *MSI-H/dMMR*, *FGFR2*, *IDH1*, or *BRAF V600E*, then you might receive drug therapy that targets the mutation.
- Best supportive care may offer symptom relief.

### 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?

# 8

## Making treatment decisions

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- 69 Questions to ask
- 80 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 care team 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.























## Resources

### **Cholangiocarcinoma Foundation**

[CureCCA.org](https://CureCCA.org)

### **Global Liver Institute**

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

### **MedlinePlus**

[medlineplus.gov/gallbladdercancer.html](https://medlineplus.gov/gallbladdercancer.html)

[medlineplus.gov/bileductcancer.html](https://medlineplus.gov/bileductcancer.html)

### **National Cancer Institute (NCI)**

[cancer.gov/types/gallbladder](https://cancer.gov/types/gallbladder)

### **Triage Cancer**

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



**share with us.**

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

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





## Words to know

### **adjuvant therapy**

Treatment that is given to lower the chances of the cancer returning.

### **alpha-fetoprotein (AFP)**

A protein that can be elevated in those with liver cancer.

### **arterially directed therapy**

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

### **ascites**

Abnormal buildup of fluid in the abdomen.

### **bile**

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

### **bile duct**

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

### **bilirubin**

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

### **biopsy**

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

### **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.

### **carcinoma in situ**

A cancer that has not grown into tissue that would allow it to spread.

### **catheter**

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

### **chemoembolization**

Treatment that blocks the blood supply to the tumor(s) and injects a chemotherapy mixture into the tumor.

### **chemoradiation**

Treatment with a combination of chemotherapy and radiation therapy.

### **chemotherapy**

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

### **cholangiography**

An x-ray of the bile ducts.

## Words to know

### **cholangitis**

An infection of the vessels that drain digestive fluid from the liver (bile ducts).

### **cholecystectomy**

An operation to remove the gallbladder.

### **cholecystitis**

Inflammation of the gallbladder.

### **cholelithiasis**

The presence of gallstones.

### **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.

### **colonoscopy**

A procedure to check inside the colon with a device that is guided through the anus.

### **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.

### **deoxyribonucleic acid (DNA)**

A chain of chemicals in cells that contains coded instructions for making and controlling cells.

### **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.

### **endoscope**

A device that is passed through a natural opening to do work inside the body.

### **endoscopic retrograde cholangiopancreatography (ERCP)**

A procedure to work on pancreatic and bile ducts with an imaging device that is guided down the throat.

### **endoscopic ultrasound (EUS)**

A procedure that takes detailed pictures of the digestive tract and nearby tissue with a device passed through a natural opening.

### **epithelium**

A thin layer of tissue that covers organs, glands, and other structures within the body.

### **esophagogastroduodenoscopy (EGD)**

A procedure to do work in the first parts of the digestive tract with a device guided down the throat. Also called an upper GI endoscopy.

### **external beam radiation therapy (EBRT)**

Radiation therapy received from a machine outside the body.

### **fine-needle aspiration (FNA)**

Removal of a tissue sample with a thin needle.

### **fluoropyrimidine-based therapy**

A combination chemotherapy regimen in which the main drug used is 5-FU (5-fluorouracil).

### **FOLFIRI**

A combination chemotherapy regimen that includes 5-FU, leucovorin, and irinotecan.

## Words to know

### **FOLFOX**

A combination chemotherapy regimen that includes 5-FU, leucovorin, and oxaliplatin.

### **gallbladder**

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

### **gastroenterologist**

A doctor who is an expert in digestive diseases.

### **gastrointestinal (GI) tract**

The group of organs through which food passes after being eaten. Also called digestive tract.

### **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.

### **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.

### **intestine**

The organ that food passes through after leaving the stomach.

### **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.

### **lamina propria**

A type of connective tissue found under the thin layer of tissues covering a mucous membrane.

### **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.

### **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.

**minimally invasive procedure**

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

**mutation**

An abnormal change.

**neoadjuvant therapy**

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

**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.

**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.

**percutaneous transhepatic cholangiography (PTC)**

A procedure to view the biliary tract with an x-ray and possibly place a catheter to drain fluid from the biliary tract.

**peritoneum**

The tissue that lines the abdominal wall and covers most of the organs in the abdomen (viscera). Also called visceral peritoneum

**positron emission tomography (PET)**

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

**primary therapy**

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.

**serosa**

The outer lining of organs and body cavities of the abdomen and chest, including the stomach. Also called serous membrane.

**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.

**stereotactic body radiation therapy (SBRT)**

Treatment with high-dose radiation within one or a few sessions.

**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.

**three-dimensional conformal radiation therapy (3D-CRT)**

A treatment with radiation that uses beams matched to the shape of the tumor.

**tumor marker**

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

**ultrasound (US)**

A test that uses sound waves to take pictures of the insides of the body.

**unresectable**

Cancer that can't be removed by surgery.

**visceral peritoneum**

The lining (serosa) that surrounds the internal organs in the abdomen.

# NCCN Contributors

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

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# NCCN Cancer Centers

**Abramson Cancer Center**  
at the University of Pennsylvania  
Philadelphia, Pennsylvania  
800.789.7366 • [pennmedicine.org/cancer](http://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](http://uhhospitals.org/services/cancer-services)  
CC Taussig Cancer Institute  
866.223.8100 • [my.clevelandclinic.org/departments/cancer](http://my.clevelandclinic.org/departments/cancer)  
Case CCC  
216.844.8797 • [case.edu/cancer](http://case.edu/cancer)

**City of Hope National Medical Center**  
Duarte, California  
800.826.4673 • [cityofhope.org](http://cityofhope.org)

**Dana-Farber/Brigham and Women's Cancer Center |  
Mass General Cancer Center**  
Boston, Massachusetts  
617.732.5500 • [youhaveus.org](http://youhaveus.org)  
617.726.5130 • [massgeneral.org/cancer-center](http://massgeneral.org/cancer-center)

**Duke Cancer Institute**  
Durham, North Carolina  
888.275.3853 • [dukecancerinstitute.org](http://dukecancerinstitute.org)

**Fox Chase Cancer Center**  
Philadelphia, Pennsylvania  
888.369.2427 • [foxchase.org](http://foxchase.org)

**Fred & Pamela Buffett Cancer Center**  
Omaha, Nebraska  
402.559.5600 • [unmc.edu/cancercenter](http://unmc.edu/cancercenter)

**Fred Hutchinson Cancer Center**  
Seattle, Washington  
206.667.5000 • [fredhutch.org](http://fredhutch.org)

**Huntsman Cancer Institute at the University of Utah**  
Salt Lake City, Utah  
800.824.2073 • [huntsmancancer.org](http://huntsmancancer.org)

**Indiana University Melvin and Bren Simon  
Comprehensive Cancer Center**  
Indianapolis, Indiana  
888.600.4822 • [www.cancer.iu.edu](http://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](http://mayoclinic.org/cancercenter)

**Memorial Sloan Kettering Cancer Center**  
New York, New York  
800.525.2225 • [mskcc.org](http://mskcc.org)

**Moffitt Cancer Center**  
Tampa, Florida  
888.663.3488 • [moffitt.org](http://moffitt.org)

**O'Neal Comprehensive Cancer Center at UAB**  
Birmingham, Alabama  
800.822.0933 • [uab.edu/onealcancercenter](http://uab.edu/onealcancercenter)

**Robert H. Lurie Comprehensive Cancer  
Center of Northwestern University**  
Chicago, Illinois  
866.587.4322 • [cancer.northwestern.edu](http://cancer.northwestern.edu)

**Roswell Park Comprehensive Cancer Center**  
Buffalo, New York  
877.275.7724 • [roswellpark.org](http://roswellpark.org)

**Siteman Cancer Center at Barnes-Jewish Hospital  
and Washington University School of Medicine**  
St. Louis, Missouri  
800.600.3606 • [siteman.wustl.edu](http://siteman.wustl.edu)

**St. Jude Children's Research Hospital/  
The University of Tennessee Health Science Center**  
Memphis, Tennessee  
866.278.5833 • [stjude.org](http://stjude.org)  
901.448.5500 • [uthsc.edu](http://uthsc.edu)

**Stanford Cancer Institute**  
Stanford, California  
877.668.7535 • [cancer.stanford.edu](http://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](http://cancer.osu.edu)

**The Sidney Kimmel Comprehensive  
Cancer Center at Johns Hopkins**  
Baltimore, Maryland  
410.955.8964  
[www.hopkinskimmelcancercenter.org](http://www.hopkinskimmelcancercenter.org)

**The UChicago Medicine Comprehensive Cancer Center**  
Chicago, Illinois  
773.702.1000 • [uchicagomedicine.org/cancer](http://uchicagomedicine.org/cancer)

**The University of Texas MD Anderson Cancer Center**  
Houston, Texas  
844.269.5922 • [mdanderson.org](http://mdanderson.org)

**UC Davis Comprehensive Cancer Center**  
Sacramento, California  
916.734.5959 • 800.770.9261  
[health.ucdavis.edu/cancer](http://health.ucdavis.edu/cancer)

UC San Diego Moores Cancer Center  
La Jolla, California  
858.822.6100 • [cancer.ucsd.edu](http://cancer.ucsd.edu)

UCLA Jonsson Comprehensive Cancer Center  
Los Angeles, California  
310.825.5268 • [cancer.ucla.edu](http://cancer.ucla.edu)

UCSF Helen Diller Family  
Comprehensive Cancer Center  
San Francisco, California  
800.689.8273 • [cancer.ucsf.edu](http://cancer.ucsf.edu)

University of Colorado Cancer Center  
Aurora, Colorado  
720.848.0300 • [coloradocancercenter.org](http://coloradocancercenter.org)

University of Michigan Rogel Cancer Center  
Ann Arbor, Michigan  
800.865.1125 • [rogelcancercenter.org](http://rogelcancercenter.org)

University of Wisconsin Carbone Cancer Center  
Madison, Wisconsin  
608.265.1700 • [uwhealth.org/cancer](http://uwhealth.org/cancer)

UT Southwestern Simmons  
Comprehensive Cancer Center  
Dallas, Texas  
214.648.3111 • [utsouthwestern.edu/simmons](http://utsouthwestern.edu/simmons)

Vanderbilt-Ingram Cancer Center  
Nashville, Tennessee  
877.936.8422 • [vicc.org](http://vicc.org)

Yale Cancer Center/Smilow Cancer Hospital  
New Haven, Connecticut  
855.4.SMILOW • [yalecancercenter.org](http://yalecancercenter.org)



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**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**

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**Galaxy Healthcare (Borivali): By**

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