Gallbladder and Bile Duct Cancers
Hepatobiliary Cancers

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Global Liver Institute

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

The Bili Project Foundation

The Bili Project Foundation is honored to work with the NCCN Foundation to provide this information to support bile duct, liver and gallbladder cancer patients and their families in our goals together to raise awareness and access to educational information to make informed decisions about their care. Susan Acquisto/Joy Stephenson Laws, Co-Founders. thebiliproject.org

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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. This book is about cancers that occur in the gallbladder and bile ducts.

The hepatobiliary system

The digestive system takes in food, breaks it down (digestion), absorbs nutrients, and removes waste from the body. The prefix “hepato” means liver, while “biliary” refers to the gallbladder and bile ducts. Together, they form the hepatobiliary system, which makes bile to aid in the digestion of fat.

The gallbladder

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

Bile ducts

Liver cells make bile. Bile is a yellow or green fluid made up of cholesterol, bilirubin, salts such as potassium and sodium, water, and other elements found in the body. It flows into small channels that drain into thin tubes called ducts. These ducts form larger and larger
channels that flow into the left and right hepatic (liver) ducts. The left and right hepatic ducts come together to form the common hepatic bile duct. The common hepatic duct joins with a duct connected to the gallbladder, called the cystic duct, to form the common bile duct. 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.

- Extrahepatic bile ducts are found 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.

### Gallbladder cancer

Gallbladder cancer is the most common type of biliary tract cancer worldwide. It 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, like sarcoma, can grow in the gallbladder. Gallbladder adenocarcinoma is a 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
- On imaging tests

### 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)
- Distal bile duct cancer

### 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 that has grown into a nearby body part and has spread to nearby lymph nodes is called a local metastasis or locally advanced.
- Cancer that has spread to a body part far from the primary tumor is called a distant metastasis. A distant metastasis could be in the lung, bone, or abdominal lining. This is metastatic cancer.

Cancer can spread to distant sites through blood and the lymphatic system. Lymph travels throughout the body in vessels like blood does. Lymph gives cells water and food. It also has white blood cells that fight germs. Lymph nodes filter lymph and remove germs. Lymph vessels and nodes are found everywhere in the body.

### Review

- 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 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.
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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. It is important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a great way to access your test results.

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

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

Create a medical binder

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

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

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

Liver disease history
Your doctor will also ask about your history of any previous liver problems, such as cirrhosis; viral hepatitis B or C infection; episodes of jaundice, gallstones, alcohol use, and fatty liver disease; or risk factors (such as obesity and diabetes).

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

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

A health care provider may:

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

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

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

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

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

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

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

Hepatitis panel
Hepatitis is a type of liver disease. Viruses called hepatitis A, hepatitis B (HBV), and hepatitis C (HCV) are the most common causes of hepatitis. A hepatitis panel is a blood test that checks to see if you have a hepatitis infection caused by one of these viruses. Chronic (long-term) HBV or prior exposure to HBV, and a current or past infection with HCV, both increase the risk for liver cancer and biliary tract cancers. Hepatitis causes the liver to become inflamed and not work as it should. HBV and HCV can cause scarring of the liver, liver failure, and cancer.

A hepatitis panel will tell your treatment team if you had hepatitis in the past or if you have it today. You may be referred to a hepatologist if you have positive results. A hepatologist is a doctor who specializes in the care of the liver, biliary tract, and gallbladder.

Tumor markers in the blood
Your doctor may order additional blood tests to look for alpha-fetoprotein (AFP), cancer antigen 19-9 (CA 19-9), and/or carcinoembryonic antigen (CEA). These are protein or glycoprotein tumor markers found in blood.
Imaging tests

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

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

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

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

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

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

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

Dynamic MRI scan
In a dynamic MRI scan, there are two scans: one without contrast and one with contrast.

First, a scan is done without contrast. Then, contrast is injected into a vein and another scan is done.

MRCP
A magnetic resonance cholangiopancreatography (MRCP) is a type of MRI scan that makes very clear pictures of the bile ducts (cholangio) and pancreas (pancreatography). No contrast is used because bile and other fluids act as their own contrast.
PET scan
A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is a substance injected into a vein to see where it is in the body and if it is using sugar to grow. Cancer cells show up as bright spots on PET scans. Not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on PET.

Sometimes, PET is combined with CT. This combined test is called a PET/CT scan. It may be done with one or two machines depending on the cancer center.

Ultrasound
An ultrasound (US) uses high-energy sound waves to form pictures of the inside of the body. A probe will be pressed onto your abdomen. Ultrasound can show small areas of cancer that are near the surface of the body. Sometimes, an ultrasound or CT are 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.

PTC
A percutaneous transhepatic cholangiography (PTC) uses contrast and an x-ray to take pictures of the biliary tract. The contrast is injected using a needle or a catheter (thin, flexible tube) passed through the skin (percutaneous) into a bile duct in the liver (transhepatic). An x-ray uses small amounts of radiation to make pictures of organs and tissues inside the body.

If necessary, a catheter can be inserted to drain fluid from the biliary tract. This can drain into a bag outside of the body or the bile bag can be removed and the bile can drain into the small intestine. A metal stent may also be placed for an obstruction or blockage of the bile duct.

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

Scopes
Some imaging tests use a thin, tube-shaped tool called a scope 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.

Imaging tests with scopes might include:

- Endoscopic ultrasound (EUS)
- Endoscopic retrograde cholangiopancreatography (ERCP)
- Esophagogastroduodenoscopy (EGD)
- Colonoscopy

EUS
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...
Testing for gallbladder and bile duct cancers

Scopes

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 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 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.

An endoscope is a thin tube-shaped tool with a camera. It is inserted through your mouth and used to look inside your body.
EGD
In an EGD, a device is guided down the throat into the esophagus, stomach, and upper parts of the 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 dilated blood vessels or ulcers. An EGD can also be referred to as an upper GI endoscopy.

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 and then into the rectum followed by the remainder of the colon. A colonoscopy is done under sedation to keep you comfortable during the procedure.

Laparoscopy
A laparoscopy is a procedure that allows your doctors to see organs in your abdomen. It uses a tool similar to an endoscope called a laparoscope that is inserted through a tiny cut in your abdomen. Laparoscopy is done under general anesthesia. This is a controlled loss of wakefulness from drugs.

Laparoscopy may only be used in certain cases. It may be used to learn the stage of cancer or for cancer that is not clearly seen on imaging. It may also be used for cancer that has not metastasized.

Biopsy
Tissue or fluid may be removed from your body and tested to diagnose cancer. A biopsy is a procedure that removes samples of fluid or tissue. The tissue could also be abnormal but not cancer.

Types of possible biopsies include:

- **Fine-needle aspiration (FNA)** uses a thin needle to remove a sample of tissue or fluid. An ultrasound (US) may guide the FNA biopsy.
- **ERCP brushings** during an ERCP procedure can also be used to look for cancer cells.
- **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 IV (intravenous) line.
- **Laparoscopic biopsy** uses a biopsy tool to take samples of tissues during laparoscopic surgery.

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

Tumor tests
A sample from a biopsy of your tumor may be tested to look for specific DNA (deoxyribonucleic acid) mutations, protein
levels, or other molecular features. This information is used to choose the best treatment for you. It is sometimes called tumor molecular profile testing.

CA 19-9, CEA, and AFP
CA 19-9, CEA, and AFP are substances found in blood that can be elevated in people with hepatobiliary cancers. CA 19-9 might be measured before and after surgery or treatment for jaundice, such as clearing a blocked bile duct. See Blood Tests section for more information on tumor markers found in blood.

Tumor mutation testing
A sample of your tumor or blood may be used to see if the cancer cells have any specific DNA mutations. Some mutations such as NTRK gene fusions, FGFR2 fusions, or IDH1 mutations can be targeted with specific therapies. This is a different type of DNA testing than the genetic testing for mutations you may have inherited from your parents. In tumor mutation testing, only the tumor is tested and not the rest of your body.

MSI/MMR testing
Microsatellites are short, repeated strings of DNA (the information inside genes). When errors or defects occur, they are fixed. Some cancers prevent these errors from being fixed. This is called microsatellite instability (MSI). Knowing this can help plan treatment.

Mismatch repair (MMR) helps fix mutations in certain genes. When MMR is lacking (dMMR), these mutations may lead to cancer. Knowing this can help plan treatment or predict how well treatment like immunotherapy will work with your type of tumor. When cancer cells have more than a normal number of microsatellites, it is called MSI-H (microsatellite instability-high).

Genetic tests
Genes are coded instructions for the proteins your cells make. A mutation is when something goes wrong in the genetic code. Mutations can be passed down in families or can occur spontaneously. In other words, they may be present before you are born (hereditary or germline) or caused by genetic damage (acquired or somatic) later in life.

Genetics can increase the risk of different cancers. 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 will speak to you about the results. A genetic counselor is an expert who has special training in genetic diseases.

Genetic counseling
Your genetic counselor or oncologist might recommend genetic testing. BRCA1 and BRCA2 gene mutations are related to hereditary breast, ovarian, and prostate cancer. Other genes may be tested as well. Tests results may be used to guide treatment planning.

BRCA tests
Everyone has genes called BRCA1 and BRCA2. Normal BRCA genes help to prevent tumor growth. They help fix damaged cells and help cells grow normally. Mutations in BRCA1 or BRCA2 increase the risk of breast, ovarian, prostate, colorectal, or melanoma skin cancer, as well as some biliary tract cancers. These mutations can also affect how well some treatments work.
Cancer stages

A cancer stage is a way to describe the extent of the cancer based on test results at the time you are first diagnosed with cancer. The American Joint Committee on Cancer (AJCC) created this to determine how much cancer is in your body, where it is located, and what subtype you have. This is called staging. Based on testing, your cancer will be assigned a stage. Staging is needed to make treatment decisions. Once treatment starts, staging does not change.

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)

There are other staging systems. Doctors may explain your cancer stage in different ways than described next.

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 imaging and pathology results, your doctor will assign a score or number to each letter. The higher the number, the larger the tumor or the more the cancer has spread to lymph nodes or other organs. 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 (metastasized) to distant parts of the body

Grade

Another factor used in staging is the cancer grade. Grade describes how abnormal the tumor cells look under a microscope (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 (G1) means the cancer cells look like normal cells. Poorly differentiated (G3) means the cancer cells look very different compared to normal cells. G3 is the highest grade for gallbladder and bile duct cancers.

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

Numbered stages

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

- Tests are used to find cancer, plan treatment, and check how well treatment is working.
- Blood tests check for signs of disease and how well organs are working.
- Imaging tests take pictures of the inside of your body.
- A biopsy removes tissue or fluid from your body to diagnose cancer or perform additional molecular tests.
- In tumor tests, samples of your tumor are tested for specific DNA mutations, protein levels, or other molecular features.
- Some mutations can run in families and increase the risk of cancer. In hereditary genetic tests, your normal cells (such as blood or cells from a saliva sample) are tested for mutations.
- Staging is a rating by your doctors of the extent of the cancer at the time you are first diagnosed. Once treatment starts, staging does not change.
- Doctors may explain your cancer stage in different ways to make it less confusing.
- Results from blood tests, imaging studies, and biopsy will determine your treatment plan. Online portals are a great way to access your test results.
3
Gallbladder and bile duct cancer treatments

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There is more than one treatment for gallbladder and bile duct cancers. This chapter describes treatment options and what to expect. Discuss with your doctor which treatment might be best for you.

Gallbladder and bile duct cancers are treatable. Treatment can be local, systemic, or a combination of both.

There are 2 types of treatment:

- Local therapy focuses treatment on a certain area. It includes surgery, ablation, embolization, and radiation therapy.
- Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.

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

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 may also be used to reduce symptoms caused by the cancer or extend life. This is called palliative surgery.

The type of surgery you receive depends on size and location of the tumor. It also depends on if there is cancer in any surrounding organs and tissues.

There are 2 types of surgery:

- Open surgery
- Minimally invasive surgery (laparoscopic or robotic surgery)

When preparing for surgery, you should seek the opinion of an experienced surgeon. You can ask for a referral to a hospital or cancer center that has experience in treating your type of cancer. Surgery for the gallbladder and bile duct cancers can be complex. The surgeon should be an expert in performing these types of surgery.

**Open surgery**

Open surgery removes tissue through one large surgical cut below your ribs. The large incision lets your doctor directly view and access the tumor to remove it.

**Minimally invasive surgery**

Minimally invasive surgery uses several small incisions or cuts instead of one large cut.

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 doctor 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 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.

Tumor resection
Imaging tests will be used to see if your cancer is resectable (can be removed completely with surgery) or unresectable (cannot be removed with surgery). The goal of surgery or tumor resection is to remove all of the cancer. To do so, the tumor is removed along with some normal-looking tissue around its edge. The normal-looking tissue is called the surgical margin.
Surgical margin
The goal of surgery is a cancer-free surgical margin. After surgery, you may receive treatment such as radiation or systemic therapy to kill any remaining cancer cells.

- In a clear or negative margin (R0), no cancerous cells are found in the tissue around the edge of the tumor.
- In an R1 positive margin, the surgeon removes all of the visible tumor, but the microscopic margins are still positive for tumor cells.
- In an R2 positive margin, the surgeon is unable to remove all of the visible tumor. Therefore, the tumor is left at the time of surgery.

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

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

Liver
The liver is divided into 8 sections or segments based on the location of the portal vein, hepatic vein, and bile ducts.
Liver resection
Surgery to remove part of the liver is called a partial hepatectomy or hepatic resection. Surgery depends on the size and location of the tumor and how healthy your liver is. You might have surgery to remove a small wedge or an entire liver lobe. The part of the liver that remains will keep working, and if the liver is healthy enough, the missing section will regrow. A partial hepatectomy is different than a liver transplant.

Liver transplant
A liver transplant is rarely an option, but might be considered for certain types of bile duct cancer. In a liver transplant, the entire liver is removed and replaced with a healthy, donor liver. The new liver may be donated from a person who recently died, or a section of liver may be donated from a living person. A liver transplant is based on certain size limits and tumor locations.

The liver is divided into 8 sections or segments based on hepatic artery, portal vein, and bile duct locations. Structures such as the inferior vena cava, portal vein, hepatic artery, and bile ducts are reconnected to the new liver.

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. For a regional lymphadenectomy, some of the lymph nodes in the tumor area are removed. For a radical lymphadenectomy, most or all of the lymph nodes in the tumor area are removed. A lymphadenectomy is sometimes called lymph node dissection.

Did you know?
The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same.

Chemotherapy, targeted therapy, and immunotherapy are all types of systemic therapy.
Systemic therapy

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

Systemic therapies that might be used include:

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

**Chemotherapy**

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

**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. It is a combination of systemic and local therapies.

**Targeted therapy**

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

Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop the action of molecules that help cancer cells grow and/or survive. Some targeted therapy drugs block the chemical signals that tell cancer cells to grow. Other targeted therapy drugs block signals that cause new blood vessels to form. Others target hormones.

Regorafenib (Stivarga®) is a targeted therapy that might be used to treat gallbladder and bile duct cancers.

Targeted therapies may be used to treat biliary cancers that have certain gene mutations like:

- Pemigatinib (Pemazyre™) for cholangiocarcinoma with FGFR2 fusions or rearrangements
- Ivosidenib (Tibsovo®) for cholangiocarcinoma with IDH1 mutations
- Entrectinib (Rozlytrek) and larotrectinib (Vitrakvi®) for NTRK gene fusion

**Immunotherapy**

Immunotherapy is a type of systemic treatment that increases the activity of your immune system. By doing so, it improves your body’s ability to find and destroy cancer cells. Immunotherapy can be given alone or with other types of treatment. Pembrolizumab (Keytruda®) is a type of immunotherapy that might be used to treat MSI-H/dMMR tumors.
Radiation therapy

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

Radiation may be given:

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

External beam radiation therapy

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

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

- **Stereotactic body radiation therapy (SBRT)** uses high-energy radiation beams to treat cancers.
- **Proton beam radiation therapy** uses streams of particles called protons to kill tumor cells.
- **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 tissues.
- **Image-guided radiation therapy (IGRT)** uses a computer to create a picture of the tumor. This helps guide the radiation beam during treatment. It is used with IMRT and 3D-CRT. Tumors can shift slightly within the body and can change shape and size between and during treatment visits. Because of this, IGRT can improve how well 3D-CRT and IMRT target the tumor.
- **Intraoperative radiation therapy (IORT)** uses radiation treatment aimed directly at the tumor during surgery.
- **Palliative EBRT** is used to treat pain caused by cancer.
Arterially directed therapy

Arterially directed therapies include embolization, chemoembolization, drug-eluting bead embolization, and radioembolization. They treat tumors by injecting particles, chemotherapy, or radioactive beads directly into the blood vessels that supply the tumor(s). A small catheter is inserted into an artery and is guided to the tumor. Once in place, the particles, chemotherapy, or beads are injected.

Types of arterially directed therapy include:

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

- **Chemoembolization (also known as TACE or transarterial chemoembolization)** blocks the blood supply to the tumor(s) plus injects a chemotherapy mixture into the tumor. TACE has risks. It might not be used if your bilirubin level is above 3 mg/mL.

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

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

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

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

Clinical trials have 4 phases.

- **Phase I trials** aim to find the safest and best dose of a new drug. Another aim is to find the best way to give the drug with the fewest side effects.
- **Phase II trials** assess if a drug works for a specific type of cancer.
- **Phase III trials** compare a new drug to a standard treatment.
- **Phase IV trials** evaluate a drug’s safety and treatment results after it has been approved.

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

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

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

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

Finding a clinical trial

- Search the National Institutes of Health (NIH) database for clinical trials. It includes publicly and privately funded clinical trials, whom to contact, and how to enroll. Look for an open clinical trial for your specific type of cancer. Go to ClinicalTrials.gov.
- The National Cancer Institute’s Cancer Information Service (CIS) provides up-to-date information on clinical trials. You can call, e-mail, or chat live. Call 1.800.4.CANCER (800.422.6237) or go to cancer.gov.
Supportive care

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

Treatment side effects

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

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

Trouble eating

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

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

Blocked bile duct

A tumor 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. 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 (cancer spread to other parts of the body), in order 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 catheter to drain the fluid into a bag placed on the outside of your body. Another option is to insert a 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.

- **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.

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

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

- **Your primary care doctor** handles medical care not related to your cancer. This person can help you express your feelings about treatments to your cancer care team.

- **A pathologist** interprets tests the cells, tissues, and organs removed during a biopsy or surgery.

- **A diagnostic radiologist** reads the results of x-rays and other imaging tests.

- **A hepatobiliary gastroenterologist** performs ERCP procedures to place and exchange stents within the biliary tract if the cancer is causing blockage. The hepatobiliary GI specialist may also perform an EUS, ERCP biopsy, or brushing procedure.

- **An interventional radiologist** performs needle biopsies, ablations, and arterially directed therapies, and places ports for treatment. This person may also place percutaneous biliary drains if the bile ducts are blocked.

- **A surgical oncologist** performs operations to remove cancer.

- **A medical oncologist** treats cancer in adults using systemic therapy. Often, this person will lead the overall treatment team and keep track of tests and exams done.
by other specialists. A medical oncologist will often coordinate your care. Ask who will coordinate your care.

- **A radiation oncologist** prescribes and plans radiation therapy to treat cancer.
- **An anesthesiologist** gives anesthesia, a medicine so you do not feel pain during surgery or procedures.
- **A gastroenterologist** is an expert in digestive diseases. A specific type of gastroenterologist that focuses on liver disease is called a hepatologist.
- **A palliative care specialist** is an expert in the treatment of symptoms caused by the cancer with the goal of improving a patient’s quality of life and easing suffering.
- **Advanced practice providers** are an important part of any team. These are registered nurse practitioners and physician assistants who monitor your health and provide care.
- **Residents and fellows** are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Nutritionists** can provide guidance on what foods or diet are most suitable for your particular condition.
- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you feel.

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

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

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

- Local therapy focuses treatment on a certain area. It includes surgery, radiation therapy, ablation, and arterially directed therapy.
- Surgery is a main treatment option for gallbladder and bile duct cancers.
- Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.
- Targeted therapies can block the ways cancer cells grow, divide, and move in the body.
- Immunotherapy uses your body’s natural defenses to find and destroy cancer cells.
- Radiation therapy (RT) uses high-energy radiation from x-rays, gamma rays, protons, and other sources to kill cancer cells and shrink tumors.
- Arterially directed therapy treats tumors by injecting particles, chemotherapy, or radioactive beads directly into the blood vessels that supply the tumor(s).
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works. It is often one of the preferred treatments for gallbladder cancer.
- Supportive care is health care that relieves symptoms caused by cancer or cancer treatment and improves quality of life.
4 Gallbladder cancer

36 Overview
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57 Metastatic disease
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The gallbladder is a pear-shaped organ found under the liver. It is made up of several layers of 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. Treatment is based on if cancer was found during surgery, during pathology review, or on imaging tests. Together, you and your doctor will choose the treatment plan that is best for you.
Gallbladder cancer stages

Cancer starts inside the gallbladder and grows through the layers of the gallbladder wall. Once cancer reaches the outer wall, it can grow or spread into nearby ducts, arteries, veins, or organs. Gallbladder cancer is staged by the how much the tumor has grown into the layers of the gallbladder wall and if the tumor is on the side nearest 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.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Tumor Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis, N0, M0</td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>T1, N0, M0</td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
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</tr>
<tr>
<td>Stage 2A</td>
<td>T2a, N0, M0</td>
<td></td>
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<tr>
<td>Stage 2B</td>
<td>T2b, N0, M0</td>
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<tr>
<td>Stage 3</td>
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<tr>
<td>Stage 3A</td>
<td>T3, N0, M0</td>
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</tr>
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<td>Stage 3B</td>
<td>T1 to T3, N1, M0</td>
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<td>Stage 4</td>
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<tr>
<td>Stage 4A</td>
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<tr>
<td>Stage 4B</td>
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</tr>
<tr>
<td></td>
<td>Any T, Any N, M1</td>
<td></td>
</tr>
</tbody>
</table>
**T = Tumor**

Carcinoma in situ (Tis) is the earliest stage of gallbladder cancer. The cancer cells are found inside the lining of the gallbladder wall (epithelium). The 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
- **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.

- **M0** means no distant metastasis
- **M1** means distant metastasis is found. This is metastatic cancer.

**Treatment options**

Gallbladder cancer is often found by chance. This is called an incidental finding.

Gallbladder cancer can be found 3 ways:

- During surgery
- During pathology review
- On imaging tests
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.

**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.

**Tests**

You will have the following tests:

- Multiphasic CT of the abdomen and pelvis with contrast
- Multiphasic MRI of the abdomen and pelvis with contrast
- Chest CT with or without contrast

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.

Imaging tests will determine if your tumor can be removed with surgery (resectable) or cannot be removed with surgery (unresectable).

**Order of treatments**

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

- **Neoadjuvant (before)** treatment is given to shrink the tumor before primary treatment (surgery). This might change an unresectable tumor into a resectable tumor.
- **Primary treatment** is the main treatment given to rid the body of cancer. Surgery is usually the main treatment for resectable gallbladder cancer.
- **Adjuvant (after) treatment** is given after primary treatment to rid the body of any cancer cells left behind from surgery. It is also used when the risk of cancer returning (recurrence) is felt to be high.
- **First-line treatment** is the first set of systemic (drug) treatment given.
- **Second-line treatment** is the next set of treatment given if cancer progresses during or after systemic therapy.

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

Treatment will be based on if the cancer is resectable or unresectable. You might have treatment before surgery called neoadjuvant therapy. This is to reduce the amount of cancer. Sometimes, neoadjuvant therapy can shrink a tumor enough that it can be removed with surgery. This means that a previously unresectable tumor might become resectable.

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

It is important to know that not everyone responds the same way to treatment. Some people respond better than expected. Others do worse. Talk with your doctor about your goals for treatment. Your wishes are important.

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 cholecystectomy 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.

Treatment after surgery

Treatment after surgery is called adjuvant therapy. It will be based on post-resection status, which is the amount of cancer that remains after surgery.

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

Those with R1 or R2 resections should be evaluated by a multidisciplinary team.

Systemic therapy or a clinical trial are the preferred adjuvant treatment options. A preferred treatment is one proven to have a better result. Other options include fluoropyrimidine-based chemoradiation used alone or with chemotherapy.

For adjuvant treatment based on post-resection status, see Guide 2.

Adjuvant systemic therapy

If you will have systemic (drug) therapy after surgery, then capecitabine is the preferred option. All adjuvant systemic therapy options can be found in Guide 3.
## Guide 2
### Adjuvant treatment based on post-resection status

<table>
<thead>
<tr>
<th>Is there cancer after surgery?</th>
<th>Treatment options</th>
</tr>
</thead>
</table>
| No cancer remains (R0) and no cancer found in regional nodes or Carcinoma in situ at surgical margin | • Observation  
• Systemic therapy (preferred) (see Guide 3)  
• Clinical trial (preferred)  
• Fluoropyrimidine-based chemoradiation |
| Microscopic cancer cells remain (R1) or Cancer found in regional nodes | • Systemic therapy (preferred) (see Guide 3)  
• Clinical trial (preferred)  
• Fluoropyrimidine-based chemoradiation  
• Fluoropyrimidine-based or gemcitabine-based chemotherapy followed by fluoropyrimidine-based chemoradiation  
• Fluoropyrimidine-based chemoradiation followed by fluoropyrimidine-based or gemcitabine-based chemotherapy |
| Visible cancer remains (R2) | • See treatment for unresectable disease |

## Guide 3
### Adjuvant systemic therapy options: Resectable gallbladder cancer

| Preferred option |  
|------------------|---|
| • Capecitabine |

| Other recommended |  
|-------------------|---|
| • 5-fluorouracil with oxaliplatin  
• Capecitabine with oxaliplatin  
• Gemcitabine with capecitabine  
• Gemcitabine with cisplatin  
• 5-fluorouracil with cisplatin  
• Capecitabine with cisplatin  
• 5-fluorouracil  
• Gemcitabine |
Unsectable
An unresectable tumor cannot be removed with surgery.

Before treatment begins, tumor tests might include:

- Microsatellite instability (MSI) and/or mismatch repair (MMR) testing
- Germline testing for those with MMR deficient (dMMR)/MSI-high (MSI-H) tumors or a family history that suggests BRCA1 or BRCA2 mutations
- Molecular testing that may include NTRK gene fusion testing

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 extent 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), see Guide 4
- Clinical trial (preferred)
- Palliative radiation therapy
- Best supportive care

Guide 4
Systemic therapy options: Unresectable gallbladder cancer

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>• Gemcitabine with cisplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other recommended</td>
<td>• 5-fluorouracil with oxaliplatin</td>
</tr>
<tr>
<td></td>
<td>• 5-fluorouracil with cisplatin</td>
</tr>
<tr>
<td></td>
<td>• Capecitabine with cisplatin</td>
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<tr>
<td></td>
<td>• Capecitabine with oxaliplatin</td>
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<td>• Gemcitabine with capecitabine</td>
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<tr>
<td></td>
<td>• Gemcitabine with oxaliplatin</td>
</tr>
<tr>
<td></td>
<td>• Gemcitabine with cisplatin and albumin-bound paclitaxel</td>
</tr>
<tr>
<td></td>
<td>• Single agents: 5-fluorouracil or capecitabine or gemcitabine</td>
</tr>
</tbody>
</table>

Used in some cases
For NTRK gene fusion-positive tumors:
• Entrectinib
• Larotrectinib

For MSI-H/dMMR tumors:
• Pembrolizumab
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.

**Systemic therapy**

Systemic therapy is one of the preferred treatments for unresectable gallbladder cancer. Gemcitabine with cisplatin is the preferred option. There are other recommended options. If you have a tumor that has *NTRK* gene fusion, then entrectinib or larotrectinib will be used. For a MSI-H/dMMR tumor, pembrolizumab will be given. Ask your medical oncologist why one systemic therapy might be chosen over another to treat your type of cancer.

For unresectable systemic therapy options, see Guide 4.

**Disease progression**

When cancer progresses during or after systemic therapy, then your medical oncologists might try a different systemic therapy found in Guide 4. For disease progression, the preferred option is FOLFOX. FOLFOX is a combination of chemotherapy drugs that includes 5-fluorouracil (5-FU), leucovorin, and oxaliplatin. FOLFIRI is a combination of 5-FU with leucovorin and irinotecan. If your tumor has a specific gene mutation, then you might receive drug therapy that targets the mutation. See Guide 5.

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**Guide 5**

**Systemic therapy options: Disease progression**

<table>
<thead>
<tr>
<th>Preferred option</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FOLFOX</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FOLFIRI</td>
</tr>
<tr>
<td>• Regorafenib</td>
</tr>
<tr>
<td>• Preferred and other recommended options listed in Guide 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Used in some cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>For <em>NTRK</em> gene fusion-positive tumors:</td>
</tr>
<tr>
<td>• Entrectinib</td>
</tr>
<tr>
<td>• Larotrectinib</td>
</tr>
<tr>
<td>For MSI-H/dMMR tumors:</td>
</tr>
<tr>
<td>• Pembrolizumab</td>
</tr>
</tbody>
</table>
Found at pathology

Gallbladder cancer can be found during pathology review following a cholecystectomy for cholelithiasis (gallstones). An expert hepatobiliary pathologist should review your pathology results. Your doctor 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.

Treatment options
Treatment is based on test results and staging. For treatment options, see Guide 6.

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 the tumor to see if it is growing.

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.

Guide 6
Treatment options: Cancer found by chance on pathology review

<table>
<thead>
<tr>
<th>T1a (with negative margins)</th>
<th>• Observation</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Cystic duct lymph node is positive for cancer</th>
<th>• Consider neoadjuvant chemotherapy (see Guide 7)</th>
<th>• Liver surgery with lymphadenectomy and possible bile duct removal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Clinical trial</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T1b or greater</th>
<th>• Liver surgery with lymphadenectomy and possible bile duct removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resectable</td>
<td>• Systemic therapy (preferred)</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial (preferred)</td>
</tr>
<tr>
<td></td>
<td>• Palliative radiation therapy</td>
</tr>
<tr>
<td></td>
<td>• Best supportive care</td>
</tr>
<tr>
<td>Unresectable</td>
<td>• MSI/MMR testing</td>
</tr>
<tr>
<td></td>
<td>• Consider additional molecular testing</td>
</tr>
</tbody>
</table>
Before starting treatment, you might have the following:

- Multiphasic abdominal and pelvic CT with IV contrast
- Multiphasic abdominal and pelvic MRI with IV contrast
- Chest CT with or without contrast
- Staging laparoscopy
- MSI/MMR testing

**Treatment before surgery**

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 nearby 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.

For neoadjuvant chemotherapy options, see Guide 7.

**Surgery**

Treatment is surgery to remove a part of the liver (hepatic resection), nearby lymph nodes (lymphadenectomy), and possibly the bile duct.

---

**Guide 7**

**Neoadjuvant chemotherapy options**

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>——</th>
</tr>
</thead>
</table>

**Other recommended**

- 5-fluorouracil with oxaliplatin
- Capecitabine with oxaliplatin
- Gemcitabine with capecitabine
- Gemcitabine with cisplatin
- 5-fluorouracil with cisplatin
- Capecitabine with cisplatin
- Gemcitabine with cisplatin and albumin-bound paclitaxel
- Gemcitabine with oxaliplatin
- Single agents: 5-fluorouracil or capecitabine or gemcitabine
Treatment after surgery
Treatment after surgery is called adjuvant therapy. It is based on the post-resection status, which is the amount of cancer that remains after surgery.

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

The preferred adjuvant treatment options are systemic therapy (capecitabine) or a clinical trial. A preferred treatment is one proven to have a better result. Other options include fluoropyrimidine-based chemoradiation used alone or with chemotherapy. Adjuvant chemotherapy or chemoradiation has been associated with survival benefit, especially in those with lymph node-positive disease.

For all treatment options, see Guide 8.

Adjuvant systemic therapies can be found in Guide 3.

### Guide 8
**Adjuvant treatment based on post-resection status**

<table>
<thead>
<tr>
<th>Is there cancer after surgery?</th>
<th>Treatment options</th>
</tr>
</thead>
</table>
| **No cancer remains (R0) and no cancer found in regional nodes or Carcinoma in situ at surgical margin** | • Observation  
• Systemic therapy (preferred) (see Guide 3)  
• Clinical trial (preferred)  
• Fluoropyrimidine-based chemoradiation |
| **Microscopic cancer cells remain (R1) or Cancer found in regional nodes** | • Systemic therapy (preferred) (see Guide 3)  
• Clinical trial (preferred)  
• Fluoropyrimidine-based chemoradiation  
• Fluoropyrimidine-based or gemcitabine-based chemotherapy followed by fluoropyrimidine-based chemoradiation  
• Fluoropyrimidine-based chemoradiation followed by fluoropyrimidine-based or gemcitabine-based chemotherapy |
| **Visible cancer remains (R2)** | • See treatment for unresectable disease |
**T1b or larger**
A T1b tumor has invaded the muscle layer of the gallbladder wall.

Before starting treatment, you might have the following:

- Multiphasic abdominal and pelvic CT with IV contrast
- Multiphasic abdominal and pelvic MRI with IV contrast
- Chest CT with or without contrast
- Staging laparoscopy

**Resectable**
A tumor that can be removed with surgery is called resectable. For a tumor that is T1b or greater, surgery might be possible. Treatment is surgery to remove a part of the liver (hepatic resection), nearby lymph nodes (lymphadenectomy), and possibly the bile duct.

**Unresectable**
An unresectable tumor cannot be removed with surgery.

Before treatment begins, tumor tests might include:

- Microsatellite instability (MSI) and/or mismatch repair (MMR) testing
- Germline testing for those with MMR deficient (dMMR)/MSI-high (MSI-H) tumors or a family history that suggests *BRCA1* or *BRCA2* mutations
- Molecular testing that may include *NTRK* gene testing

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 for an unresectable tumor include:

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

Systemic therapy or a clinical trial are the preferred treatments. Palliative radiation therapy is treatment to help with pain or discomfort. Best supportive care is used with other treatments to improve quality of life.

Systemic therapy options for tumor that is T1b or larger can be found in Guide 4.

---

Surgery should be performed by an experienced surgeon who is prepared to completely remove the tumor.
Found on imaging

Sometimes, gallbladder cancer 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. Treatment will be based on if the tumor is resectable or unresectable.

Tests
Before starting treatment, you might have imaging and blood tests. Tumor markers known as CA 19-9 and CEA might be measured as a baseline before treatment to see if there are any changes after treatment.

An operation called a staging laparoscopy might be done to stage your cancer. 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. If you have jaundice, biliary drainage might be done to see if it can relieve any bile duct blockage.

Ask questions about the tests and procedures you might have. You will meet with a surgeon during this time.

For possible tests and procedures you might have, see Guide 9.

Guide 9
Tests: Tumor found on imaging

- Medical history and physical exam
- Multiphasic CT with contrast of the abdomen and pelvis
- Multiphasic MRI with contrast of the abdomen and pelvis
- Chest CT with or without contrast
- Liver function tests (LFTs)
- Appointment with a surgeon
- Assess liver function and health (liver reserve)
- Consider CEA as a baseline for future CEA tests
- Consider CA 19-9 as a baseline for future CA 19-9 tests
- Consider staging laparoscopy
- Biliary drainage
Resectable
For a tumor that is resectable, you will have surgery to remove the entire gallbladder (cholecystectomy), part of the liver (en bloc hepatic resection), lymph nodes (lymphadenectomy), and possibly the bile duct. You might have systemic therapy before surgery called neoadjuvant therapy. Neoadjuvant therapy is used to reduce the size of the tumor or amount of cancer. This might make it easier to remove the tumor.

Treatment after surgery
Adjuvant therapy is treatment after surgery. It is based on how much cancer remains after surgery called post-resection status. The preferred adjuvant treatment options are systemic therapy or a clinical trial. Other options include fluoropyrimidine-based chemoradiation used alone or with chemotherapy. Adjuvant chemotherapy or chemoradiation has been associated with survival benefit, especially in those with lymph node-positive disease.

For all adjuvant treatment options, see Guide 8.

Unresectable
When a tumor cannot be removed with surgery, it is called unresectable. A sample of your tumor might have MSI/MMR testing and molecular testing. For those with dMMR/MSI-H tumors or a family history suggestive of BRCA1 or BRCA2 mutations, germline testing might be done and you might be referred to a genetic counselor. Testing may also include NTRK gene fusion testing.

Guide 10
Adjuvant systemic therapy options: Resectable gallbladder cancer

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>Capecitabine</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-fluorouracil with oxaliplatin</td>
</tr>
<tr>
<td>Capecitabine with oxaliplatin</td>
</tr>
<tr>
<td>Gemcitabine with capecitabine</td>
</tr>
<tr>
<td>Gemcitabine with cisplatin</td>
</tr>
<tr>
<td>5-fluorouracil with cisplatin</td>
</tr>
<tr>
<td>Capecitabine with cisplatin</td>
</tr>
<tr>
<td>5-fluorouracil</td>
</tr>
<tr>
<td>Gemcitabine</td>
</tr>
</tbody>
</table>
Treatment options
Unresectable treatment options include the following:

- Systemic therapy (preferred), see Guide 11
- Clinical trial (preferred)
- Palliative radiation therapy
- Best supportive care

Systemic therapy or a clinical trial are the preferred treatment options. Palliative radiation therapy is treatment to help with pain or discomfort. Best supportive care is used with other treatments to improve quality of life.

Guide 11
Systemic therapy options: Unresectable gallbladder cancer

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>Gemcitabine with cisplatin</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
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</thead>
<tbody>
<tr>
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<tr>
<td>5-fluorouracil with cisplatin</td>
</tr>
<tr>
<td>Capecitabine with cisplatin</td>
</tr>
<tr>
<td>Capecitabine with oxaliplatin</td>
</tr>
<tr>
<td>Gemcitabine with capecitabine</td>
</tr>
<tr>
<td>Gemcitabine with oxaliplatin</td>
</tr>
<tr>
<td>Gemcitabine with cisplatin and albumin-bound paclitaxel</td>
</tr>
<tr>
<td>Single agents: 5-fluorouracil or capecitabine or gemcitabine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Used in some cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>For NTRK gene fusion-positive tumors:</td>
</tr>
<tr>
<td>Entrectinib</td>
</tr>
<tr>
<td>Larotrectinib</td>
</tr>
<tr>
<td>For MSI-H/dMMR tumors:</td>
</tr>
<tr>
<td>Pembrolizumab</td>
</tr>
</tbody>
</table>
Disease progression

When unresectable cancer progresses during or after systemic therapy, then your medical oncologists might try a different systemic therapy from Guide 11.

For disease progression, the preferred option is FOLFOX. FOLFOX is a combination of chemotherapy drugs that includes 5-fluorouracil (5-FU), leucovorin, and oxaliplatin. FOLFIRI is a combination of 5-FU with leucovorin and irinotecan. If your tumor has a specific gene mutation, then you might receive drug therapy that targets the mutation. See Guide 12.

Guide 12
Systemic therapy options: Disease progression

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>FOLFOX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other recommended</td>
<td>FOLFIRI</td>
</tr>
<tr>
<td></td>
<td>Regorafenib</td>
</tr>
<tr>
<td></td>
<td>Preferred and other recommended options listed in Guide 11</td>
</tr>
<tr>
<td>Used in some cases</td>
<td>For NTRK gene fusion-positive tumors:</td>
</tr>
<tr>
<td></td>
<td>Entrectinib</td>
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<td>For MSI-H/dMMR tumors:</td>
</tr>
<tr>
<td></td>
<td>Pembrolizumab</td>
</tr>
</tbody>
</table>

A preferred treatment option is proven to be more effective.
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 may turn white.

Testing

If you have jaundice with gallbladder cancer, you will have tests found in Guide 13.

Your doctor will conduct a medical history and physical exam. You will have blood tests, imaging tests, and a cholangiography. A cholangiography is an x-ray of the bile ducts. Magnetic resonance cholangiopancreatography (MRCP) is preferred type of cholangiography.

During this time, you might meet with a surgeon to learn about treating your jaundice and cancer. You might have a staging laparoscopy.

Guide 13
Tests: Jaundice with gallbladder cancer

Medical history and physical exam
Liver function tests (LFTs)
Chest CT with or without contrast
Multiphasic CT with contrast of the abdomen and pelvis
Multiphasic MRI with contrast of the abdomen and pelvis
Cholangiography (magnetic resonance cholangiopancreatography [MRCP] is preferred)
Appointment with a surgeon
Consider CEA as a baseline for future CEA tests
Consider CA 19-9 as a baseline for future CA 19-9 tests
Consider staging laparoscopy
Biliary drainage
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) with percutaneous transhepatic cholangiography (PTC) are often used together to treat jaundice.

**Treatment**
Jaundice may be caused by the cancer. The tumor can grow large and block the fluid from draining from the bile ducts. If you have jaundice, your doctor will consider draining the fluid before chemotherapy starts.

Treatment will be based on if the tumor is resectable or unresectable. See Guide 14.

### Guide 14
**Treatment options: Jaundice with gallbladder cancer**

<table>
<thead>
<tr>
<th>Resectable</th>
<th>Cholecystectomy with surgery to remove:</th>
<th>Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Consider neoadjuvant therapy (see Guide 15)</td>
<td>• Part of the liver (en bloc hepatic resection)</td>
<td>• MSI/MMR testing</td>
</tr>
<tr>
<td>• Clinical trial</td>
<td>• Lymph nodes (lymphadenectomy)</td>
<td>• Consider additional molecular testing</td>
</tr>
<tr>
<td></td>
<td>• Bile duct</td>
<td></td>
</tr>
</tbody>
</table>

**Unresectable**

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

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Gallbladder and Bile Duct Cancers, 2020
Resectable
A tumor that can be removed with surgery is resectable. If the disease is spreading outside of the gallbladder and the tumor is large, your doctor may suggest a clinical trial or neoadjuvant therapy.

Neoadjuvant therapy is given to shrink the tumor and slow the spread of cancer. After this therapy, your doctor may drain the fluid of the blocked bile ducts. For neoadjuvant chemotherapy options, see Guide 15.

Surgery
For a tumor that is resectable, you will have surgery to remove the gallbladder (cholecystectomy), part of the liver (en bloc hepatic resection), lymph nodes (lymphadenectomy), and the bile duct.

Treatment after surgery
Adjuvant therapy is treatment after surgery. It is based on how much cancer remains after surgery called post-resection status. The preferred adjuvant treatment options are systemic therapy or a clinical trial. Other options include fluoropyrimidine-based chemoradiation used alone or with chemotherapy.

Guide 15
Neoadjuvant chemotherapy options: Resectable gallbladder cancer

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>–</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other recommended</strong></td>
<td></td>
</tr>
<tr>
<td>• 5-fluorouracil with oxaliplatin</td>
<td></td>
</tr>
<tr>
<td>• Capecitabine with oxaliplatin</td>
<td></td>
</tr>
<tr>
<td>• Gemcitabine with capecitabine</td>
<td></td>
</tr>
<tr>
<td>• Gemcitabine with cisplatin</td>
<td></td>
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<tr>
<td>• 5-fluorouracil with cisplatin</td>
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<tr>
<td>• Capecitabine with cisplatin</td>
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<tr>
<td>• Gemcitabine with cisplatin and albumin-bound paclitaxel</td>
<td></td>
</tr>
<tr>
<td>• Gemcitabine with oxaliplatin</td>
<td></td>
</tr>
<tr>
<td>• Single agents: 5-fluorouracil or capecitabine or gemcitabine</td>
<td></td>
</tr>
</tbody>
</table>
Gallbladder cancer

Jaundice with cancer

For all adjuvant treatment options, see Guide 16.

For adjuvant systemic (drug) therapy options only, see Guide 17.

Guide 16
Adjuvant treatment based on post-resection status

<table>
<thead>
<tr>
<th>Is there cancer after surgery?</th>
<th>Treatment options</th>
</tr>
</thead>
</table>
| No cancer remains (R0) and no cancer found in regional nodes or Carcinoma in situ at surgical margin | • Observation  
• Systemic therapy (preferred) (see Guide 17)  
• Clinical trial (preferred)  
• Fluoropyrimidine-based chemoradiation |
| Microscopic cancer cells remain (R1) or Cancer found in regional nodes | • Systemic therapy (preferred) (see Guide 17)  
• Clinical trial (preferred)  
• Fluoropyrimidine-based chemoradiation  
• Fluoropyrimidine-based or gemcitabine-based chemotherapy followed by fluoropyrimidine-based chemoradiation  
• Fluoropyrimidine-based chemoradiation followed by fluoropyrimidine-based or gemcitabine-based chemotherapy |
| Visible cancer remains (R2) | • See treatment for unresectable disease |

Guide 17
Adjuvant systemic therapy options

| Preferred | • Capecitabine |
| Other | • 5-fluorouracil with oxaliplatin  
• Capecitabine with oxaliplatin  
• Gemcitabine with capecitabine  
• Gemcitabine with cisplatin  
• 5-fluorouracil with cisplatin  
• Capecitabine with cisplatin  
• 5-fluorouracil  
• Gemcitabine |
Unresectable
When a tumor cannot be removed with surgery, it is called unresectable. The tumor will be biopsied and tested for MSI/MMR, gene fusions, and other mutations using molecular testing. You might have germline testing and/or be referred to a genetic counselor.

Unresectable treatment options include:

- Systemic therapy (preferred), see Guide 18
- Clinical trial (preferred)
- Palliative radiation therapy
- Best supportive care

Systemic therapy or a clinical trial are the preferred treatment options. Palliative radiation therapy is treatment to help with pain or discomfort. Best supportive care is used with other treatments to improve quality of life.

Guide 18
Systemic therapy options: Unresectable and metastatic gallbladder cancer

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>• Gemcitabine with cisplatin</th>
</tr>
</thead>
</table>
| Other recommended | • 5-fluorouracil with oxaliplatin  
|                  | • 5-fluorouracil with cisplatin  
|                  | • Capecitabine with cisplatin  
|                  | • Capecitabine with oxaliplatin  
|                  | • Gemcitabine with capecitabine  
|                  | • Gemcitabine with oxaliplatin  
|                  | • Gemcitabine with cisplatin and albumin-bound paclitaxel  
|                  | • Single agents: 5-fluorouracil or capecitabine or gemcitabine |

Used in some cases
For NTRK gene fusion-positive tumors:
• Entrectinib  
• Larotrectinib
For MSI-H/dMMR tumors:
• Pembrolizumab
Surveillance

After completing treatment, 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.

Metastatic disease

Metastatic cancer is cancer that has spread to distant sites in the body. Your doctor will do a biopsy and MSI testing. Treatment options are based on the size and location of the cancer.

Treatment options for metastatic gallbladder cancer include:

- Systemic therapy (preferred), see Guide 18
- 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.

Disease progression

If metastatic disease 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. FOLFIRI is a combination of 5-FU with leucovorin and irinotecan. If your tumor has a specific gene mutation, then you might receive drug therapy that targets the mutation. See Guide 19.

Guide 19
Systemic therapy options: Metastatic disease progression

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>• FOLFOX</th>
</tr>
</thead>
</table>
| Other recommended | • FOLFIRI  
• Regorafenib  
• Preferred and other recommended options listed in Guide 18 |
| Used in some cases | For NTRK gene fusion-positive tumors:  
• Entrectinib  
• Larotrectinib  
For MSI-H/dMMR tumors:  
• Pembrolizumab |
Review

- 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), or has spread to other parts of the body (metastatic).

- Treatment options for gallbladder cancer may include surgery, chemotherapy, chemoradiation, palliative radiation therapy, clinical trial, 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 specific gene mutation, then you might receive drug therapy that targets the mutation.

- Best supportive care may offer symptom relief.
5
Intrahepatic bile duct cancer

60 Overview
61 Cancer stages
62 Testing
64 Treatment
65 Resectable
67 Unresectable
68 Metastatic
69 Review
A cholangiocarcinoma is a cancer of the bile duct. Intrahepatic cholangiocarcinoma (ICC) is cancer that is found in the bile ducts of the liver. It is also known as intrahepatic bile duct cancer. Together, you and your doctor will choose the treatment plan that is best for you.

**Overview**

A cholangiocarcinoma 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 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.

**Liver anatomy**

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. It is not liver cancer.
There can be more than one tumor and it can be found in the small ductules or in the larger hepatic ducts. In most cases, surgery cannot remove all of the tumor. Treatment is to prevent or slow the spread of cancer.

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.

The layers of the bile duct wall are:

- Epithelium - A thin, moist (mucous) layer of tissue that covers the inside of the duct
- Lamina propria - A type of connective tissue found under the epithelium membrane
- Muscle – A type of soft tissue
- Perimuscular fibrous tissue – A type of connective tissue that surrounds muscle
- Serosa – An outer membrane

Cancer stages for intrahepatic bile duct cancer can be found in Guide 20.

<table>
<thead>
<tr>
<th>Guide 20 Intrahepatic bile duct cancer stages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 0</strong></td>
</tr>
<tr>
<td>• Tis, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 1</strong></td>
</tr>
<tr>
<td><strong>Stage 1A</strong></td>
</tr>
<tr>
<td>• T1a, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 1B</strong></td>
</tr>
<tr>
<td>• T1b, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 2</strong></td>
</tr>
<tr>
<td>• T2, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 3</strong></td>
</tr>
<tr>
<td><strong>Stage 3A</strong></td>
</tr>
<tr>
<td>• T3, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 3B</strong></td>
</tr>
<tr>
<td>• T4, N1, M0</td>
</tr>
<tr>
<td><strong>Stage 4</strong></td>
</tr>
<tr>
<td>• Any T, Any N, M1</td>
</tr>
</tbody>
</table>
**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)
- **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
- **T2a** One tumor that has grown into blood vessels inside the liver (intrahepatic) or multiple tumors that may or may not be in intrahepatic 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 pancreatoduodenal, and portal vein lymph nodes.

- **N0** No cancer in regional lymph nodes
- **N1** Cancer is found in 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 lung.

- **M0** means no distant metastasis
- **M1** means distant metastasis is found. This is metastatic cancer.

**Testing**
Once it is confirmed that the isolated tumor found on imaging is not liver cancer (hepatocellular carcinoma), then you will have tests found in Guide 21.

Blood tests will measure CEA, CA 19-9, AFP (alpha-fetoprotein), 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 treatment can wake up (or reactivate) the virus. If this happens, it can cause harm to the liver.

During this time, 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 multiphasic CT of the abdomen and pelvis, and a multiphasic MRI of the abdomen and pelvis. Imaging of this area allows your doctor to see 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.

### Guide 21

**Tests: Intrahepatic bile duct cancer**

- Medical history and physical exam
- Multiphasic CT with contrast of the abdomen and pelvis
- Multiphasic MRI with contrast of the abdomen and pelvis
- Chest CT with or without contrast
- Consider CEA as a baseline for future CEA tests
- Consider CA 19-9 as a baseline for future CA 19-9 tests
- Liver function tests (LFTs)
- Appointment with a surgeon
- Esophagogastroduodenoscopy (EGD) and colonoscopy
- Consider viral hepatitis tests
- Consider biopsy
- Consider alpha-fetoprotein (AFP)
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 will be done. For those with dMMR/MSI-H tumors or a family history that suggests BRCA1 or BRCA2 mutations, then you might have germline testing. You might be referred to a genetic counselor. Additional molecular testing might be considered.

Treatment options can be found in Guide 22.

<table>
<thead>
<tr>
<th>Guide 22</th>
<th>Treatment options: Intrahepatic bile duct cancer</th>
</tr>
</thead>
</table>
| **Resectable** | • Consider staging laparoscopy  
• Resection with possible lymphadenectomy  
• For adjuvant therapy, see Guide 23  
• Surveillance |
| **Unresectable** | • MSI/MMR testing  
• Consider additional molecular testing  
• Systemic therapy, see Guide 25  
• Clinical trial  
• Chemoradiation (EBRT with fluoropyrimidine)  
• Consider locoregional therapy (EBRT or arterially directed therapy)  
• Best supportive care |
| **Metastatic** | • MSI/MMR testing  
• Consider additional molecular testing  
• Systemic therapy, see Guide 25  
• Clinical trial  
• Consider locoregional therapy (EBRT or arterially directed therapy)  
• Best supportive care |
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 wedge 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 based on the post-resection status, which is the amount of cancer that remains after surgery.

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

For all treatment options, see Guide 23.

Guide 23
Adjuvant treatment based on post-resection status

<table>
<thead>
<tr>
<th>Does cancer remain after surgery?</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No cancer remains (R0)</strong></td>
<td>• Observation</td>
</tr>
<tr>
<td></td>
<td>• Systemic therapy (preferred) (<a href="#">see Guide 24</a>)</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial (preferred)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Microscopic cancer cells remain (R1)</strong> or Cancer found in regional nodes</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Systemic therapy (<a href="#">see Guide 24</a>)</td>
<td></td>
</tr>
<tr>
<td>• Fluopyrimidine-based chemoradiation</td>
<td></td>
</tr>
<tr>
<td>• Fluopyrimidine-based or gemcitabine-based chemotherapy followed by fluopyrimidine-based chemoradiation</td>
<td></td>
</tr>
<tr>
<td>• Fluopyrimidine-based chemoradiation followed by fluopyrimidine-based or gemcitabine-based chemotherapy</td>
<td></td>
</tr>
<tr>
<td>• Clinical trial</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Visible cancer remains (R2)</strong></th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• See treatment for unresectable disease</td>
<td></td>
</tr>
</tbody>
</table>
Adjuvant systemic therapies can be found in Guide 24.

R0
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.

R1
If microscopic cancer cells remain (R1) or cancer is found in nearby lymph nodes, then treatment options include systemic therapy, fluoropyrimidine-based chemoradiation used alone or with chemotherapy, or a clinical trial. Adjuvant chemotherapy or chemoradiation has been associated with survival benefit, especially in those with lymph node-positive disease. After treatment, you will enter surveillance.

R2
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 see if cancer returns called recurrence. During this time you might have multiphasic CT and MRI scans every 3 to 6 months for 2 years, then every 6 to 12 months for up to 5 years, or as needed. Your doctor will discuss a surveillance plan with you. It is important to keep any follow-up doctor visits and imaging test appointments.

---

**Guide 24**

**Adjuvant systemic therapy options: Intrahepatic bile duct cancer**

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>• Capecitabine</th>
</tr>
</thead>
</table>
| Other recommended | • 5-fluorouracil with oxaliplatin  
|                   | • Capecitabine with oxaliplatin  
|                   | • Gemcitabine with capecitabine  
|                   | • Gemcitabine with cisplatin  
|                   | • 5-fluorouracil with cisplatin  
|                   | • Capecitabine with cisplatin  
|                   | • 5-fluorouracil  
|                   | • Gemcitabine |
Unresectable

An unresectable tumor cannot be removed with surgery. However, there are a number of treatment options.

These include the following:

- Systemic therapy, see Guide 25
- Clinical trial
- Chemoradiation (EBRT with fluoropyrimidine)
- Locoregional radiation therapy or arterially directed therapy
- Best supportive care

Guide 25

Systemic therapy options: Unresectable and metastatic

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>• Gemcitabine with cisplatin</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 5-fluorouracil with oxaliplatin</td>
</tr>
<tr>
<td>• 5-fluorouracil with cisplatin</td>
</tr>
<tr>
<td>• Capecitabine with cisplatin</td>
</tr>
<tr>
<td>• Capecitabine with oxaliplatin</td>
</tr>
<tr>
<td>• Gemcitabine with capecitabine</td>
</tr>
<tr>
<td>• Gemcitabine with oxaliplatin</td>
</tr>
<tr>
<td>• Gemcitabine with cisplatin and albumin-bound paclitaxel</td>
</tr>
<tr>
<td>• Single agents: 5-fluorouracil or capecitabine or gemcitabine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Used in some cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>For NTRK gene fusion-positive tumors:</td>
</tr>
<tr>
<td>• Entrectinib</td>
</tr>
<tr>
<td>• Larotrectinib</td>
</tr>
<tr>
<td>For MSI-H/dMMR tumors:</td>
</tr>
<tr>
<td>• Pembrolizumab</td>
</tr>
</tbody>
</table>
**Disease progression**

If metastatic 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. FOLFIRI is a combination of 5-FU with leucovorin and irinotecan. If your tumor has a specific gene mutation such as *NTRK*, MSI-H/dMMR, *FGFR2*, or *IDH1*, then you might receive drug therapy that targets the mutation. See Guide 26.

**Metastatic**

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

Treatment options include the following:

- Systemic therapy, see Guide 25
- Clinical trial
- Locoregional therapy radiation therapy or arterially directed therapy
- Best supportive care

Treatment options will be based on your wishes and your doctor’s recommendations. Best supportive care is always given.

---

**Guide 26**

**Systemic therapy options: Disease progression**

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>• FOLFOX</th>
</tr>
</thead>
</table>
| Other recommended | • FOLFIRI  
• Regorafenib  
• Preferred and other recommended options listed in Guide 25 |
| Used in some cases | For *NTRK* gene fusion-positive tumors:  
• Entrectinib  
• Larotrectinib  
For MSI-H/dMMR tumors:  
• Pembrolizumab  
For cholangiocarcinoma with *FGFR2* fusions or rearrangements:  
• Pemigatinib  
For cholangiocarcinoma with *IDH1* mutations:  
• Ivosidenib |
Disease progression
If metastatic 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. FOLFIRI is a combination of 5-FU with leucovorin and irinotecan. If your tumor has a specific gene mutation, then you might receive drug therapy that targets the mutation. If your tumor has a specific gene mutation such as \textit{NTRK}, MSI-H/dMMR, \textit{FGFR2}, or \textit{IDH1}, then you might receive drug therapy that targets the mutation. See Guide 26.

Review

- Not all bile duct cancers are the same.
- A cholangiocarcinoma 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), or if it has spread to other parts of the body (metastatic).
- 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 specific gene mutation such as \textit{NTRK}, MSI-H/dMMR, \textit{FGFR2}, or \textit{IDH1}, then you might receive drug therapy that targets the mutation.
Extrahepatic bile duct cancer

71 Overview
72 Testing
73 Perihilar cancer stages
74 Distal cancer stages
76 Treatment options
76 Resectable
80 Unresectable
82 Metastatic
83 Review
Extrahepatic bile ducts are small tubes that carry bile outside of the liver. They are made up of the common hepatic duct and the common bile duct. Extrahepatic bile duct cancers include distal and perihilar types. The type is based on the location of the cancer. 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. Together, you and your doctor will choose the treatment plan that is best for you.

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.
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.

A cholangiocarcinoma is a rare cancer that forms in the bile ducts. Intrahepatic cholangiocarcinoma (ICC) is found inside the liver. Extrahepatic cholangiocarcinoma (ECC) is found outside the liver. Extrahepatic bile duct cancers are also known as ECC.

A team of experts should manage your care.

**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. If your doctor suspects extrahepatic bile duct cancer, then you might have the tests found in Guide 27.

**Imaging tests**

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

**Guide 27**

**Tests: Extrahepatic bile duct cancer**

- Medical history and physical exam
- Multiphasic abdominal and pelvic CT and MRI with IV contrast (to look for blood vessel involvement)
- Chest CT with or without contrast
- Cholangiography (magnetic resonance cholangiopancreatography [MRCP] is preferred)
- Consider CEA as a baseline for future CEA tests
- Consider CA 19-9 as a baseline for future CA 19-9 tests
- Liver function tests (LFTs)
- Consider endoscopic ultrasound (EUS) after appointment with a surgeon
- Consider serum IgG4 to rule out autoimmune cholangitis. Those with with IgG-4–related cholangiopathy should be referred to an expert treatment center.
You may have a test called a cholangiography to see if the bile ducts are blocked. A type of cholangiography called a magnetic resonance cholangiopancreatography (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.

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### Perihilar cancer stages

Perihilar bile duct 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 28.

**Guide 28**

**Perihilar bile duct cancer stages**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 0</strong></td>
<td>Tis, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 1</strong></td>
<td>T1, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 2</strong></td>
<td>T2, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 3</strong></td>
<td></td>
</tr>
<tr>
<td>Stage 3A</td>
<td>T3, N0, M0</td>
</tr>
<tr>
<td>Stage 3B</td>
<td>T4, N0, M0</td>
</tr>
<tr>
<td>Stage 3C</td>
<td>Any T, N1, M0</td>
</tr>
<tr>
<td><strong>Stage 4</strong></td>
<td></td>
</tr>
<tr>
<td>Stage 4A</td>
<td>Any T, N2, M0</td>
</tr>
<tr>
<td>Stage 4B</td>
<td>Any T, Any N, M1</td>
</tr>
</tbody>
</table>
**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)
- **T1** Tumor is confined to the duct, but has grown through the muscle layer or the perimuscular fibrous tissue
- **T2** Tumor has grown beyond the wall of the bile duct to surrounding adipose (fat) tissue, or 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**
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. These include hilar, cystic duct, common bile duct, hepatic artery, posterior pancreatoduodenal, and portal vein lymph nodes.

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

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

**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 29.
**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**
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. These include hilar, cystic duct, common bile duct, hepatic artery, posterior pancreaticoduodenal, and portal vein lymph nodes.

- **N0** No cancer is found in regional lymph node
- **N1** Cancer is found in 1 to 3 lymph nodes
- **N2** Cancer is found in 4 or more 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 liver, lungs, and the lining that surrounds the abdominal organs (visceral peritoneum).

- **M0** means no distant metastasis
- **M1** means distant metastasis is found. This is metastatic cancer.

---

**Guideline 29**
**Distal bile duct cancer stages**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 0</strong></td>
<td>• Tis, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 1</strong></td>
<td>• T1, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 2</strong></td>
<td>• T2, N1, M0</td>
</tr>
<tr>
<td><strong>Stage 2A</strong></td>
<td>• T1, N1, M0</td>
</tr>
<tr>
<td><strong>Stage 2B</strong></td>
<td>• T2, N1, M0</td>
</tr>
<tr>
<td><strong>Stage 3</strong></td>
<td>• T3, N1, M0</td>
</tr>
<tr>
<td><strong>Stage 3A</strong></td>
<td>• T1, N2, M0</td>
</tr>
<tr>
<td><strong>Stage 3B</strong></td>
<td>• T4, N0, M0</td>
</tr>
<tr>
<td><strong>Stage 4</strong></td>
<td>• Any T, Any N, M1</td>
</tr>
</tbody>
</table>
Treatment options

Treatment is based on if the cancer is:

- Resectable
- Unresectable
- Metastatic

For an overview of treatment options, see Guide 30.

Resectable

Before surgery you might have biliary drainage. Exploratory surgery may be performed when suspicion of cancer is high. A staging laparoscopy might be used to gain a better understanding of the size and location of the tumor. 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

Guide 30
Treatment options: Extrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Resectable</th>
<th>Unresectable</th>
<th>Metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Exploratory surgery</td>
<td>• Biliary drainage, if needed</td>
<td>• Biliary drainage, if needed</td>
</tr>
<tr>
<td>• Consider staging laparoscopy</td>
<td>• Evaluate if candidate for liver transplant</td>
<td>• Biopsy</td>
</tr>
<tr>
<td>• Consider biliary drainage before surgery</td>
<td>• MSI/MMR testing</td>
<td>• MSI/MMR testing</td>
</tr>
<tr>
<td>• Multidisciplinary review</td>
<td>• Consider additional molecular testing</td>
<td>• Additional molecular testing</td>
</tr>
<tr>
<td>• Surgery followed by adjuvant therapy (see Guide 31)</td>
<td>• Systemic therapy, see Guide 33</td>
<td>• Systemic therapy, see Guide 33</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial</td>
<td>• Clinical trial</td>
</tr>
<tr>
<td></td>
<td>• Chemoradiation (EBRT with fluoropyrimidine)</td>
<td>• Clinical trial</td>
</tr>
<tr>
<td></td>
<td>• Palliative EBRT</td>
<td>• Best supportive care</td>
</tr>
<tr>
<td></td>
<td>• Best supportive care</td>
<td></td>
</tr>
</tbody>
</table>
discuss if surgery is safe for you and whether the cancer can be removed. This is called multidisciplinary review.

Surgery
Surgery is based on where the cancer is located in your body. 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
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
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) may be needed for tumors in the hilar area.

Whipple procedure
The image on the left shows cancer in the head of the pancreas. The image on the right shows how the organs might be reconnected during a Whipple procedure.
Treatment after surgery
Treatment after surgery is called adjuvant therapy. It is based on the post-resection status, which is the amount of cancer that remains after surgery. The goal is to kill any remaining microscopic cancer cells.

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

For adjuvant treatment options, see Guide 31.

Guide 31
Adjuvant treatment based on post-resection status

<table>
<thead>
<tr>
<th>Does cancer remain after surgery?</th>
<th>Treatment options</th>
</tr>
</thead>
</table>
| **No cancer remains (R0) and no cancer found in regional nodes or Carcinoma in situ at surgical margin** | • Observation  
• Systemic therapy (see Guide 32)  
• Fluoropyrimidine chemoradiation  
• Clinical trial |
| **Microscopic cancer cells remain (R1) or Cancer found in regional nodes** | • Systemic therapy (see Guide 32)  
• Fluoropyrimidine-based chemoradiation  
• Fluoropyrimidine-based or gemcitabine-based chemotherapy followed by fluoropyrimidine-based chemoradiation  
• Fluoropyrimidine-based chemoradiation followed by fluoropyrimidine-based or gemcitabine-based chemotherapy  
• Clinical trial |
| **Visible cancer remains (R2)** | • See treatment for unresectable disease |

Adjuvant systemic therapies can be found in Guide 32.
Extrahepatic bile duct cancer

Resectable

R0
If no cancer remains (R0), options include observation, systemic therapy, fluoropyrimidine chemoradiation, or a clinical trial. Observation is sometimes called watch-and-wait. After treatment, you will enter surveillance.

R1
If microscopic cancer cells remain (R1) or cancer is found in nearby lymph nodes, then treatment options include systemic therapy, fluoropyrimidine-based chemoradiation used alone or with chemotherapy, or a clinical trial. Adjuvant chemotherapy or chemoradiation has been associated with survival benefit, especially in those with lymph node-positive disease. After treatment, you will enter surveillance.

R2
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 see if cancer returns called recurrence. 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. Your doctor will discuss with you a surveillance plan. It is important to keep any follow-up doctor visits and imaging test appointments.

Guide 32
Adjuvant systemic therapy options: Extrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>• Capecitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• 5-fluorouracil with oxaliplatin</td>
</tr>
<tr>
<td></td>
<td>• Capecitabine with oxaliplatin</td>
</tr>
<tr>
<td></td>
<td>• Gemcitabine with capecitabine</td>
</tr>
<tr>
<td></td>
<td>• Gemcitabine with cisplatin</td>
</tr>
<tr>
<td></td>
<td>• 5-fluorouracil with cisplatin</td>
</tr>
<tr>
<td></td>
<td>• Capecitabine with cisplatin</td>
</tr>
<tr>
<td></td>
<td>• 5-fluorouracil</td>
</tr>
<tr>
<td></td>
<td>• Gemcitabine</td>
</tr>
</tbody>
</table>
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

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 bridging therapy.

Treatment

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 doctor why one treatment might work better in your situation. Not everyone responds the same way to treatment. Some people do better than expected. Others do worse. Talk to your doctor about what to expect from treatment.

Treatment options include the following:

- Systemic therapy, see Guide 33
- Clinical trial
- Chemoradiation (EBRT with fluoropyrimidine)
- Palliative radiation therapy (EBRT)
- Best supportive care
Systemic therapy
If you have jaundice, then your doctor will consider biliary drainage before starting systemic therapy. The preferred systemic therapy is gemcitabine with cisplatin. However, there are many recommended options. See Guide 33.

Disease progression
If unresectable 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. FOLFIRI is a combination of 5-FU with leucovorin and irinotecan. If your tumor has a specific gene alteration such as NTRK, MSI-H/dMMR, FGFR2, or IDH1, then you might receive drug therapy that targets the mutation. See Guide 34.

Guide 33
Systemic therapy options: Unresectable and metastatic

<table>
<thead>
<tr>
<th>Preferred option</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Gemcitabine with cisplatin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 5-fluorouracil with oxaliplatin</td>
</tr>
<tr>
<td>• 5-fluorouracil with cisplatin</td>
</tr>
<tr>
<td>• Capecitabine with cisplatin</td>
</tr>
<tr>
<td>• Capecitabine with oxaliplatin</td>
</tr>
<tr>
<td>• Gemcitabine with capecitabine</td>
</tr>
<tr>
<td>• Gemcitabine with oxaliplatin</td>
</tr>
<tr>
<td>• Gemcitabine with cisplatin and albumin-bound paclitaxel</td>
</tr>
<tr>
<td>• Single agents: 5-fluorouracil or capecitabine or gemcitabine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Used in some cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>For NTRK gene fusion-positive tumors:</td>
</tr>
<tr>
<td>• Entrectinib</td>
</tr>
<tr>
<td>• Larotrectinib</td>
</tr>
<tr>
<td>For MSI-H/dMMR tumors:</td>
</tr>
<tr>
<td>• Pembrolizumab</td>
</tr>
</tbody>
</table>
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, your doctor will attempt to treat the blocked bile duct. A biopsy may be done of the metastasis to confirm that the cancer is bile duct cancer.

**Treatment**

Treatment options include the following:

- Systemic therapy, see Guide 33
- Clinical trial
- Best supportive care

Treatment options will be based on your wishes and your doctor’s recommendations. Best supportive care is always given. You may consider joining a clinical trial. If you have jaundice, you might have biliary drainage before starting systemic therapy. Systemic therapy options can be found in Guide 33.

### Guide 34

**Systemic therapy options: Disease progression**

<table>
<thead>
<tr>
<th>Preferred option</th>
<th>FOLFOX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other recommended</td>
<td>FOLFIRI, Regorafenib, Preferred and other recommended options listed in Guide 33</td>
</tr>
<tr>
<td>Used in some cases</td>
<td>For NTRK gene fusion-positive tumors: Entrectinib, Larotrectinib</td>
</tr>
</tbody>
</table>
Disease progression
If metastatic 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. FOLFIRI is a combination of 5-FU with leucovorin and irinotecan. If your tumor has a specific gene mutation, then you might receive drug therapy that targets the mutation. If your tumor has a specific gene mutation such as NTRK, MSI-H/dMMR, FGFR2, or IDH1, then you might receive drug therapy that targets the mutation.

See Guide 34.

Review

- Not all bile duct cancers are the same.
- Extrahepatic bile ducts are small tubes that carry bile outside of the liver. They include the common hepatic duct and the common bile duct.
- A cholangiocarcinoma 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), or has spread to other parts of the body (metastatic).
- Treatment before surgery is called neoadjuvant. Treatment after surgery is called adjuvant.
- If your tumor has a specific gene mutation such as NTRK, MSI-H/dMMR, FGFR2, or IDH1, then you might receive drug therapy that targets the mutation.
7
Making treatment decisions

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

**It’s your choice**

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

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

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

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

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

**Second opinion**

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

Things you can do to prepare:

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

**Support groups**

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

**Questions to ask your doctors**

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

1. Where did the cancer start? In what type of cell? Is this cancer common?

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

3. What stage is the cancer? What does this mean?

4. What tests do you recommend for me? Will I have any genetic tests?

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

6. What if I am pregnant or want to become pregnant?

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

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

9. Who will talk with me about the next steps? When?

10. What can I do before my next appointment?
Questions to ask about options

1. What will happen if I do nothing?

2. How do my age, overall health, and other factors affect my options?

3. What if I am pregnant? What if I’m planning to get pregnant in the near future?

4. Which option is proven to work best?

5. Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?

6. What are the possible complications and side effects?

7. Is surgery an option? Why or why not?

8. How do you know if treatment is working? How will I know if treatment is working?

9. What are my options if my treatment stops working?

10. What can be done to prevent or relieve the side effects of treatment?

11. Are there any life-threatening side effects of this treatment? How will I be monitored?

12. Can I stop treatment at any time? What will happen if I stop treatment?

13. Are there any clinical trials I should consider for my condition?
Questions to ask about treatment

1. What are my treatment choices? What are the benefits and risks?

2. Which treatment do you recommend and why?

3. How long do I have to decide?

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

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

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

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

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

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

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

11. Which treatment will give me the best quality of life? Which treatment will extend my life? By how long? What will happen if I decide not to get any active treatment?

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

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

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

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

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

5. Will I have more than one surgery? Why?

6. Will surgery be open or laparoscopic? What will the recovery from surgery be like?

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

8. Will I have surgery to remove the tumor or part of my liver (partial hepatectomy)? Am I a candidate for a liver transplant?

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

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

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

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

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

3. What does the treatment do?

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

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

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

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

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

9. How will you know the treatment is working?

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

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

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

American Cancer Society
cancer.org/cancer/gallbladder-cancer/about.html
cancer.org/cancer/bile-duct-cancer.html

Global Liver Institute
globalliver.org

MedlinePlus
medlineplus.gov/gallbladdercancer.html
medlineplus.gov/bileductcancer.html

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

Sharsheret
sharsheret.org

The Bili Project Foundation
thebiliproject.org

The Cholangiocarcinoma Foundation
cholangiocarcinoma.org

Young Survival Coalition (YSC)
youngsurvival.org
Words to know

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

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

**advanced cancer**
Cancer that has spread beyond the area near the main tumor.

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

**alpha-fetoprotein (AFP)**
A protein made by some cancers that is usually present in babies growing in the womb.

**ascites**
Abnormal buildup of fluid in the abdomen.

**best supportive care**
Treatment that improves quality of life.

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

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

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

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

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

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

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

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

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

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

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

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

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

**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 cancer cells by damaging or disrupting the making of the genetic code.

**cholangiography**
An x-ray of the exam 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.

cholelithiasis
The presence of gallstones.

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

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

colonoscopy
A procedure to work 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 uses x-rays from many angles to make a picture of the insides of the body.

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

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

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

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

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)
A cancer treatment with radiation received from a machine outside the body.

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

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.

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 DNA instructions in cells for making new cells and controlling how cells behave.

general anesthesia
A drug-induced, sleep-like state for pain relief.

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

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

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

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

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

infection
An illness caused by germs.

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

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

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.

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

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

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

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

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

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

medical history
A report of all your health events and medications.
medical oncologist
A doctor who is an expert in cancer drugs.

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

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)
The presence of 2 or more abnormal DNA parts called 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 treatment
A treatment that is given before the main treatment to reduce the cancer. Also called preoperative treatment if given before an operation.

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

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

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

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

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

pelvis
The body area between the hipbones.

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

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

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

positron emission tomography (PET)
A test that uses radioactive material to see the shape and function of body parts.

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

primary tumor
The first mass of cancer cells.

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

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

radiation therapy
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.
Words to know

**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.

**small intestine**
A digestive organ that absorbs nutrients from eaten food.

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

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

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

**surgery**
An operation to remove or repair a part of the body.

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

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

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

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

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

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

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

**visceral peritoneum**
The lining that surrounds the organs in the abdomen.

**widespread metastatic disease**
The spread of cancer from the first tumor to many new sites in the body.
This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers. It was adapted, reviewed, and published with help from the following people:

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