Hepatobiliary Cancers

LIVER, GALLBLADDER, AND BILE DUCT CANCERS

Presented with support from:

NCCN GUIDELINES FOR PATIENTS®

Available online at NCCN.org/patients
LEARNING that you have cancer can be overwhelming.

The goal of this book is to help you get the best care. It explains which cancer tests and treatments are recommended by experts in hepatobiliary cancers.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 27 leading cancer centers. Experts from NCCN have written treatment guidelines for doctors who treat hepatobiliary cancers. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of hepatobiliary cancers. Key points of the book are summarized in the related NCCN Quick Guide™. NCCN also offers patient books on colon, pancreatic, esophageal, and many other cancer types. Visit NCCN.org/patients for the full library of patient books, summaries, and other resources.
These patient guidelines for cancer care are produced by the National Comprehensive Cancer Network® (NCCN®).

The mission of NCCN is to improve cancer care so people can live better lives. At the core of NCCN are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). NCCN Guidelines® contain information to help health care workers plan the best cancer care. They list options for cancer care that are most likely to have the best results. The NCCN Guidelines for Patients® present the information from the NCCN Guidelines in an easy-to-learn format.

Panels of experts create the NCCN Guidelines. Most of the experts are from NCCN Member Institutions. Their areas of expertise are diverse. Many panels also include a patient advocate. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors.

For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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NCCN Foundation was founded by NCCN to raise funds for patient education based on the NCCN Guidelines. NCCN Foundation offers guidance to people with cancer and their caregivers at every step of their cancer journey. This is done by sharing key information from leading cancer experts. This information can be found in a library of NCCN Guidelines for Patients® and other patient education resources. NCCN Foundation is also committed to advancing cancer treatment by funding the nation’s promising doctors at the center of cancer research, education, and progress of cancer therapies.

For more information about NCCN Foundation, visit NCCNFoundation.org.
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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 NCCN to provide this information to support liver and bile duct cancer patients and their families in the hope that together we can make the cancer journey easier and more successful.
Donna R. Cryer, JD, President & CEO, Global Liver Institute. www.globalliver.org

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The Cholangiocarcinoma Foundation
The Cholangiocarcinoma Foundation is pleased to endorse this comprehensive guide that provides a reliable wealth of vital information in a readable and understandable format. It is an invaluable resource that provides patients the knowledge they need to partner with their healthcare team as they navigate the often complicated world of hepatobiliary cancers.
www.cholangiocarcinoma.org.

With generous support from

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Carl Schmidt in honor of “Prof SS”
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How to use this book

Who should read this book?

This book is about treatment for hepatobiliary cancers. These include liver (hepatocellular carcinoma), gall bladder, and bile duct (intrahepatic and extrahepatic cholangiocarcinoma) cancers. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with doctors what care is best.

Does this book include all options?

This book includes information for many situations. Thus, you will likely not get every test and treatment listed. Your treatment team can help with options. They can point out what sections apply to you. They can also give you more information. As you read this book, you may find it helpful to make a list of questions to ask your doctors.

Are the book chapters in a certain order?

Yes, early chapters may help you with treatment options found in later chapters. Starting with Part 1 may be helpful; it explains what the hepatobiliary cancers are. Knowing more about these types of cancers may help you better understand their treatment. Part 2 explains the tests doctors use for these types of cancers and what the test results mean.


Part 7 is the last chapter of the guideline. It offers some helpful tips for making treatment decisions. Here you can get sample questions to ask your doctors. You can also visit the websites listed in this section for more information on hepatobiliary cancers.

Help! What do the words mean?

In this book, many medical words are included. These are words you will likely hear from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Feel free to ask your treatment team to explain a word or phrase that you don’t understand.

Words that you may not know are defined in the text or in the Dictionary. Acronyms are also defined when first used and in the Glossary. One example is HCC for hepatocellular carcinoma.
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Learning that you have or may have cancer can be overwhelming. Part 1 briefly describes the hepatobiliary system and cancer that starts here. You will also learn about risk factors and symptoms for each type of hepatobiliary cancer.

The hepatobiliary system

The hepatobiliary system is a part of the digestive system. The digestive system involves taking in food, breaking it down (digestion), absorbing nutrients, and removing waste from the body. The function of the hepatobiliary system is to help absorb nutrients and help remove waste from the body. The main parts of the hepatobiliary system include the liver, gallbladder, and bile ducts. Some doctors consider the pancreas to be a part of this system. See Figure 1.

The liver, gallbladder, and bile ducts

The liver is the largest organ inside the body. It has two lobes, a right and left lobe. It is on the upper right side of the abdomen (belly area), under your rib cage. It filters blood, helps with blood clotting, makes bile, breaks down fats, and helps process sugar for energy. Bile is the yellow or green liquid that is made by the liver. Bile stays in the gallbladder while you eat, and then passes through the bile ducts to help with the digestion of food. The bile ducts are tubes. The gallbladder is a smaller organ in the upper right side of your abdomen (belly area), under the liver.

Figure 1. Hepatobiliary system

The hepatobiliary system includes the liver, gallbladder, and bile ducts. “Hepato” refers to the liver. “Biliary” refers to the gallbladder and bile ducts.
The gallbladder holds bile from the liver. It releases bile after food is eaten to aid with digestion. The gallbladder has an inner and outer layer, a layer of muscle, and another layer of connective tissue.

The gallbladder releases bile. The bile then passes through the bile ducts. The bile then goes from the common hepatic duct (left and right ducts from the liver) to the cystic duct (small duct from the gallbladder). These ducts come together 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 so your small intestine can absorb nutrients and send waste to your large intestine, also known as the colon.

Cancer basics

Cancer is a disease that starts in the cells of your body. Cells are the building blocks of tissue in the body. The human body contains trillions of cells. DNA (deoxyribonucleic acid) is found within each cell and controls the cells, instructing them on what to do. The coded instructions for your cells found in DNA are called genes.

Normal cells grow and divide and repeat the process over and over again. See Figure 2. Normal genes tell cells that they are supposed to die when they become old or damaged. If they don’t die, and new cells start to form, this growth can get out of control.

Figure 2.
Normal cell growth vs. cancer cell growth

Normal cells increase in number when they are needed. They also die when old or damaged. In contrast, cancer cells quickly make new cells and live longer.
Cancer growth
Abnormal out-of-control growth can be caused by a problem with the genes, and can lead to the growth of a solid mass of cells called a tumor. Some tumors are malignant (cancer). Some tumors are benign (not cancer). Solid tumors can grow anywhere in the body and can affect the way the body works.

Unlike normal cells, cancer cells can spread to other parts of the body. This process is called metastasis. The uncontrolled growth and spread of cancer cells makes cancer dangerous. Cancer cells can replace or deform normal tissue causing organs to stop working.

Hepatobiliary cancers
In general, cancer is named after the place where it starts in the body. The cancer keeps the same name even if it happens to spread. Thus, cancer that starts in the liver is called liver cancer. The term “hepato” refers to the liver. Gall bladder cancer and bile duct cancers are known as biliary tract cancers. Together, liver, gallbladder, and bile duct cancers are known as the hepatobiliary cancers.

If there is concern for one of these cancers, a biopsy may be done to confirm a diagnosis of cancer. A sample of fluid or tissue is taken during a biopsy and examined under a microscope. Since there are different cells in the body, there are different cell types of hepatobiliary cancers, which grow and behave differently in the body.

Your doctor can test for the cell type of hepatobiliary cancer. This is known as histology. Histology is an important piece of a cancer diagnosis and helps the doctors determine how to treat the cancer. A pathologist will classify the cell type based on the size, shape, and structure of the cells. A pathologist is a doctor who is an expert in examining cells under a microscope to find cancer or other diseases.

Risk factors for hepatobiliary cancers
Keeping track of your medical history and your family’s health history are important. Sharing this information with your doctor is important. It will help your doctor with testing for a disease like cancer. However, doctors are not exactly sure what causes the hepatobiliary cancers. They have learned that certain risk factors can be seen with these cancers. A risk factor is anything that increases your chances of having a disease like cancer.

Risk factors can be activities that people do, things in the environment, or traits passed from parents to children through genes. Genes are coded instructions for your cells. The process of mutation is when something goes wrong in the genetic code. Mutations can be passed down in families. They may be present before you are born (inherited), or caused by genetic damage (acquired) occurring later in life. People with inherited genetic mutations have a higher risk for certain cancers, but that doesn’t mean they will definitely develop cancer.

Learn about the risk factors for the hepatobiliary cancers. If you are at risk, or showing any signs or symptoms of these cancers, your doctor may order tests to assess your health. It is helpful to ask questions about medical tests.
This patient guideline will focus on:

- Liver cancer (hepatocellular carcinoma)
- Gallbladder cancer
- Bile duct cancers (intrahepatic and extrahepatic cholangiocarcinoma)

NCCN experts recommend that people with hepatobiliary cancers seek care with an experienced team of doctors. These doctors should specialize in the treatment of these cancers. It is helpful to discuss the treatment options available to you. Ask your treatment team questions about your next steps of care.
Liver cancer (hepatocellular carcinoma)

Cancer that starts in the liver is called primary liver cancer. Other types of primary cancer can spread to the liver. For example, cancer can start in the intestines (colon) and spread to the liver. This is called metastatic colon cancer. Cancer that spreads to the liver from another site is more common than primary liver cancer.

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

Other primary liver cancers in adults include rare types of sarcoma that start in the blood vessel cells of the liver. Another rare type is made of both hepatocellular and cholangiocarcinoma (bile duct) cancer cells. This patient guideline will focus on HCC and its treatment.

Guide 1 has some risk factors that can be seen with HCC. HBV and HCV may put someone at risk for HCC. HBV and HCV are spread by contact with blood and other bodily fluids. These viruses may cause chronic infection of the liver and cirrhosis. Cirrhosis is when scar tissue replaces normal tissue, causing damage to the liver. Certain things like drinking too much alcohol or HBV/HCV may cause cirrhosis. Doctors have found that a large number of people with HCC have cirrhosis.

Genetic hemochromatosis is an inherited condition that causes the liver to store too much iron from food. Other metabolic disorders like diabetes, obesity, or other problems processing sugar may put someone at risk for HCC.

Guide 1. HCC risk factors

<table>
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<th>Risk factors</th>
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<tbody>
<tr>
<td>• HBV (hepatitis B virus) and HCV (hepatitis C virus)</td>
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<tr>
<td>• Cirrhosis</td>
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<tr>
<td>• Genetic hemochromatosis</td>
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<tr>
<td>• Metabolic disorders</td>
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<tr>
<td>• Drinking too much alcohol</td>
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<tr>
<td>• Contact with aflatoxin in certain foods</td>
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<tr>
<td>• NAFLD (non-alcoholic fatty liver disease)</td>
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Drinking too much alcohol can cause damage to the liver. Eating grains or nuts with possible aflatoxin (a fungus) on them may also put someone at risk. Having NAFLD, which is an inflamed liver, may lead to scarring in people who drink little or no alcohol. NAFLD is seen in obese people or people with diabetes, high cholesterol, and a few other conditions. This also increases someone's risk for HCC.

Screening

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

NCCN experts recommend screening with:

- An ultrasound every 6 months, and
- Possible AFP (alpha-fetoprotein) testing
An ultrasound is a test that uses sound waves to take pictures of the inside of the body. A blood test checks for AFP. AFP is a glycoprotein that may be related to HCC. AFP levels in the blood can be elevated in patients with HCC. Doctors use it as a tumor marker for HCC. However, it may also be present with other medical conditions that are not cancer. If a blood test shows a high AFP and/or there is a liver nodule (lump) 10 mm or larger, a CT (computed tomography) scan or MRI (magnetic resonance imaging) scan of the abdomen is recommended. See Part 2 on page 18 for more information on tests.

**Symptoms**

Doctors need to assess your health and learn about your symptoms. Keep in mind, symptoms of HCC may be similar to those of other medical conditions. Some people with HCC may have symptoms, while others may have no symptoms at all. See Guide 2.

Your doctor may think you have this cancer when he or she finds abnormal levels on a regular blood test, you have symptoms, or something is seen on an imaging test. These things can be found during a routine doctor’s visit.

It is important to tell the doctor how you are feeling during your visit or call if you have any symptoms. Ask what tests you will have and why you are having these tests. If your doctor suspects HCC, he or she will check your upper abdomen for swelling or fluid, and will order tests to learn more about your health. Read more about testing for HCC in Part 2.

Guide 2. HCC symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
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<tbody>
<tr>
<td>• Jaundice (yellow-colored skin or whites of the eyes)</td>
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<tr>
<td>• Loss of appetite</td>
</tr>
<tr>
<td>• Weight loss</td>
</tr>
<tr>
<td>• Feeling ill (malaise)</td>
</tr>
<tr>
<td>• Upper abdomen (belly) pain</td>
</tr>
<tr>
<td>• Enlarged liver</td>
</tr>
<tr>
<td>• Ascites (fluid buildup)</td>
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</table>

Stages of Liver Damage

- Healthy Liver
- Fatty Liver
- Liver Fibrosis
- Cirrhosis
Gallbladder cancer

Bile travels through the biliary tract, which includes the gallbladder, to the first part of the small intestine called the duodenum. Gallbladder cancer is the most common type of biliary tract cancer. This cancer starts in the gallbladder. It is a rare cancer that can grow and spread quickly.

Adenocarcinoma is the most common cell type of gallbladder cancer. Adenocarcinoma is a cancer of cells that line the organs, and makes fluids or hormones. Other rare cell types of cancer like sarcoma can grow in the gallbladder.

Guide 3 lists risk factors for gallbladder cancer. The most common risk factor is having gallbladder stones. The risk increases with the size of the stones. Calcification (hardening of the wall) of the gallbladder is considered a lesser risk. Other risk factors include anomalous pancreaticobiliary duct junctions (abnormal connecting duct); polyps, which are usually benign (not cancer) growths; and long-standing typhoid infection. Primary sclerosing cholangitis causes inflammation and damage to the bile ducts and inflammatory bowel disease can do the same. This damage increases the risk for gallbladder cancer. Not all doctors agree that adenomyomatosis of the gallbladder (wall thickening from gallstones) puts someone at risk.

Symptoms

Doctors need to assess your health and learn about your symptoms. Keep in mind, symptoms of gallbladder cancer may be similar to those of other medical conditions. Some people with gallbladder cancer may have symptoms, while others may have no symptoms at all. See Guide 4.

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<table>
<thead>
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<th>Risk factors</th>
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<tr>
<td>• Gallstones (choleliathiasis)</td>
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<tr>
<td>• Calcification of the gallbladder (porcelain gallbladder)</td>
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<tr>
<td>• Anomalous pancreaticobiliary duct junctions</td>
</tr>
<tr>
<td>• Gallbladder polyps</td>
</tr>
<tr>
<td>• Chronic typhoid infection</td>
</tr>
<tr>
<td>• Primary sclerosing cholangitis</td>
</tr>
<tr>
<td>• Inflammatory bowel disease</td>
</tr>
<tr>
<td>• Adenomyomatosis of the gallbladder</td>
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Guide 4. Gallbladder cancer symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Jaundice (yellow-colored skin or whites of the eyes)</td>
</tr>
<tr>
<td>• Chronic upper abdomen (belly) pain</td>
</tr>
<tr>
<td>• Lumps in the abdomen</td>
</tr>
<tr>
<td>• Nausea and vomiting</td>
</tr>
<tr>
<td>• Feeling bloated</td>
</tr>
</tbody>
</table>
Your doctor may think you have this cancer when he or she finds abnormal levels on a regular blood test, you have symptoms, or something is seen on an imaging test. For an example, a tumor in the gallbladder may be found on an ultrasound being done for other reasons.

Some gallbladder cancers are found during surgery to remove gallstones. This surgery is called a cholecystectomy. Upper abdomen pain that continues and jaundice from a blockage of the bile ducts may also be signs of gallbladder cancer. Yet, these symptoms may be caused by other medical conditions.

It is important to tell the doctor how you are feeling during your visit or call if you have any symptoms. Ask what tests you will have and why they are being done. If your doctor suspects gallbladder cancer, he or she may assess your upper abdomen for lumps and order tests to get more information about your health. Currently, there is no screening test for gallbladder cancer. Learn more about testing for gallbladder cancer in Part 2. See Figure 3.

**Figure 3. Gallstones**

Gallstones are hard stones that form in the gallbladder or the bile ducts. They are made from bile and other digestive material and can vary in size. Some people may have one or more gallstones.
Bile duct cancers (cholangiocarcinoma)

The bile ducts carry bile from the liver to the small intestine. Cholangiocarcinoma, also known as bile duct cancer, starts in the bile ducts. This cancer is also called a biliary tract cancer. The most common cell type is adenocarcinoma.

Bile duct cancer can be intrahepatic or extrahepatic. 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. Hilar bile duct cancer (Klatskin tumors) and distal bile duct cancer are subtypes of extrahepatic bile duct cancers.

Guide 5 lists risk factors for intrahepatic and extrahepatic bile duct cancers. Growths such as gallbladder stones can block the bile ducts. Cysts (fluid-filled sacs) and infection are also risk factors for bile duct cancers. Inflammatory bowel disease, which causes inflammation of the bowel, may also be a risk factor. However, it may be confused with primary sclerosing cholangitis, which also causes inflammation. Inflammation is the immune system’s reaction to protect your body, but it can cause problems depending on where it occurs. Long-term inflammation is a risk factor for bile duct cancer.

Intrahepatic bile duct cancer has certain risk factors like HCC (see page 12). This includes HBV, HCV, cirrhosis, diabetes, obesity, alcohol, and NAFLD. Tobacco use is also a risk factor for intrahepatic bile duct cancer.

**Symptoms**

Doctors need to assess your health and learn about your symptoms. Keep in mind, symptoms of bile duct cancer may be similar to those of other medical conditions. Some people with bile duct cancer may have symptoms, while many may have no symptoms at all. See Guide 6.
Slight changes in liver function tests may occur with bile duct cancer. Some people with intrahepatic bile duct cancer have general symptoms like fever, pain in the upper abdomen, and weight loss. Jaundice from a blockage of the bile ducts can happen with extrahepatic bile duct cancer. Jaundice is yellow-colored skin or whites of the eyes due to a buildup of bilirubin in the body.

It is important to tell the doctor how you are feeling during your visit or call if you have any symptoms. Ask what tests you will have to find out what is causing the symptoms. If your doctor suspects bile duct cancer, he or she will check your blood and order other tests. Currently, there is no screening test for bile duct cancers. Find out more about testing for bile duct cancer in Part 2.

Review

- The liver, gallbladder, and bile ducts are part of the hepatobiliary system.
- In general, cancer is named after the place where it starts in the body.
- A risk factor is anything that increases your chances of having a disease like cancer.
- Symptoms of cancer may be similar to those of other medical conditions.
- Screening is when tests are done on a regular basis to detect a disease in someone without symptoms.
- It is important to tell the doctor how you are feeling during your visit or call if you have any symptoms.

“When I was diagnosed with cholangiocarcinoma in 2015 at 28 years old, I read the statistics and was certain I would not live to see my 30th birthday. Thanks to an outstanding, invested, multidisciplinary team, I celebrated 31 in January and show no signs of slowing down.

-Cait, cholangiocarcinoma survivor
2 Testing for hepatobiliary cancers

- 19 Medical history & physical exam
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Part 2 discusses tests used to diagnose a hepatobiliary cancer. Doctors will test your blood and tissue samples to confirm a diagnosis of cancer. The test results will help your doctors and you decide on a treatment plan.

Medical history & physical exam

Two basic tools of diagnosis include a medical history and physical exam. Your doctor will ask about your medical history, which should include everything that has ever happened to you, related to your health. He or she will also do an exam of your body. Doctors often perform a physical exam along with taking a medical history.

Your doctor will ask you about:

- Health events in your life, including surgeries, accidents, and past illnesses
- Recent sickness
- Medications you are taking now and those you may be allergic to (It is helpful to keep a list of your meds. Include any supplements and over-the-counter medicine you take.)
- Family history of disease such as cancer, heart disease, or diabetes

Your doctor may:

- Check your eyes, ears, nose, and neck
- Listen to your lungs, heart, and abdomen (belly)
- Feel and use pressure on your body to see if organs are of normal size, soft or hard, or cause pain when touched

Blood tests

Doctors test blood to look for signs of disease and assess your general health. Blood tests are not used to find or diagnose (confirm) hepatobiliary cancer. Blood tests may be done along with other tests before, during, and after treatment.

Blood tests are done for many different reasons. After treatment starts, blood tests may help your doctors assess your response to cancer-fighting drugs. Abnormal levels of certain chemicals in the blood may be a sign that the cancer has spread in the body. Below is a list of common blood tests and some that are specific to hepatobiliary cancers.

**Complete blood count with differential**

A CBC (complete blood count) measures the number of blood cells in a blood sample. It includes numbers of white blood cells, red blood cells, and platelets. Your blood counts may be low or high because of cancer or another health problem. A CBC is an essential test that gives a picture of your overall health.

There are several types of white blood cells in your body. A white cell differential counts the number of each type. It also checks if the counts are in balance with each other. Your doctor can learn from this test what the cause of an abnormal white blood count is. It is also used to stage the cancer and check if treatment is working.

**Comprehensive metabolic panel**

Chemicals in your blood come from your liver, bone, and other organs. A comprehensive metabolic panel often includes tests for up to 14 chemicals. The tests show if the level of chemicals is too low or high. Abnormal levels can be caused by cancer or other health problems. Your doctor will check certain levels like BUN (blood urea nitrogen) and creatinine for kidney function. These levels may be abnormal because of liver disease.
Liver function panel
A liver function panel test will assess the health of your liver. Your liver does many important jobs, such as remove toxins from your blood. Liver function tests measure chemicals that are made or processed by the liver. It is recommended that the levels of bilirubin, albumin, AST (aspartate aminotransferase), ALT (alanine transaminase), ALP (alkaline phosphatase), PT (prothrombin time), INR (international normalized ratio), and platelet count be measured. Levels that are too high or low may be a sign of liver damage or cancer spread.

Hepatitis panel
This panel of blood tests can check for HBV or HCV. Chronic (long-term) hepatitis B and a current or past infection with hepatitis C increase the risk for HCC and biliary tract cancers. Hepatitis causes the liver to become inflamed and not work as it should.

Your doctor will want to know if you have had any of the viruses in the past, or if you still have them today. The tests will look for antibodies that may have tried to fight the virus, or certain parts of the actual virus itself. It is helpful to tell your treatment team if you’ve ever had hepatitis. You may be referred to a hepatologist if you have positive results. A hepatologist is a doctor who specializes in the care of the liver, biliary tract, gallbladder, and pancreas. He or she can help manage the treatment of hepatitis.

Your doctor may also test for AFP, CA 19-9 (cancer antigen 19-9), or other tumor markers that can be elevated in certain types of liver tumors.

Imaging tests
Imaging tests are used to take pictures (images) of the inside of your body. Your doctor will want to check the primary tumor, or original site of the tumor. Imaging can be used to see if there is cancer in the body. CT and MRI scans are common imaging tests for hepatobiliary cancers.

What to know about imaging tests:

- Imaging tests can see if the cancer is in more than one part of the body.
- They continue during treatment to see how the disease is responding.
- They can be used after treatment to check for signs of disease (recurrence).

You may not learn of the results of your imaging tests for a few days since a radiologist needs to see the pictures. A radiologist is a doctor who is an expert in reading the pictures from imaging tests.

CT scan
A CT scan uses x-rays to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the x-ray pictures are combined to make one detailed picture of the body part. A CT scan of the abdomen and pelvis may be given along with other tests to look for cancer. A CT scan of the chest may also be done to assess the extent of cancer (staging). See Figure 5.

Before the CT scan, you may be given a contrast dye to make the pictures clearer. You may drink the dye, have it injected into your vein, or both. It may cause you to feel flushed or get hives. Rarely, serious allergic reactions occur. Tell your doctors if you have had bad reactions in the past.
MRI scan
An MRI scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. This type of scan is good for assessing the abdomen and pelvis. An MRI scan can also be used to check the spine and soft tissues like the brain.

An MRI may be used as an initial test to check treatment results, and to check for the spread of cancer to other parts of the body. Getting an MRI scan is similar to getting a CT scan. But, MRI scans take longer to complete. For the scan, you will need to lie on a table that moves through a large tunnel in the scanning machine. The machine may make loud noises during the test. The tunnel of the machine may be close to your body, so let the doctor know if you are claustrophobic (fear of small spaces). Like a CT scan, a contrast dye may be used to make the pictures clearer.

MRCP
An MRCP (magnetic resonance cholangiopancreatography) is a type of MRI scan that makes very clear pictures of the pancreas and bile ducts. No contrast dye is used because bile and other fluids serve as contrast. An MRCP is often done along with a normal MRI scan. This is the case for gallbladder and bile duct cancers. If you have jaundice, an MRCP may be the recommended method to assess the biliary tract.

PET scan
A PET (positron emission tomography) scan shows how your cells are using a simple form of sugar. To create pictures, a sugar radiotracer first needs to be put into your body with an injection into a vein. The radiotracer emits a small amount of energy that is detected by the machine that takes pictures. Active cancer cells use sugar faster than normal cells. Thus, cancer cells look brighter in the pictures.
When PET is combined with CT, it is called a PET/CT scan. Sometimes a PET/CT scan is used to check the results of a CT or MRI that is not clear. In some cases, it may also be done to check for distant metastases.

**Ultrasound**
An ultrasound is a test that uses sound waves to take pictures of the inside of the body. Ultrasound is good at showing small areas of cancer that are superficial (on the surface of the body). A gel is placed on the skin and a small device is lightly pressed and moved over a specific area of the body. Ultrasounds are generally painless.

**PTC**
PTC (percutaneous transhepatic cholangiography) uses contrast and an x-ray to take pictures of the biliary tract. The contrast is injected 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 (thin, flexible tube) can be inserted to drain fluid from the biliary tract, into a bag outside of the body or into the small intestine. A metal stent may also be placed for an obstruction.

For this test, your doctor will first give you medicine to make you feel relaxed and then numb the area where the needle will be inserted. You will be awake during this test and able to tell the medical team if you have any issues.

**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. At the other end of the scope is an eyepiece that your doctor looks through to see the images shown by the camera. The scope is guided into the body through a natural opening, such as the mouth or nose. It may also be inserted through a small surgical cut. More than one type of scope may be used for imaging tests.

**EUS**
An EUS (endoscopic ultrasound) uses an endoscope that has a small ultrasound probe at the end. The endoscope is inserted through your mouth and guided down your throat and stomach to the first part of the small intestine (duodenum). The ultrasound probe bounces sound waves off your organs to make pictures of the inside of your body. EUS may get a closer look at your bile ducts and any tumor that might be in this area. Sometimes an EUS can detect lesions (abnormal areas) that are difficult to see on a CT or MRI. An FNA (fine-needle aspiration) or needle biopsy can be performed during an EUS if needed.

**ERCP**
An ERCP (endoscopic retrograde cholangiopancreatography) uses an endoscope and x-rays to make 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 dye into the bile ducts. Then, an x-ray machine will take pictures. The contrast dye allows the bile ducts to be clearly seen on the x-ray pictures. This test helps your doctor get access to any obstructed bile ducts so he or she can place a stent. See Figure 6.
Laparoscopy
This method uses small cuts in the abdomen instead of one big one. Small tools are inserted through the cuts to perform a biopsy or surgery. One of the tools is called a laparoscope. It is a long tube with a light and camera at the end. The camera lets your doctor see organs and other tissues inside your abdomen. The other tools are used to remove tissue.

Laparoscopy may only be used in certain cases. It may be used to learn the stage of cancer. It may also be used if the cancer has not spread to distant sites. It may also be used if the cancer is not clearly seen on imaging. See Part 3 on page 28 for more information on surgery methods.

Figure 6. ERCP
The endoscope is inserted through your mouth and guided down your throat and stomach to the duodenum.
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. If surgery is possible and you are at high risk for a hepatobiliary cancer, a biopsy may not be needed.

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

If you have a biopsy, your doctor will recommend one of the types listed here:

- **Core needle biopsy** removes a core (large) sample of the tumor. This is the preferred biopsy for getting more tissue to test or freeze to be tested at a later time.

- **FNA biopsy** uses a thin needle to take a sample of tissue. An ultrasound may guide the FNA biopsy. This is good for deep tissue tumors or those near blood vessels.

- **Laparoscopy** uses a device that passes through a small cut near the belly button to do work inside. A tool then takes samples of tissue. Your doctor can also assess the extent of cancer in this area. See the next section for more on staging.

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

Test results

The results from the exam of your body, imaging tests, and in some cases a biopsy will determine your next steps of care. These results help doctors learn the cancer stage. The cancer stage is based on how far the cancer has grown and spread in the body.

Once your doctors know more about your diagnosis, they can talk to you about what to expect. Talking with your doctor about the type of hepatobiliary cancer and cancer stage will help with treatment planning. Your treatment team will come together and decide on a treatment plan. This treatment plan will be based on the extent of cancer in your body and your other health needs, as well as your personal choices. A treatment plan is a written course of action that covers every stage of the treatment process.

“My treatment team was amazing, they always provided me with hope and the feeling that we were in this together and that I would never be alone in deciding the future of my treatments.”

-Lisa, cholangiocarcinoma survivor
Your medical tests:

✓ Your doctors will order tests and schedule visits to talk about your care plan.

✓ It is helpful to keep track of your test results at all times. Ask your doctors questions about the results.

✓ Your treatment team will gather your test results and suggest treatment options.
Cancer stage

Cancer staging is a rating by your doctors of the extent of the cancer. It is used to plan which treatments are best for you.

The AJCC (American Joint Committee on Cancer) staging system is a common staging system used for the hepatobiliary cancers seen below.

- Hepatocellular cancer
- 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 four stages—I, II, III, and IV for each type of hepatobiliary cancer.

In this system, the letters T (tumor), N (node), and M (metastasis) describe a different area of cancer growth. The T, N, and M scores are combined to assign the cancer a stage.

- **T score** describes the growth of the primary tumor.
- **N score** describes spread of cancer growth to lymph nodes.
- **M score** tells if the cancer has spread to distant sites.

Another factor used in staging is the cancer grade. Higher-grade cancers tend to grow and spread faster than lower-grade cancers. The letter G notes the grade. "Well differentiated" means the cancer cells look like normal cells under a microscope, and these cancer cells tend to grow slowly. "Poorly differentiated" means the cancer cells look nothing like normal cells under a microscope, and these cancer cells tend to grow quickly.

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

GX–G3 are used for all hepatobiliary cancers. GX–G4 are used to assign a cancer grade for HCC.

**Other scores for HCC**

HCC has one more set of scores according to a scoring system called the Ishak system. Fibrosis is scored from 0–6. Fibrosis is mild scarring of liver tissue. Cirrhosis is when this scarring becomes severe.

This F scoring system is a factor for prognosis. Prognosis is the likely course and outcome of a disease based on tests.

- **F0** Fibrosis score of 0–4 is none to moderate fibrosis
- **F1** Fibrosis score of 5–6 is severe fibrosis to cirrhosis
HCC also uses a Child-Pugh score to assess liver damage caused by disease. This disease is mostly cirrhosis. This score helps your treatment team see how the liver is working, decide if surgery is an option, and plan treatment.

This system includes:

- **Class A** (lowest operative risk)
- **Class B** (intermediate operative risk)
- **Class C** (highest operative risk)

The class is based on points from blood tests (albumin, bilirubin, PT), and points for encephalopathy (liver failure) and ascites (fluid buildup). The points are from 1–3 and go up with each abnormal result.

**Review**

- Cancer tests are used to find cancer, plan treatment, and check how well treatment is working.
- Your health history and a body exam inform your doctor about your health.
- Blood tests check for signs of disease.
- Imaging tests that take pictures of the inside of your body may show cancer.
- A biopsy removes tissue or fluid from your body to diagnose cancer.
- A treatment plan is a written course of action that covers every stage of the treatment process.
- Cancer staging is a rating by your doctors of the extent of the cancer.
3
Overview of cancer treatments

29 Surgery
33 Ablation
33 Embolization
34 Radiation therapy
35 Chemotherapy
36 Targeted therapy
37 Immunotherapy
38 Clinical trials
39 Review
Part 3 describes the main treatments for hepatobiliary cancers. Knowing what a treatment is will help you understand your treatment options listed in the Treatment guide for Part 4, Part 5, and Part 6. There is more than one treatment for each type of hepatobiliary cancer. Not every person with a hepatobiliary cancer will receive every treatment listed in this chapter.

### Types of treatment

**Local treatments** are used to treat a focused area of cancer. Surgery and radiation therapy are common local treatments. Liver transplantation may be an option in certain cases meeting very specific criteria.

**Locoregional** is another word you will see in this guideline. These procedures are minimally invasive, meaning small incisions are used and there may be less side effects. Examples of locoregional therapies include ablation and embolization. Ablation is used for small tumors (<2–3 cm) in the liver. Embolization is often used for liver tumors that can’t treated with surgery.

**Systemic treatments** are able to treat cancer cells throughout the body. This type of treatment is an option for people with hepatobiliary cancers. It comes in the form of drug treatment that includes chemotherapy, targeted therapy, and immunotherapy.

### Surgery

Surgery is a primary treatment for hepatobiliary 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 or supportive care.

The method and extent of surgery for hepatobiliary cancers varies. It depends on where the cancer is in the body and the size of the tumor. Surgery may not be an option for some people if the cancer has spread or because of other medical conditions. Your doctor will assess your health including your liver function before offering surgery as an option.

When preparing for surgery, you should seek the opinion of an experienced surgeon. Patients can seek care or ask for a referral to a hospital or cancer center that has experience in treating hepatobiliary cancers. Surgery for the hepatobiliary cancers can be complex. The surgeon should be an expert in performing these types of surgery.

**Surgery for HCC**

Partial hepatectomy is surgery to remove a section of the liver. This section can be an entire lobe or part of the liver where the cancer has grown. Some normal tissue around the area is also removed. The part of the liver that is not removed will keep working, and the missing section may regrow.

This type of surgery may only be an option for some people. The cancer must not involve the blood vessels, be too large, or have spread beyond the liver. You must also have a working liver and be able to have the actual surgery.
Liver transplant is another option for some people with HCC or bile duct tumors. This is based on certain size limits and tumor locations. Transplants completely replace the diseased liver with a new one. The new liver may be donated from a person who recently died, or a section of liver may be donated from a healthy, living person. The new liver will take over and function in the body.

A liver transplant may be an option for people who can’t have a partial hepatectomy. They may not be able to have surgery because the liver has too much disease (ie, cirrhosis), or the cancer may be in an area that is hard to reach.

Keep in mind, other treatments may be given if you are waiting for a transplant. These methods may also be used to treat smaller cancers or those in places that are hard to reach. These treatments are ablation and embolization. See page 33 to read more about these treatment options.

**Surgery for gallbladder cancer**
Cholecystectomy is the type of surgery used for gallbladder cancer. This surgery involves removing the gallbladder and some tissue around it. The goal is to have negative margins with no cancer remaining.

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 where the cancer is located will help your surgeon decide on the extent of surgery. Smaller tumors may only require a simple cholecystectomy without the other steps of removal.

**Surgery for bile duct cancers**
For intrahepatic bile duct cancers, a hepatic resection with negative margins 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 the cancer spread beyond the nearby lymph nodes or to distant sites, other treatment besides surgery may be offered.

For extrahepatic bile duct cancers, surgery includes removing the bile duct and nearby lymph nodes. People with distal extrahepatic bile duct cancer may also need a Whipple procedure (pancreatoduodenectomy). Distal tumors are in the common bile duct that passes through the pancreas. A Whipple procedure involves removing the pancreas, duodenum, and other nearby organs. Cancer in the hilar area is in the common bile duct and close to the liver. A hepatic resection may be needed for tumors in the hilar area.

**Surgical margin**
With most surgery methods, your surgeon will try to remove a cancer-free surgical margin. A surgical margin is a ring of normal-looking tissue around the tumor. Sometimes a cancer-free margin can’t be removed. After surgery, you may receive adjuvant treatment such as radiation, or systemic therapy like chemotherapy or targeted therapy. Adjuvant treatment is given after surgery to kill any remaining cancer cells.

**Possible side effects of surgery**
Side effects are unhealthy or unpleasant physical or emotional responses to treatment. You may experience side effects from the anesthesia or surgery. Often, general anesthesia is used for surgery. General anesthesia is the use of drugs that put you into a deep sleep-like state so you won’t feel pain. Ask your treatment team for a full list of side effects once you know more about the type of surgery you have planned.
Liver transplant

Who can have a liver transplant?

- People with HCC who meet certain criteria, known as UNOS (United Network for Organ Sharing) criteria:
  - People with an HCC tumor 2–5 cm in width, or 2–3 tumors ≤3 cm each
  - No cancer spread to large blood vessels
  - No extrahepatic disease (no disease outside the liver)
- People who fall a little outside of the UNOS criteria may have a transplant at select centers.
- People can get treatment before the transplant to reduce the size of the cancer. This treatment is directed into or near the tumor. It is called downstaging therapy.
- Some centers also offer transplant for small bile duct tumors in the perihilar location, along with chemotherapy and radiation.

What happens during the transplant?

- The diseased liver is removed completely along with the tumor and replaced with a living donor’s section of a liver or a deceased person’s liver.
- The surgery can take hours and should be led by an experienced transplant surgeon.

What happens after the transplant?

- You remain in the hospital and recover for a number of days.
- You may have many blood tests and doctor’s visits. Your transplant team will help with your follow-up schedule.
- You will stay on medicine for the rest of your life. Some medicines stop the immune system from attacking the liver, while others prevent infection and help you stay healthy.

How long can I wait for a liver?

- You will be placed on a waiting list and watched closely by your treatment team.
- The wait is based on many things including your liver function and prognosis. A prognosis is the likely course and outcome of a disease based on tests.
Biliary drainage
When the bile ducts are obstructed (blocked), a person may have jaundice or other problems like pain or an infection (cholangitis). Biliary drainage may be an option for some people with gallbladder or bile duct cancer.

Your treatment team will discuss ways to drain the biliary tract. You may have surgery to add a new path for the fluid to drain (bypass), or a catheter or stent placed to drain the fluid. A catheter is a thin, flexible plastic tube. It can be used to give medicine or drain fluid from the body. A stent is a thin metal or plastic tube. Stents may need to be replaced after a certain time.

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. Chemotherapy may be given to treat metastatic disease but usually requires intact liver function and biliary drainage to be given safely. Thus, your doctor may recommend you have biliary drainage before chemotherapy begins.

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 the drainage using surgical bypass, ERCP, or a PTC.

- 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.

- ERCP is when an endoscope is used 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.

- PTC involves placing 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.

Ask your doctor about the possible side effects of biliary drainage. See Parts 5 and 6 for more on treatment options for people with jaundice.

Resection of your liver is certainly a large operation, and it has all of the issues associated with a large operation. However, the liver regenerates, and the difficulties you may face right after surgery will resolve themselves with time. You will be a lot more tired than usual for a while, and your diet may change a bit, but that is a small price to pay to have your life back.

-Steven,
inhahepatic cholangiocarcinoma survivor
Ablation

Other treatment may be given if you are waiting for a liver transplant or if your tumors can’t be treated with surgery. One of these treatments is ablation. This treatment may be an option for some people with HCC. Ablation methods include heat, cold, lasers, or chemicals like alcohol to treat the cancer. RFA (radiofrequency ablation) is an example of an ablation technique used to treat smaller liver tumors.

Ablation may be done through small incisions (laparoscopic), through the skin, or by an open approach. Your doctor will check the tumor size, where the cancer is located, and how well your liver is working before doing this treatment. Through research, we know that ablation works best on tumors less than 3 cm in size. These tumors must also not be near other organs, in major blood vessels, or close to the bile ducts.

Possible side effects of ablation
Ablation may affect the normal tissue in the liver. Common side effects may include pain or bleeding in the abdomen. Serious side effects of ablation are not common. Ask your doctor for a full list of side effects of ablation.

Embolization

ADT (arterially directed therapies) are a treatment option for some people with HCC. There are different methods of ADT just like there are for ablation, and no option has been proven to be better than another. For this procedure, an object or substance is inserted through a catheter into the hepatic artery leading to the cancer.

The common types of ADT for hepatobiliary cancers include:

- **Bland embolization** involves blocking the blood supply to the tumor by injecting tiny particles into the blood vessels feeding the tumor(s). Stopping the blood flow cuts off the oxygen supply to the tumor and causes cancer cells to die.

- **Chemoembolization (also known as TACE or transarterial chemoembolization)** involves injecting a chemotherapy mixture into the tumor and blocking the feeding blood vessels to the tumor(s).

- **DEB-TACE (drug-eluting bead transarterial chemoembolization)** is when tiny particles loaded with chemotherapy are injected into the blood vessels feeding the tumor(s). The particles give off small amounts of chemotherapy to the tumor over several days.

- **Radioembolization (also known as 90Y)** involves injecting glass or resin beads that deliver high-dose radiation directly to the tumor.

Tumor location is not a main factor when deciding on using embolization as a treatment. This treatment may be an option if a large amount of cancer is in the liver but has not spread beyond the liver, your liver is working well, and the hepatic artery can be accessed. Embolization may be an option for patients that can’t have surgery or ablation as a single treatment. Embolization can also be combined with ablation to treat some tumors. Combining these treatments is an option for tumors 3–5 cm in size.

Possible side effects of embolization
Embolization may cause some side effects. Your doctor can explain what is likely to happen with this treatment. Common side effects may include pain, fever, and nausea or vomiting. Ask your doctor for a full list of possible side effects of embolization.
Radiation therapy

Radiation therapy uses high-energy rays or protons to treat cancer. The rays damage DNA. DNA is a chain of chemicals in cells that contains genes. This either kills the cancer cells right away or stops new cancer cells from being made.

There are different ways to give radiation. Which method you get depends on the type of hepatobiliary cancer and the purpose of radiation therapy. Some methods are discussed next. You may feel side effects from radiation although not everyone does. Ask your treatment team for a full list of side effects.

**External beam radiation therapy**
Radiation is delivered from a machine outside the body. This method is called EBRT (external beam radiation therapy). To receive EBRT, you must first have a simulation session. For simulation, imaging scans are used to help target the tumor with radiation while trying to minimize how much radiation goes to normal healthy organs.

Using the scans, your treatment team will plan the best radiation dose, number and shape of radiation beams, and number of treatment sessions. Beams are shaped with computer software and hardware added to the radiation machine. Radiation beams are aimed at the tumor. This is done with help from ink marks on the skin or marker seeds in the tumor.

During treatment, you will lie on a table in the same position as you did for simulation. Devices may be used to keep you still so the radiation targets the tumor in the same place every day of treatment. You will be alone while the technician operates the machine from a nearby room. He or she will be able to see, hear, and speak with you at all times. As treatment is given, you may hear noises from the machine.

There are multiple types of EBRT given as a treatment for hepatobiliary cancers. EBRT may be an option when surgery is not possible. It may be given after surgery as an adjuvant treatment. Some types of EBRT focus on controlling the cancer growth and relieving the symptoms caused by the cancer. This is called palliative EBRT.

The types of EBRT for hepatobiliary cancers include:

- **3D-CRT (three-dimensional conformal radiation therapy)** uses beams matched to the shape of the tumor.
- **IMRT (intensity-modulated radiation therapy)** is a more advanced type of radiation that uses small beams of different strengths to limit the radiation dose more to the tumor and reduce the dose to the nearby healthy tissue.
- **SBRT (stereotactic body radiation therapy)** involves high-dose radiation within one or a few sessions. The advantage of this method is the ability to deliver a more intense treatment that may kill or ablate the tumor. It can be given in a shorter timeframe. The drawback of this treatment is the potential for damage to nearby organs.
- **PBT (proton beam therapy)** uses proton beams, instead of x-rays, to treat the tumor. The advantage of protons is that the radiated area can be better confined to the tumor away from normal tissue compared with standard photon radiation. The drawback of proton therapy is the limited number of facilities that offer proton therapy and the higher cost of treatment.
Drugs can also be given to treat cancer throughout the body. This is called systemic therapy. Doctors use systemic drugs to treat cancer cells that may have spread beyond the first site of cancer. The types of drugs given are based on the type of hepatobiliary cancer. See the drug treatments listed in Guides 7 and 8.

Chemotherapy

Chemotherapy is the use of drugs to destroy abnormal cells in the body. But, the drugs can also affect normal cells. Many people refer to this treatment as “chemo.”

Different types of chemotherapy drugs work in different ways to kill abnormal cells or stop new ones from being made.

Guide 7. Drug treatment for gallbladder cancer and bile duct cancer

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**Immunotherapy**

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Guide 8. Drug treatment for HCC

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**Targeted therapy**

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More than one drug may be used. When only one drug is used, it's called a single agent. A combination regimen is the use of two or more chemotherapy drugs. Chemotherapy can also be combined with other treatment. For example, chemotherapy can be given with radiation. This is called chemoradiation. The type of chemotherapy used is fluoropyrimidine (fluorouracil or capecitabine). Chemoradiation may be a treatment option for gallbladder and bile duct cancers.

Some chemotherapy drugs are liquids that are injected into a vein or under the skin with a needle. Some drugs may require a large IV (intra-venous) called a port or central venous catheter to be placed for safe administration. Sometimes, chemotherapy can also be injected into an artery that leads to the tumor (intra-arterial chemotherapy). Other chemotherapy drugs may be given as a pill that is swallowed.

Chemotherapy is usually given for gallbladder and bile duct cancers. It may be a primary treatment option or after-surgery (adjuvant) option for these cancers. Both adjuvant chemotherapy and chemoradiation have shown some benefit in treating bile duct cancer that has spread to the lymph nodes.

At this time, there are not enough data to support the use of standard chemotherapy for HCC. In some cases, chemotherapy may be suggested if surgery or a liver transplant is not an option. It may also be an option for metastatic disease.

**Possible side effects of chemotherapy**
The side effects of chemotherapy can differ between people. Some people have many side effects. Others have few or none at all. Some side effects can be very serious while others can be hard to deal with but not serious. Side effects of chemotherapy depend on the drug type, amount taken, length of treatment, and the person.

Common side effects of chemotherapy may include:

- Extreme tiredness
- Infection
- Low blood cell and platelet counts
- Not feeling hungry
- Nausea and/or vomiting
- Diarrhea
- Hair loss
- Mouth sores
- Neuropathy (nerve irritation causing numbness, tingling, burning, or cold sensitivities in hands, feet, or sometimes mouth)

Not all side effects of chemotherapy are listed here. It is helpful to ask your treatment team for a full list of side effects. Learn how you can prepare and cope with possible side effects of chemotherapy.

**Targeted therapy**
Targeted therapy stops the action of molecules involved in the growth of cancer cells. Some targeted therapy drugs block the chemical signals that tell the cancer cells to grow. Other targeted therapy drugs block signals that cause new blood vessels to form. Other drugs target hormones.

Targeted therapy with a drug called sorafenib is usually the first-line systemic therapy option for more advanced stages of HCC. Targeted therapies may
be used to treat other hepatobiliary tumors that have certain gene mutations. Targeted therapy generally harms normal cells less than chemotherapy but still has side effects. Side effects differ between drugs. Most targeted therapies come in pill form but some need to be injected.

Possible side effects of targeted therapy
The side effects of targeted therapy depend on the drug and dose. Some of the side effects listed are caused by only one targeted drug. Others are caused by many targeted drugs but differ in how likely they are to occur. Common side effects of targeted therapy drugs may include:

- Extreme tiredness
- Low blood cell counts
- Body aches
- Skin rash
- Pain, redness, or blistering on palms of hands and soles of feet
- Mouth sores
- High blood pressure
- Fever
- Nausea and/or vomiting
- Diarrhea

Not all side effects of targeted therapy drugs are listed here. Be sure to ask your treatment team for a complete list of side effects. If a side effect bothers you, tell your treatment team.

Immunotherapy
The immune system is the body’s natural defense against infection and disease. The immune system includes many chemicals and proteins. These chemicals and proteins are made naturally in your body. Immunotherapy increases the activity of your immune system. By doing so, it improves your body’s ability to find and destroy cancer cells. The side effects of immunotherapy depend on the drug and dose.

Immunotherapy with the drug nivolumab can help to shrink tumors in people with advanced stages of HCC after progression on sorafenib. Doctors are studying whether immunotherapy can be an earlier treatment option for HCC, or used in combination with other treatments. See page 49. Pembrolizumab, an immunotherapy drug, may be an option for treating certain types of tumors seen with gallbladder and bile duct cancers. Ask your doctor for more information on immunotherapy.

Possible side effects of immunotherapy
The side effects of immunotherapy depend on the drug being used. Common side effects of immunotherapy may include:

- Extreme tiredness
- Skin rash
- Nausea and/or vomiting
- Diarrhea
- Mouth sores
- Bone, joint, and/or muscle pain

Not all side effects are listed here. It is helpful to learn about the drug treatment your doctor recommends. Ask for a complete list of side effects.
Clinical trials

Clinical trials are research studies that people choose to take part in. Because of clinical trials, doctors learn how to prevent, diagnose, and treat a disease like cancer. Because of clinical trials, the tests and treatments in this book are now widely used to help people with hepatobiliary cancers.

One of your treatment choices may be to join a clinical trial. NCCN experts strongly support clinical trials as a treatment option. Clinical trials are an important option for people with cancer.

Phases of a clinical trial
Clinical trials go through levels or phases of testing to find safe and helpful ways to manage a hepatobiliary cancer. These phases help move the research along to find out what works best for people with cancer.

- **Phase I** looks at how much drug to give, its side effects, and how often to give the treatment.

- **Phase II** tests for side effects and how it works on the cancer type.

- **Phase III** compares the new treatment (or new use of treatment) to what is commonly used.

- **Phase IV** follows late side effects and if the treatment still works after a long period.

Taking part in a clinical trial
Your medical team will carefully manage your care and follow a plan. Patients in a clinical trial are often alike with their cancer type and general health. You can join a clinical trial when you meet certain terms (eligibility criteria).

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

Some benefits of a clinical trial:

- You will have access to the most current cancer care.

- You will be closely watched by your medical team.

- You may help other patients with cancer.

Some risks of a clinical trial:

- Like any test or treatment, there may be side effects.

- New tests or treatments may not work.

- You may have to visit the hospital more for treatment and appointments.

Next steps
Ask your doctor or nurse if a clinical trial may be an option for you. There may be clinical trials where you are getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 7 on page 74.
Review

- Surgery is a main treatment option for hepatobiliary cancers.
- Doctors may consider a liver transplant for HCC if people meet certain criteria for this treatment.
- Other locoregional treatments for hepatobiliary cancers include radiation therapy, ablation, and embolization.
- Drug treatments may include chemotherapy, targeted therapy, and immunotherapy depending on the type of hepatobiliary cancer.
- Clinical trials are a treatment option for hepatobiliary cancers. They help doctors learn how to prevent, diagnose, and treat a disease like cancer.

Complementary and alternative medicine

CAM (complementary and alternative medicine) is a group of treatments sometimes used by people with cancer. Many CAMs are being studied to see if they are truly helpful.

Complementary medicines are meant to be used alongside standard therapies, most often for relaxation, improving your health, or to prevent or reduce side effects.

Alternative medicine is treatment or techniques that are used instead of standard treatments such as chemotherapy or radiation. Some are sold as cures even though they haven’t been proven to work in clinical trials.

Many cancer centers or local hospitals have complementary therapy programs that offer acupuncture, yoga, and other types of therapy.

It’s important to tell your treatment team if you are using any complementary medicine, especially supplements, vitamins, or herbs. Some of these things can interfere with your cancer treatment. For more information about CAM, ask your doctor and visit the websites listed in Part 7.
## Treatment guide: Liver cancer (hepatocellular carcinoma)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
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<td>Treatment planning</td>
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<td>Treatment for metastatic disease or widespread tumors</td>
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<td>46</td>
<td>Review</td>
</tr>
</tbody>
</table>
Part 4 is about a type of liver cancer known as hepatocellular carcinoma. This chapter begins with treatment planning. After a diagnosis, more tests help your doctors learn about the extent of cancer. The type of treatment you get depends on how much cancer is in the liver and where the cancer may have spread in the body. Treatment options will also depend on whether or not you have a working or damaged liver.

This information is taken from the treatment guidelines written by NCCN experts of HCC. These treatment guidelines list options for people with HCC in general. Thus, your doctors may suggest other treatment for you based on your health and personal needs. Discuss and decide on your treatment plan with your doctor.

Helpful tips for reading the treatment guides in the next 3 chapters

✓ The treatment guides (that look like charts) are numbered and list test or treatment options.

✓ It is helpful to read the guides from left to right, using the arrows to follow a path. The titles of the guides are important.

✓ The symbol ± means with or without. This is used to show when a test or treatment is given "with or without" another test or treatment.

✓ Acronyms (a group of letters using the first letters of words or phrases) found in the treatment guides are defined on page 80.
Treatment planning


<table>
<thead>
<tr>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Medical history and physical exam</td>
</tr>
<tr>
<td>• Hepatitis panel test</td>
</tr>
<tr>
<td>• CBC and platelets</td>
</tr>
<tr>
<td>• Other blood tests</td>
</tr>
<tr>
<td>• AFP</td>
</tr>
<tr>
<td>• CT of chest</td>
</tr>
<tr>
<td>• Bone scan, if needed</td>
</tr>
<tr>
<td>• CT or MRI of abdomen and pelvis</td>
</tr>
</tbody>
</table>

Your performance status

Which treatment is recommended for you depends on your health status rating, also called performance status. Your health status is a rating by your doctor based on your overall health, cancer symptoms, and ability to do daily activities.

- **Good health status** means that your overall health is good and you’re able to continue doing all of your regular daily activities very well. You also have very few or very mild symptoms of the cancer and you’re able to eat well.

- **Poor health status** means that your overall health is poor. You aren’t able to do your regular daily activities well, and you are suffering from a number of cancer symptoms.

A team of experts who have experience with HCC should be managing your care. The team will create a plan designed for your needs. After your doctor has confirmed that you have HCC, he or she will talk with you about the diagnosis and may order more tests. Your doctors will take a medical history, including your lifetime medical conditions; do an exam of your body; and order imaging tests and blood tests. See Guide 9.

Certain blood tests will check for a past or current hepatitis viral infection. Hepatitis puts someone at risk for HCC. Some cancer treatment can wake up (reactivate) the virus. If this happens, it can cause harm to the liver. In many patients, a blood test for AFP will also let your doctor know if HCC may be present.
## Treatment with surgery or liver transplant

### Guide 10. Treatment with surgery or liver transplant

<table>
<thead>
<tr>
<th>Surgery assessment</th>
<th>Treatment options</th>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery is an option</td>
<td>• Surgery or Ablation • ADT • Radiation therapy</td>
<td>• Imaging tests every 3–6 months for 2 years, then every 6–12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• AFP every 3–6 months for 2 years then every 6–12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Treat if disease comes back (recurs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Refer to hepatologist, if antiviral therapy needed for hepatitis</td>
</tr>
<tr>
<td>Liver transplant is an option</td>
<td>• Refer to liver transplant center • Consider bridge therapy, then complete transplant</td>
<td></td>
</tr>
</tbody>
</table>

Imaging tests may include a CT of the chest. HCC tends to spread to the lungs, so this area may be assessed. Other imaging tests include a CT or MRI of the abdomen and pelvis. Imaging of this area allows your doctor to see the size of the tumor, if the cancer has spread in this area, or if the tumor has invaded the lymph nodes or blood vessels. Your doctor can also check the underlying health of your liver.

### Test results

Once your doctors review your test results, they can talk to you about your options. Talking with your doctor about treatment and its side effects is important. It is helpful to ask questions and understand what comes next in your treatment plan.

Guide 10 shows when surgery, in this case a partial hepatectomy, or a liver transplant may be an option. Your doctor will use the test results and consider other factors, including your overall health and liver function, when it comes to treatment. Surgery or a liver transplant are primary (main) treatment options for people with HCC.

If you can have surgery, you and your doctor may decide on this option. Other options include locoregional therapy such as ablation, ADT, or radiation therapy. (See page 33 for more on locoregional therapies). ADT includes different forms of embolization.

Surgery is not an option for everyone with HCC. Sometimes parts of the liver can’t be saved and keep working as they should in the body. Thus, other treatment options may be offered. If you can have a liver transplant, you should go to a liver transplant center with an experienced transplant team.

You may have bridge therapy while you wait for a liver transplant. Bridge therapy may include ablation, embolization, radiation, or drug treatment. Other treatment is given because some people need to be on the waiting list for a longer time. Thus, bridge therapy may be considered.
Treatment without surgery

Guide 11. Treatment without surgery (partial hepatectomy)

<table>
<thead>
<tr>
<th>Transplant assessment</th>
<th>Treatment options</th>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver transplant is an option</td>
<td>• Refer to liver transplant center&lt;br&gt;• Consider bridge therapy, then complete transplant</td>
<td>• Imaging tests every 3–6 months for 2 years, then every 6–12 months&lt;br&gt;• AFP every 3–6 months for 2 years then every 6–12 months&lt;br&gt;• Treat if disease comes back (recurs)</td>
</tr>
<tr>
<td>Liver transplant is not the best option because of:&lt;br&gt;◦ Liver damage&lt;br&gt;◦ Tumor location&lt;br&gt;◦ Other illness or poor health status</td>
<td>• Locoregional therapy preferred:&lt;br&gt;◦ Ablation&lt;br&gt;◦ ADT&lt;br&gt;◦ Radiation therapy&lt;br&gt;• Systemic therapy:&lt;br&gt;◦ Sorafenib&lt;br&gt;◦ Chemotherapy&lt;br&gt;◦ Systemic&lt;br&gt;◦ Intra-arterial&lt;br&gt;• Clinical trial&lt;br&gt;• Best supportive care</td>
<td>• If progression on or after sorafenib:&lt;br&gt;◦ Regorafenib&lt;br&gt;◦ Nivolumab</td>
</tr>
</tbody>
</table>

Whether you have surgery or a liver transplant, you will start surveillance soon after. Surveillance consists of testing on a regular basis. Your doctors watch for tumor growth so that treatment can be started later, if needed, instead of right away. During surveillance, your doctor will plan a testing schedule just for you. Keep in mind, these and other tests may be given more or less often than listed in Guide 10. If the cancer comes back, your treatment team may suggest more treatment.

Guide 11 starts with an assessment to see if a liver transplant is an option. Sometimes surgery (partial hepatectomy) is not possible because of where the tumor is located, it invaded the blood vessels, or the liver is too damaged. Yet, a liver transplant may be possible in some cases. If a transplant is possible, you should seek expert care and your treatment team may consider bridge therapy before the transplant.

After a transplant, your treatment team will watch you closely. Surveillance will begin and will consist of testing on a regular basis. Your doctors will watch for tumor growth so that treatment can be started later, if needed, instead of right away.
## Treatment for local disease

### Guide 12. Treatment for local disease

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Treatment options</th>
<th>Further treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local disease or Local disease with minimal extrahepatic disease only</td>
<td>• Locoregional therapy preferred:</td>
<td>• If progression on or after sorafenib:</td>
</tr>
<tr>
<td></td>
<td>◦ Ablation</td>
<td>◦ Regorafenib</td>
</tr>
<tr>
<td></td>
<td>◦ ADT</td>
<td>◦ Nivolumab</td>
</tr>
<tr>
<td></td>
<td>◦ Radiation therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Systemic therapy:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Sorafenib</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Chemotherapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Systemic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Intra-arterial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Clinical trial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Best supportive care</td>
<td></td>
</tr>
</tbody>
</table>

During surveillance, your doctor will plan a testing schedule just for you. Keep in mind, these and other tests may be given more or less often.

If a liver transplant is not the best option, you may get locoregional therapy such as ablation, ADT, or radiation therapy. According to NCCN experts, these therapies are a preferred option of care. Systemic therapy using drug treatment may also be an option. This includes a targeted therapy called sorafenib and chemotherapy. However, it is recommended you receive chemotherapy in a clinical trial. More data are needed to learn how well chemotherapy works in treating HCC. Thus, your doctor may suggest you join a clinical trial.

Another option is to seek best supportive care to ease any discomfort you may have. Best supportive care does not treat the cancer; the goal is to control the symptoms and make you comfortable to provide the best possible quality of life.

There are other options if you need more treatment. If the cancer gets worse (progresses) while taking sorafenib, you may take regorafenib or nivolumab. Ask your doctor if you will start surveillance or need more treatment.

**Guide 12** lists treatment options for local disease. This means the tumor localized mostly within the liver, and without spread, or with very minimal spread outside the liver. Treatment options include locoregional therapy as seen in Guide 12. These therapies are the preferred options for local disease.

Systemic therapy may include sorafenib or chemotherapy. If the cancer continues to grow during or after taking sorafenib, you may take regorafenib or nivolumab. Joining a clinical trial is strongly encouraged. If you need relief from symptoms, you can seek best supportive care. Ask your doctor which options are best for the stage of cancer you have. It is helpful to learn what you can expect during and after treatment is complete.
Liver cancer                   Treatment for metastatic disease or widespread tumors

Guide 13. Treatment for metastatic disease or widespread tumors in the liver

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Treatment options</th>
<th>Further treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic disease or Widespread tumors in the liver</td>
<td>• Systemic therapy:</td>
<td>• If progression on or after sorafenib:</td>
</tr>
<tr>
<td></td>
<td>◦ Sorafenib</td>
<td>◦ Regorafenib</td>
</tr>
<tr>
<td></td>
<td>◦ Chemotherapy</td>
<td>◦ Nivolumab</td>
</tr>
<tr>
<td></td>
<td>◦ Systemic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Intra-arterial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Clinical trial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Best supportive care</td>
<td></td>
</tr>
</tbody>
</table>

Guide 13 lists treatment options for HCC that has spread to distant sites in the body. It also lists options for when there are many tumors throughout the liver. At this stage of disease, options include systemic therapy with sorafenib or chemotherapy. It is recommended you receive chemotherapy in a clinical trial. If the cancer gets worse (progresses) during or after taking sorafenib, your doctor may offer regorafenib or nivolumab. Another option is to seek best supportive care to relieve any discomfort you may have.

Review

- Assessing the extent of liver disease is important when deciding on treatment for HCC.
- Partial hepatectomy is helpful for tumors that have not invaded the blood vessels.
- Doctors may consider a liver transplant if you meet certain criteria for this treatment.
- Your doctor may suggest locoregional therapy such as ablation, ADT, or radiation therapy.
- Systemic therapy using drug treatment may be an option.
- Surveillance consists of testing on a regular basis to watch for tumor growth.
5
Treatment guide: Gallbladder cancer

48 Treatment planning
49 Treatment for gallbladder cancer
54 Treatment for advanced disease
55 Review
Part 5 is a treatment guide for gallbladder cancer. This type of cancer may be found during surgery, from the results of a biopsy, or on an imaging test. This chapter starts with treatment planning. Followed by primary treatment options. Then, treatment options for advanced gallbladder cancer.

This information is taken from the treatment guidelines written by NCCN experts of gallbladder cancer. These treatment guidelines list options for people with gallbladder cancer in general. Thus, your doctors may suggest other treatment for you based on your health and personal needs. Discuss and decide on your treatment plan with your doctor.

Treatment planning

A team of experts who have experience with gallbladder cancer should be managing your care. The team will create a plan designed for your needs. Gallbladder cancer tends to be diagnosed at a later stage of disease. Sometimes the cancer is found during a biopsy or surgery that was planned for another reason. Others have an abnormal finding on an imaging test. Some people go to the doctor’s because they have jaundice (yellow-colored skin and whites of the eyes) and don’t know the cause of the jaundice.

If your doctor is concerned you have gallbladder cancer, he or she will take a medical history, including your lifetime medical conditions; do an exam of your body; and may order imaging and blood tests if not done before. Your doctor will want to assess the extent of disease and see how your gallbladder and liver are working. Your tests results will help guide your treatment options. Ask questions so you can understand what is available to you.

Your care plan:

- Keep a list of contact information of all of your health care providers.
- Use a calendar or ask a caregiver to make note of your treatment schedule and follow-up appointments.
# Treatment for gallbladder cancer

Guide 14. Treatment for gallbladder cancer found during surgery

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>Primary treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery is an option</td>
<td>• Cholecystectomy + hepatic resection + lymphadenectomy ± bile duct removal</td>
</tr>
<tr>
<td>Completing the surgery is not an option</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td>• MSI testing before other treatment</td>
<td>• Chemoradiation</td>
</tr>
<tr>
<td></td>
<td>• Radiation therapy</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial</td>
</tr>
<tr>
<td></td>
<td>• Best supportive care</td>
</tr>
<tr>
<td></td>
<td>• Pembrolizumab (only for MSI-H tumors)</td>
</tr>
</tbody>
</table>

Guide 14 shares treatment options for gallbladder cancer that was found during surgery. This could be a surgery like a simple cholecystectomy, when your doctor may be planning to remove the gallbladder for reasons other than cancer. If it seems you could have a more serious condition like cancer, your surgeon may do a biopsy to confirm. He or she may see the cancer has spread beyond the gallbladder and have to decide if more advanced surgery is needed. Sometimes imaging tests of the abdomen and pelvis will be done to assess the extent of cancer. For most, the surgery will involve taking out more than the gallbladder. Your doctor may also remove a section or whole lobe of the liver, some lymph nodes, and possibly the common bile duct.

If the cancer has spread to distant lymph nodes or organs, or covered the blood vessels, fully removing the cancer may not be possible. Thus, other treatment options may be suggested. They include chemotherapy, chemoradiation, radiation therapy, a clinical trial, or best supportive care to relieve your discomfort.

Chemotherapy options include gemcitabine and cisplatin given together, or another fluoropyrimidine-or gemcitabine-based chemotherapy. Chemoradiation for gallbladder cancer, or any biliary tract cancer, that has not spread to distant sites usually includes fluorouracil or capecitabine.

MSI (microsatellite instability) testing may be done if you are not able to have surgery. Your doctor is checking if you have an MSI-H (microsatellite instability-high) tumor. The genes are abnormal in these tumors. There is a problem with the cell being able to repair itself. Pembrolizumab, an immunotherapy drug, may be an option for treating these MSI-H tumors. This drug helps the immune system find and fight the cancer.
Guide 15. Treatment for gallbladder cancer found during pathology review

<table>
<thead>
<tr>
<th>Pathology results</th>
<th>Tests</th>
<th>Primary treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1a (with negative margins)</td>
<td></td>
<td>• Observe</td>
</tr>
<tr>
<td>Cystic duct node positive</td>
<td>• CT or MRI of abdomen and pelvis</td>
<td>• Consider neoadjuvant chemotherapy</td>
</tr>
<tr>
<td></td>
<td>• CT of chest</td>
<td>• Clinical trial</td>
</tr>
<tr>
<td></td>
<td>• Consider staging laparoscopy</td>
<td>• Hepatic resection + lymphadenectomy ± bile duct removal</td>
</tr>
<tr>
<td></td>
<td>• MSI testing</td>
<td></td>
</tr>
<tr>
<td>T1b or greater</td>
<td>• CT or MRI of abdomen and pelvis</td>
<td>• If surgery is an option, see treatment in row above</td>
</tr>
<tr>
<td></td>
<td>• CT of chest</td>
<td>• If surgery is not an option, have MSI testing and see these options:</td>
</tr>
<tr>
<td></td>
<td>• Consider staging laparoscopy</td>
<td>◦ Chemotherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Chemoradiation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Radiation therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Clinical trial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Best supportive care</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Pembrolizumab (only for MSI-H tumors)</td>
</tr>
</tbody>
</table>

Guide 15 shows the primary treatment options for gallbladder cancer found during a pathology review. An expert hepatobiliary pathologist should review your pathology results. Your doctor will check the pathology report for details on the tumor size and location. Imaging tests will be done to assess the extent of disease. A diagnostic laparoscopy may also be done if your doctor suspects the cancer has spread.

If the tumor is small (T1a) with negative margins, then observation will be considered. If there is cancer in the cystic duct lymph nodes or if the margins are positive, treatment may include chemotherapy before surgery. This would be a fluoropyrimidine- or gemcitabine-based chemotherapy. You may also consider joining a clinical trial or having more surgery to remove the liver, lymph nodes, and/or the common bile duct.

If the tumor is larger (T1b or greater), your doctor will decide if surgery is possible. If surgery is not possible, you have more than one option. The treatment options are listed in Guide 15. NCCN experts support joining a clinical trial, especially if you and your doctor consider chemotherapy.
Guide 16. Tests after a tumor is found on imaging

Your doctor will check tumor markers known as CEA (carcinoembryonic antigen) and CA 19-9. They may be elevated with gallbladder cancer. Other medical conditions can also cause higher levels of these markers. Thus, your doctor will use these tests along with other tests to confirm cancer. CA 19-9 may also be assessed after the bile ducts are drained. This level may be higher with cancer.

Ask questions about the tests you will have. You should also meet with a surgeon during this time. He or she may do a staging laparoscopy to explore the gallbladder and surrounding area for cancer.

Chemotherapy includes gemcitabine and cisplatin given together, or another fluoropyrimidine- or gemcitabine-based chemotherapy. EBRT given with fluoropyrimidine may be considered. Another option is radiation therapy. This may be an option for most tumors no matter where they are located. Best supportive care is another option to relieve the symptoms caused by the cancer.

Guide 16 lists tests that may be done if an abnormal tumor is found on imaging. Sometimes cancer may be found in other ways, like on an imaging test being done for other medical reasons. If there is concern for gallbladder cancer based on the results, more tests will be ordered. This may include more imaging tests and blood tests, including a liver function panel.

Tests

- Medical history and physical exam
- CT or MRI of abdomen and pelvis
- CT of chest
- Liver function tests
- Meet with a surgeon
- Assess hepatic function
- Consider CEA and CA 19-9 tests
- Consider staging laparoscopy

NCCN Guidelines for Patients®: Hepatobiliary Cancers, 2018
Guide 17. Primary treatment for gallbladder cancer found on imaging

<table>
<thead>
<tr>
<th>Assess for surgery</th>
<th>Primary treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery is an option</td>
<td>• Cholecystectomy + hepatic resection + lymphadenectomy ± bile duct removal</td>
</tr>
<tr>
<td>Completing the surgery is not an option</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td>• Biopsy</td>
<td>• Chemoradiation</td>
</tr>
<tr>
<td>◦ MSI testing before treatment</td>
<td>• Radiation therapy</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial</td>
</tr>
<tr>
<td></td>
<td>• Best supportive care</td>
</tr>
<tr>
<td></td>
<td>• Pembrolizumab (only for MSI-H tumors)</td>
</tr>
</tbody>
</table>

Guide 17 lists the primary treatment options for gallbladder cancer that was found on an imaging test and confirmed by the tests listed in Guide 16. Your doctor will assess if surgery is an option for you. If so, you will have the gallbladder, a section or whole lobe of the liver, some lymph nodes, and possibly the common bile duct removed.

If your doctor can’t complete the surgery, you still have other options. Your treatment may include chemotherapy with gemcitabine and cisplatin given together, or another fluoropyrimidine- or gemcitabine-based chemotherapy. EBRT given with fluoropyrimidine may be considered. Radiation therapy, a clinical trial, or best supportive care may also be recommended. Pembrolizumab may be an option for people with MSI-H tumors.

Guide 18 lists the tests you may have if you have jaundice. Jaundice is a yellowing of the skin and whites of the eyes due to a buildup of bilirubin in the body. Bilirubin is a yellow-brown substance in bile. Bile is a chemical made by the liver that flows through bile ducts in the liver into the intestines to help digest food.

Guide 18. Tests if jaundice occurs

<table>
<thead>
<tr>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Medical history and physical exam</td>
</tr>
<tr>
<td>• Liver function tests</td>
</tr>
<tr>
<td>• CT of chest</td>
</tr>
<tr>
<td>• CT or MRI of abdomen and pelvis</td>
</tr>
<tr>
<td>• Cholangiography</td>
</tr>
<tr>
<td>• Meet with a surgeon</td>
</tr>
<tr>
<td>• Consider CEA and CA 19-9 tests</td>
</tr>
<tr>
<td>• Consider staging laparoscopy</td>
</tr>
</tbody>
</table>
Your doctor will do some tests to check your health. They will include taking your medical history and doing a physical exam, along with imaging and blood tests. MRCP is the preferred type of cholangiography to assess the blockage.

During this time, you should meet with a surgeon to learn about your options. He or she may consider doing a staging laparoscopy to find out the extent of disease and why there is a blockage causing the jaundice.

**Guide 19** offers primary treatment options for people who have jaundice. Jaundice may be caused by the cancer. The tumor can grow large and block the fluid from draining from the bile ducts. Thus, if you have jaundice, your doctor will want to confirm gallbladder cancer. He or she will consider draining the fluid before chemotherapy starts.

Your doctor will consider surgery. If the disease is spreading outside of the gallbladder and the tumor is large, your doctor may suggest neoadjuvant treatment. Chemotherapy combination regimens include gemcitabine/cisplatin, gemcitabine/oxaliplatin, gemcitabine/capecitabine, capecitabine/cisplatin, capecitabine/oxaliplatin, 5-fluorouracil/oxaliplatin, and 5-fluorouracil/cisplatin. Single agents include gemcitabine, capecitabine, and 5-fluorouracil.

Neoadjuvant therapy is given to shrink the tumor and slow the spread of cancer. After this therapy, your doctor may drain the fluid that is blocking the bile ducts. A part or wedge of the liver, lymph nodes, and the common bile duct may also be removed.
Treatment for advanced disease

Guide 20. Treatment for metastatic disease if jaundice occurs

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Tests</th>
<th>Primary treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic disease</td>
<td>• Biopsy</td>
<td>• Biliary drainage</td>
</tr>
<tr>
<td></td>
<td>◦ MSI testing</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Clinical trial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Best supportive care</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pembrolizumab (only for MSI-H tumors)</td>
</tr>
</tbody>
</table>

Guide 21. Treatment after surgery

<table>
<thead>
<tr>
<th>Status after surgery</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No cancer remains or Carcinoma in situ (very small amount) at margin</td>
<td>• Observe</td>
</tr>
<tr>
<td></td>
<td>• Chemoradiation</td>
</tr>
<tr>
<td></td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial</td>
</tr>
<tr>
<td>• Positive margin or Some cancer remains or Cancer remains and can be seen</td>
<td>• Chemoradiation followed by chemotherapy</td>
</tr>
<tr>
<td></td>
<td>• Chemotherapy ± chemoradiation</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial</td>
</tr>
</tbody>
</table>

If surgery is not an option, the cancer may be too large to be completely removed. Your doctor will do a biopsy and MSI testing. Other options your doctor may suggest include draining the fluid, chemotherapy, chemoradiation, radiation therapy, joining a clinical trial, or best supportive care for symptom relief. Chemotherapy includes gemcitabine and cisplatin given together, or another fluoropyrimidine- or gemcitabine-based chemotherapy. Pembrolizumab may be an option for people with MSI-H tumors.

Guide 20 lists primary treatment options for metastatic gallbladder cancer. This cancer 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. You may have fluid drained from the bile ducts if you have jaundice. This is recommended if you are going to have chemotherapy.
Chemotherapy may be gemcitabine and cisplatin given together, or another fluoropyrimidine- or gemcitabine-based chemotherapy. Other options include joining a clinical trial, or best supportive care. Pembrolizumab may be an option for people with MSI-H tumors.

Guide 21 shares the possible results of surgery. Once surgery is complete, your doctors will want to know if any cancer remains. The results will guide your next treatment option. If none or very little cancer remains, you may be observed or receive chemoradiation or chemotherapy. Chemoradiation includes fluoropyrimidine. Chemotherapy would include a fluoropyrimidine- or gemcitabine-based chemotherapy. You may also consider joining a clinical trial.

If you have cancer that remains at the margin, or can be seen by your doctor, you will have further treatment. This may include chemoradiation followed by chemotherapy, or chemotherapy followed by chemoradiation. A clinical trial is also a good option. Clinical trials are an option for any stage of cancer. Ask your doctor or nurse about clinical trials that may be available to you.

You will start surveillance after treatment is complete. During surveillance, your doctor will plan a testing schedule just for you. See Guide 22.

A CT scan of the chest and CT or MRI scan of the abdomen and pelvis are recommended. If needed, your doctor may order a blood test to check tumor markers CEA and CA 19-9. If the levels rise, it may be a sign the cancer is growing. Keep in mind, these and other tests may be given more or less often than listed in the guide. If the cancer comes back, your treatment team may suggest more treatment.

Guide 22. Surveillance

<table>
<thead>
<tr>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Consider imaging tests every 6 months for 2 years if needed, then every year up to 5 years</td>
</tr>
<tr>
<td>• Consider CEA and CA 19-9 tests</td>
</tr>
</tbody>
</table>

Review

- If your doctor is concerned you have gallbladder cancer, he or she will take a medical history, do an exam of your body, and may order imaging and blood tests.

- Sometimes gallbladder cancer is found during surgery, during a review of pathology, or on an imaging test.

- Some people have jaundice because of gallbladder cancer. This is a yellowing of the skin and whites of the eyes due to a buildup of bilirubin in the body.

- Treatment options for gallbladder cancer may include surgery, chemotherapy, chemoradiation, radiation therapy, clinical trial, best supportive care, or pembrolizumab for MSI-H tumors.

- Best supportive care may offer symptom relief.
# Treatment guide: Bile duct cancer (cholangiocarcinoma)

<table>
<thead>
<tr>
<th>Page</th>
<th>Treatment Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>57</td>
<td>Treatment planning for intrahepatic bile duct cancer</td>
</tr>
<tr>
<td>58</td>
<td>Treatment for intrahepatic bile duct cancer</td>
</tr>
<tr>
<td>60</td>
<td>Treatment after surgery for intrahepatic bile duct cancer</td>
</tr>
<tr>
<td>60</td>
<td>Treatment planning for extrahepatic bile duct cancer</td>
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<tr>
<td>62</td>
<td>Treatment for extrahepatic bile duct cancer</td>
</tr>
<tr>
<td>64</td>
<td>Treatment after surgery for extrahepatic bile duct cancer</td>
</tr>
<tr>
<td>65</td>
<td>Review</td>
</tr>
</tbody>
</table>
Part 6 starts with treatment planning. Primary treatment and treatment after surgery (adjuvant treatment) are listed for intrahepatic bile duct cancer. Next, primary treatment and treatment after surgery (adjuvant treatment) are listed for extrahepatic bile duct cancer. Surveillance is recommended for both types of bile duct cancer.

This information is taken from the treatment guidelines written by NCCN experts of bile duct cancer. These treatment guidelines list options for people with bile duct cancer in general. Thus, your doctors may suggest other treatment for you based on your health and personal needs. Discuss and decide on your treatment plan with your doctor.

### Treatment planning for intrahepatic bile duct cancer

A team of experts who have experience with intrahepatic bile duct cancer should be managing your care. The team will create a plan designed for your needs. Your doctors will take a medical history, including your lifetime medical conditions, do an exam of your body, and order imaging and blood tests. See Guide 23.

Certain blood tests will check for a past or current hepatitis viral infection. See page 20. Hepatitis is a risk factor for bile duct cancer. Some cancer treatment can wake up (reactivate) the virus. If this happens, it can cause harm to the liver.

---

**Guide 23. Tests for intrahepatic bile duct cancer**

<table>
<thead>
<tr>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Medical history and physical exam</td>
</tr>
<tr>
<td>• CT or MRI of abdomen and pelvis</td>
</tr>
<tr>
<td>• CT of chest</td>
</tr>
<tr>
<td>• Consider CEA and CA 19-9 tests</td>
</tr>
<tr>
<td>• Liver function tests</td>
</tr>
<tr>
<td>• Meet with a surgeon</td>
</tr>
<tr>
<td>• EGD (esophagogastroduodenoscopy) and colonoscopy</td>
</tr>
<tr>
<td>• Consider hepatitis panel test</td>
</tr>
<tr>
<td>• Consider biopsy</td>
</tr>
<tr>
<td>• Consider AFP test</td>
</tr>
</tbody>
</table>
Treatment for intrahepatic bile duct cancer

Guide 24 offers treatment options for intrahepatic bile cancer that has not spread. First, your treatment team will assess if surgery is an option. This depends on the extent of cancer. If you have surgery, lymph nodes may also be removed since cancer can spread there. Some doctors decide to do a staging laparoscopy to see where the disease is located. If the cancer spreads in the area or to distant sites, surgery may not be possible. In this case, your doctor may consider MSI testing before treatment starts.

If surgery can’t be done, other options will be suggested. They include chemotherapy with gemcitabine and cisplatin given together, or another fluoropyrimidine or gemcitabine type of chemotherapy. Other options include chemoradiation, joining a clinical trial, or locoregional therapies. Radiation therapy or arterially directed therapies have been found to be safe and work well in some cases. If the MSI test is positive, you may take pembrolizumab. Best supportive care is an option for symptom relief.

Guide 25 lists treatment options for metastatic intrahepatic bile duct cancer. The cancer has spread to distant sites in the body. MSI testing will be done before treatment. It will help your doctor decide if pembrolizumab is an option. Chemotherapy including gemcitabine and cisplatin given together, or another fluoropyrimidine- or gemcitabine-based chemotherapy may be suggested. Other options include a clinical trial, locoregional therapies such as radiation therapy and arterially directed therapies, or best supportive care.
### Guide 24. Primary treatment for non-metastatic intrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>Primary treatment options</th>
</tr>
</thead>
</table>
| Surgery is an option | - Consider staging laparoscopy  
- Surgery  
  - Consider removing the lymph nodes for staging |
| Surgery is not an option  
  - MSI testing before treatment | - Chemotherapy  
- Clinical trial  
- Chemoradiation  
- Consider locoregional therapy:  
  - Radiation therapy  
  - ADT  
- Best supportive care  
- Pembrolizumab (only for MSI-H tumors) |

### Guide 25. Primary treatment for metastatic intrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Tests</th>
<th>Primary treatment options</th>
</tr>
</thead>
</table>
| Metastatic disease | - Consider molecular testing, including MSI testing | - Chemotherapy  
- Clinical trial  
- Consider locoregional therapy:  
  - Radiation therapy  
  - ADT  
- Pembrolizumab (only for MSI-H tumors)  
- Best supportive care |
Guide 26 shares other treatment that may be given after surgery is complete. The options you have are based on whether or not cancer remains at the surgical margin. If there is no cancer at the margin, you may be observed, or you may join a clinical trial to find new or better ways to prevent cancer from returning. You may also start adjuvant treatment using chemotherapy.

If some cancer remains or you have cancer in lymph nodes near the original tumor, you may also consider a clinical trial, start chemoradiation, or start chemotherapy with or without chemoradiation. The goal of this adjuvant treatment is to kill the cancer cells and prevent them from spreading in the body.

If cancer remains and can be seen by your doctor, he or she may suggest you join a clinical trial. Your doctor may also suggest chemotherapy. It may be given with or without chemoradiation. If possible, you may have locoregional therapy using embolization methods. Best supportive care may be an option if you need relief for any symptoms you have.

A team of experts who have experience with extrahepatic bile duct cancer should be managing your care. The team will create a plan designed for your needs. Your doctors will take a medical history, including your lifetime medical conditions; do an exam of your body; and order imaging tests and blood tests. See Guide 27.
### Tests for extrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Medical history and physical exam</td>
</tr>
<tr>
<td>• CT or MRI of abdomen and pelvis</td>
</tr>
<tr>
<td>• CT of chest</td>
</tr>
<tr>
<td>• Cholangiography</td>
</tr>
<tr>
<td>• Consider CEA and CA 19-9 tests</td>
</tr>
<tr>
<td>• Liver function tests</td>
</tr>
<tr>
<td>• Meet with a surgeon</td>
</tr>
<tr>
<td>• Consider EUS (after meeting with a surgeon)</td>
</tr>
<tr>
<td>• Consider serum IgG4 to rule out autoimmune cholangitis</td>
</tr>
</tbody>
</table>

You may have a test called a cholangiography to see if the bile ducts are blocked. Your doctor may also test for CEA and CA 19-9 tumor markers. However, these tumor markers are not used alone to confirm cancer. AFP testing will be another part of blood testing that helps support the diagnosis of extrahepatic bile duct cancer. Your level of IgG4 may also be checked to rule out an autoimmune cholangitis. This disease of the immune system may be long-term and affect the liver and biliary tract.

During this time, it is helpful to meet with a surgeon. He or she can assess if you are healthy enough to have surgery. He or she will let you know if the cancer can be removed or if you need other treatment. If you are not able to have surgery or a liver transplant, you may have a biopsy to confirm the cancer type.

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. Sometimes an EUS is done to get a closer look at the bile ducts. Your doctor will want to do more than one test and gather the results to diagnose extrahepatic bile duct cancer.

**Test results**

Once your doctors review your test results, they can talk to you about your options. Talking with your doctor about treatment and its side effects is important. It is helpful to ask questions and understand what comes next in your treatment plan.
Bile duct cancer

Treatment for extrahepatic bile duct cancer

Guide 28. Treatment planning for non-metastatic extrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>Treatment planning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery is not an option</td>
<td>• Biliary drainage, if needed</td>
</tr>
<tr>
<td></td>
<td>• Biopsy (before surgery, not transplant)</td>
</tr>
<tr>
<td></td>
<td>◦ Consider molecular testing, including MSI testing</td>
</tr>
<tr>
<td></td>
<td>• Consider referral to transplant center</td>
</tr>
<tr>
<td>Surgery is an option</td>
<td>• Surgical exploration</td>
</tr>
<tr>
<td></td>
<td>• Consider laparoscopic staging</td>
</tr>
<tr>
<td></td>
<td>• Consider biliary drainage before surgery</td>
</tr>
<tr>
<td></td>
<td>• Seek expert opinion of multidisciplinary (ie, medical, radiation, and surgical oncologists) doctors</td>
</tr>
</tbody>
</table>

Guide 28 starts with your treatment team considering whether surgery is possible. This decision is based on where the cancer is located in your body. If it has spread to a distant area, you may have a biopsy, as well as fluid drained from the biliary tract. MSI testing will also be considered. If you are able to have a liver transplant, your doctor may not do a biopsy before the transplant.

If surgery is possible, your doctor may explore the area to check the extent of cancer. This involves laparoscopic surgery. Fluid may also be drained if needed. Your treatment team of experts will discuss if surgery is safe for you and whether the cancer can be removed.

Guide 29 lists primary treatment options for extrahepatic bile duct cancer. Your treatment team has considered surgery. If this is not the best first option, you may have chemotherapy. This includes gemcitabine and cisplatin given together, or another fluoropyrimidine- or gemcitabine-based chemotherapy. You may consider joining a clinical trial or receiving chemoradiation, radiation therapy, or pembrolizumab for MSI-H tumors. Best supportive care may be given for symptom control and relief of any pain or discomfort you are feeling.

It is helpful to ask your doctors to explain your treatment options. You will also want to learn about the possible side effects of each option. Being your own advocate, and asking questions, may help you prepare for your treatment plan.
Guide 29. Primary treatment for non-metastatic extrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>Primary treatment options</th>
</tr>
</thead>
</table>
| Surgery is not an option | • Chemotherapy  
                        | • Clinical trial  
                        | • Chemoradiation  
                        | • Radiation therapy  
                        | • Pembrolizumab (only for MSI-H tumors)  
                        | • Best supportive care |
| Surgery is an option     | • Complete surgery  
                        | • Then, see adjuvant treatment and surveillance in Guide 32    |

Guide 30. Treatment planning for metastatic extrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Treatment planning</th>
</tr>
</thead>
</table>
| Metastatic disease  | • Biliary drainage, if needed  
                        | • Biopsy  
                        | ◦ Consider molecular testing, including MSI testing |

Guide 30 lists care you may have before treatment, if you have metastatic disease. At this stage, your cancer has spread to distant sites in the body. The fluid may be blocking the bile ducts, causing jaundice. If you have jaundice, your doctor will attempt to drain the fluid. He or she may do a biopsy to confirm that the cancer in distant sites is extrahepatic bile duct cancer. Your treatment team will want to know the extent of disease. They will consider both local and systemic treatment options.
Guide 31 shares primary treatment options for metastatic disease. The options include systemic treatment options. This includes gemcitabine and cisplatin given together, or another fluoropyrimidine or gemcitabine chemotherapy. You may also consider joining a clinical trial or best supportive care for relief of any pain or discomfort you are feeling. Pembrolizumab may be an option for MSI-H tumors.

Guide 32 has adjuvant treatment options. This treatment follows a primary treatment like surgery. The goal is to kill any remaining cancer cells. This may be cancer cells that are seen by the human eye or cancer cells that may be there but can’t be easily seen.

Guide 31. Primary treatment for metastatic extrahepatic bile duct cancer

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Primary treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic disease</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial</td>
</tr>
<tr>
<td></td>
<td>• Pembrolizumab (only for MSI-H tumors)</td>
</tr>
<tr>
<td></td>
<td>• Best supportive care</td>
</tr>
</tbody>
</table>

Guide 32. Adjuvant treatment and surveillance

<table>
<thead>
<tr>
<th>Surgical margin status</th>
<th>Adjuvant treatment options</th>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No cancer at the margin and negative lymph nodes</td>
<td>• Observe</td>
<td>• Consider imaging tests every 6 months for 2 years if needed, then every year up to 5 years</td>
</tr>
<tr>
<td>or</td>
<td>• Chemoradiation</td>
<td></td>
</tr>
<tr>
<td>• Carcinoma in situ at margin</td>
<td>• Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>or</td>
<td>• Clinical trial</td>
<td></td>
</tr>
<tr>
<td>• Some cancer at the margin</td>
<td>• Chemoradiation followed by chemotherapy</td>
<td></td>
</tr>
<tr>
<td>or</td>
<td>• Chemotherapy ± chemoradiation</td>
<td></td>
</tr>
<tr>
<td>• Cancer at the margin can be seen</td>
<td>• Clinical trial</td>
<td></td>
</tr>
<tr>
<td>or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Positive regional lymph nodes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The treatment options are based on whether there is cancer at the margin or it spread to the lymph nodes. Your doctor will consider systemic therapy using chemotherapy. Chemoradiation may also be an option for some people. If the cancer is seen, your doctor may give you chemotherapy and chemoradiation.

Clinical trials are also suggested as an adjuvant treatment option. There may be research studies for people with extrahepatic bile duct cancer using systemic therapy or other treatment to find new and better ways to treat this type of cancer. Ask your treatment team if there are any clinical trials available to you.

Review

- Treatment planning may include imaging tests; blood tests for tumor markers, liver function, and the hepatitis virus; and a biopsy.

- Surgery may be a treatment option for both intrahepatic bile duct cancer and extrahepatic bile duct cancer.

- Other options, depending on the extent of cancer, may include chemotherapy, chemoradiation, locoregional therapy, radiation therapy, pembrolizumab for MSI-H tumors, a clinical trial, or best supportive care.

“There have been various turning points in my treatment when the way forward hasn’t been crystal clear. In those moments, I’ve learned—and am still learning—how to hear and to trust my own gut, my own heart.

-Andrea, intrahepatic cholangiocarcinoma survivor
Making treatment decisions

67 It’s your choice
67 Questions to ask
73 Deciding between options
74 Websites
74 Review
Having cancer can feel very stressful. While absorbing the fact that you have cancer, you must also learn about tests and treatments. And, the time you have to decide on a treatment plan may feel short.

Parts 1 through 6 described the hepatobiliary cancers along with the tests and treatment options recommended by NCCN experts. These options are based on science and agreement among these experts. Part 7 aims to help you make decisions and talk with your treatment team about your next steps of care.

It’s your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don’t know much about cancer. You’ve never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn’t any better than your doctors’.

Letting others decide which option is best may make you feel more at ease. However, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, your treatment team may still ask that you sign a consent form.

On the other hand, you may want to take the lead or share in decision-making. In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you can decide on a plan that works best for you when it comes to your personal and health needs.

Questions to ask

You will likely meet with experts from different fields of medicine. It is helpful to talk with each person. Prepare questions before your visit and ask questions if the information isn’t clear. You can get copies of your medical records. It may be helpful to have a family member or friend with you at these visits to listen carefully and even take notes. A patient advocate or navigator might also be able to come. They can help you ask questions and remember what was said.

The questions below are suggestions for information you read about in this book. Feel free to use these questions or come up with your own personal questions to ask your doctor and other members of your treatment team.
Questions about testing and the results

1. What tests will I have for this type of cancer?
2. Where and when will the tests take place?
3. How long will they take?
4. What are the risks?
5. How do I prepare for testing?
6. How soon will I know the results and who will explain them to me?
7. Where did the hepatobiliary cancer start? In what type of cell?
8. Is this cancer common?
9. Have any cancer cells spread to other parts of my body?
10. What is the cancer stage?
Questions about treatment options

1. What treatment options do I have?

2. Can I join a clinical trial?

3. Does this hospital or center offer the best treatment for me?

4. Can you provide me with the research that supports this treatment plan?

5. How often will I get treatment?

6. Do I have time to get a 2nd opinion?

7. How do I prepare for treatment?

8. Will I have to go to the hospital or elsewhere? How many times? How long is each visit?

9. Should I bring someone with me when I get treated?
Questions about clinical trials

1. What clinical trial is right for me?

2. How many people will be in the clinical trial?

3. What are the tests and treatments for this study? And how often will they be?

4. How long will I be in the clinical trial?

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

6. How will you know the treatment is working?

7. Who will help me understand the costs of the clinical trial?
Questions about side effects

1. What are the side effects?
2. When can they start?
3. How long will the side effects last?
4. When should I call the doctor about my side effects?
5. Are there any medications that can prevent or relieve these side effects?
6. Are there any complementary therapies that might help?
7. Are there any long-term effects from this treatment?
8. Is home care after treatment needed? If yes, what type?
9. How soon will I be able to manage my own health?
Questions about a doctor’s experience

1. Are you board certified? If yes, in what area?

2. How many patients like me have you treated?

3. How many procedures like the one you’re suggesting have you done?

4. Is this treatment a major part of your practice?

5. How many of your patients have had complications?
Deciding between options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn’t been shown to work better than another, so science isn’t helpful. Some ways to decide on treatment are discussed next.

Getting a 2nd opinion

Even if you like and trust your doctor, it is helpful to get a 2nd opinion. You will want to have another doctor review your test results. He or she can suggest a treatment plan or check the one you already heard about.

Things you can do to prepare:

- Check with your insurance company about its rules on 2nd opinions. You want to know about out-of-pocket costs for doctors who are not part of your insurance plan.

- Reach out to patient advocacy organizations (see the websites listed on page 74) for help with 2nd opinions. Some may also give referrals to hospitals or cancer centers that specialize in treating hepatobiliary cancers.

- Make plans to have copies of all your records sent to the doctor you will see for your 2nd opinion. Do this well before your appointment. If you run into trouble having records sent, pick them up and bring them with you.

If the new doctor offers other advice, make an appointment with your first doctor to talk about the differences. Do whatever you need to feel confident about your diagnosis and treatment plan.

Getting support

Support groups often include people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with hepatobiliary cancers. If your hospital or community doesn’t have support groups for people with hepatobiliary cancers, check out the websites listed on the next page.

You can also reach out to a social worker or psychologist. They can help you find ways to cope or refer you to support services. These services may also be available to your family, friends, and to those with children so they can connect and get support.

Keep in mind:

- Every treatment option has benefits and risks. Consider these when deciding which option is best for you.

- Talking to others may help identify benefits and risks you hadn’t thought of.
Websites

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

**Global Liver Institute**  
globalliver.org/livercancer

**National Cancer Institute**  
cancer.gov/types/liver  
cancer.gov/types/gallbladder  
cancer.gov/about-cancer/treatment/clinical-trials/search

**The Cholangiocarcinoma Foundation**  
cholangiocarcinoma.org

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- Getting a 2nd opinion, attending support groups, and comparing the benefits and risks may help you decide which treatment is best for you.

“ Never be afraid to take control of your cancer journey by asking questions, doing your own research, and getting 2nd or 3rd opinions. Educating yourself is crucial especially when fighting a rare cancer. 

-Patty, intrahepatic cholangiocarcinoma survivor
### Dictionary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>abdomen</td>
<td>The belly area between the chest and pelvis.</td>
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<tr>
<td>ablation</td>
<td>A treatment that destroys very small tumors with heat, cold, lasers, or chemicals. Also called ablative therapy.</td>
</tr>
<tr>
<td>adjuvant therapy</td>
<td>Treatment that is given to lower the chances of the cancer returning.</td>
</tr>
<tr>
<td>advanced cancer</td>
<td>Cancer that has spread beyond the area near the main tumor.</td>
</tr>
<tr>
<td>allergic reaction</td>
<td>An abnormal response by the body to a foreign substance that is harmless.</td>
</tr>
<tr>
<td>alpha-fetoprotein (AFP)</td>
<td>A protein made that is usually present in babies growing in the womb.</td>
</tr>
<tr>
<td>ascites</td>
<td>Abnormal buildup of fluid in the belly area.</td>
</tr>
<tr>
<td>bile</td>
<td>A yellowish-brown fluid that is made by the liver and helps to digest food.</td>
</tr>
<tr>
<td>bile duct</td>
<td>A small tube-shaped structure that drains digestive fluid (bile) from the liver.</td>
</tr>
<tr>
<td>bilirubin</td>
<td>A yellow-brown substance that is part of a digestive fluid called bile.</td>
</tr>
<tr>
<td>biopsy</td>
<td>A procedure that removes fluid or tissue samples to be tested for disease.</td>
</tr>
<tr>
<td>blood clot</td>
<td>A thickened mass of blood. Also called a thrombosis.</td>
</tr>
<tr>
<td>blood vessel</td>
<td>A tube-shaped structure that carries blood throughout the body.</td>
</tr>
<tr>
<td>bypass</td>
<td>An operation to re-route the flow of fluid in the body.</td>
</tr>
<tr>
<td>cancer antigen 19-9 (CA 19-9)</td>
<td>A protein made by certain cancer cells and found in blood.</td>
</tr>
<tr>
<td>cancer grade</td>
<td>A rating of how much cancer cells look like normal cells.</td>
</tr>
<tr>
<td>cancer stage</td>
<td>A rating of the outlook of a cancer based on its growth and spread.</td>
</tr>
<tr>
<td>carcinoembryonic antigen (CEA)</td>
<td>A protein that is present when some types of cancer form.</td>
</tr>
<tr>
<td>carcinoma in situ</td>
<td>A cancer that has not grown into tissue that would allow it to spread.</td>
</tr>
<tr>
<td>catheter</td>
<td>A tube-shaped device that is used to give treatment or drain fluid from the body.</td>
</tr>
<tr>
<td>cell</td>
<td>The “building blocks” of tissues in the body.</td>
</tr>
<tr>
<td>chemoradiation</td>
<td>Treatment with a combination of chemotherapy and radiation therapy.</td>
</tr>
<tr>
<td>chemotherapy</td>
<td>Drugs that kill cancer cells by damaging or disrupting the making of the genetic code.</td>
</tr>
<tr>
<td>cholangitis</td>
<td>An infection of the vessels that drain digestive fluid from the liver (bile ducts).</td>
</tr>
<tr>
<td>cholecystectomy</td>
<td>An operation to remove the gallbladder.</td>
</tr>
<tr>
<td>clinical trial</td>
<td>A type of research that assesses health tests or treatments.</td>
</tr>
<tr>
<td>colon</td>
<td>The hollow organ in which eaten food turns from a liquid into a solid form.</td>
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</tbody>
</table>
colonscopy
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 dye put into your body to make clearer pictures during
imaging tests.

core needle biopsy
A procedure that removes tissue samples with a hollow
needle. Also called core biopsy.
deoxyribonucleic acid (DNA)
A chain of chemicals in cells that contains coded instructions
for making and controlling cells. Also called the “blueprint of
life.”
donor
A person who gives their organs, tissues, or cells to another
person.
embolization
A treatment that cuts off 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.
esophagastroduodenoscopy (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.
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 track.
gene
Coded 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.
hives
A skin rash caused by the body trying to rid itself of a foreign
substance.
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.

intestine
The organ that food passes through after leaving the stomach.

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.

laparoscopic surgery
An operation with tools that are passed through small cuts in the belly area.

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

liver function test
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.

metastasectomy
Surgery to remove cancer that has spread far from the first tumor.

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.

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

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

pelvis
The body area between the hipbones.

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

performance status
A rating of one’s ability to do daily activities.
physical exam
A study of the body by a health expert for signs of disease.

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.

sarcoma
A cancer of bone or soft tissue cells.

sedative
A drug that helps a person to relax or go to sleep.

side effect
An unhealthy or unpleasant physical or emotional response to treatment.

simulation
The steps needed to prepare for treatment with radiation.

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

social worker
An expert in meeting social and emotional needs.

stereotactic body radiation therapy (SBRT)
Treatment with high-dose radiation within one or a few sessions. Also called stereotactic ablative radiotherapy (SABR).

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

Whipple procedure
An operation that removes the head of the pancreas and parts of other nearby organs. Also called pancreatoduodenectomy.

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

3D-CRT
three-dimensional conformal radiation therapy

ADT
arterially directed therapies

AFP
alpha-fetoprotein

AJCC
American Joint Commission on Cancer

ALP
alkaline phosphatase

ALT
alanine transaminase

AST
aspartate aminotransferase

BUN
blood urea nitrogen

CA 19-9
cancer antigen 19-9

CAM
complementary and alternative medicine

CBC
complete blood count

CEA
carcinoembryonic antigen

CT
computed tomography

DEB-TACE
drug-eluting bead transarterial chemoembolization

DNA
deoxyribonucleic acid

EBRT
external beam radiation therapy

EGD
esophagastroduodenoscopy

ERCP
endoscopic retrograde cholangiopancreatography

EUS
endoscopic ultrasound

FLHC
fibrolamellar hepatocellular carcinoma

FNA
fine-needle aspiration

HBV
hepatitis B virus

HCC
hepatocellular carcinoma

HCV
hepatitis C virus

IMRT
intensity-modulated radiation therapy

INR
international normalized ratio

IV
Intravenous

MRI
magnetic resonance imaging

MRCP
magnetic resonance cholangiopancreatography

MSI
microsatellite instability

MSI-H
microsatellite instability-high

NAFLD
non-alcoholic fatty liver disease

PET
positron emission tomography

PT
prothrombin time

PTC
percutaneous transhepatic cholangiography

RFA
radiofrequency ablation

SBRT
stereotactic body radiation therapy

TACE
transarterial chemoembolization

T,N,M
tumor, node, metastasis

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United Network for Organ Sharing
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