

cancer.org | 1.800.227.2345

Treating Bile Duct Cancer

If you've been diagnosed with bile duct cancer, your treatment team will discuss your options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

How is bile duct cancer treated?

The main types of treatment for bile duct cancer include:

- Surgery for Bile Duct Cancer
- Radiation Therapy for Bile Duct Cancer
- Chemotherapy for Bile Duct Cancer
- Targeted Therapy for Bile Duct Cancer
- Immunotherapy for Bile Duct Cancer
- Palliative Therapy for Bile Duct Cancer

Common treatment approaches

Your treatment options will depend on several factors:

- The location and extent of the cancer.
- Whether the cancer is resectable (removable by surgery)
- The likely side effects of treatment
- · Your overall health
- The chances of curing the disease, extending life, or relieving symptoms
- Treatment Options Based on the Extent of Bile Duct Cancer

Who treats bile duct cancer?

Based on your treatment options, you might have different types of doctors on your cancer care team. These might include:

- A surgeon or a surgical oncologist: a surgeon who specializes in cancer treatment
- A radiation oncologist: a doctor who uses radiation to treat cancer
- A medical oncologist: a doctor who uses chemotherapy and other medicines to treat cancer
- A gastroenterologist (GI doctor): a doctor who treats diseases of the digestive system
- A hepatologist: a doctor who treats disease of the liver and bile ducts
- Health Professionals Associated with Cancer Care

Making treatment decisions

It's important to discuss all treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. You may feel that you need to make a decision quickly, but it's important to give yourself time to absorb the information you have learned. Ask your cancer care team questions.

If time permits, it is often a good idea to seek a second opinion, particularly for a rare cancer like bile duct cancer. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

- Questions to Ask About Bile Duct Cancer
- Seeking a Second Opinion

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they're not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

Clinical Trials

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

Complementary and Alternative Medicine

Help getting through cancer treatment

People with cancer need support and information, no matter what stage of illness they may be in. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all, you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and can be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists.

Palliative Care

Find Support Programs and Services in Your Area

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors and you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

If Cancer Treatments Stop Working

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Surgery for Bile Duct Cancer

There are 2 general types of surgery for bile duct cancer: potentially curative surgery (resectable and unresectable) and palliative surgery.

Potentially curative surgery for bile duct cancer

Resectable (potentially curative surgery) means imaging tests or the results of earlier surgeries show there's a good chance that the surgeon can remove all of the cancer along with a rim (margin) of healthy tissue around it.

Only a small percentage of bile duct cancers are resectable when they're first found.

If potentially curative surgery is being considered, you may want to get a <u>second</u> <u>opinion</u>¹ or even be referred to a large<u>cancer center</u>². Nearly all doctors agree that surgery offers the only realistic chance for curing people with bile duct cancer. But there are differences of opinion about how advanced a bile duct cancer can be and still be treatable with surgery. The surgery needed for bile duct cancer is often complex and requires an experienced surgeon. These operations are most often done at major cancer centers.

If a tumor is unresectable, itmeans doctors think the cancer is too advanced, it has spread too far, or is in too difficult a place to be entirely removed by surgery.

Laparoscopy to plan bile duct surgery

If your surgical team is planning curative surgery, they first may do a laparoscopy (a type of minor surgery) to look for any spread of the cancer that could make curative surgery not an option. This procedure is described in <u>Tests for Bile Duct Cancer</u>³. During the laparoscopy, the surgeon can look for areas of cancer that did not show up on imaging tests. If the cancer is resectable, laparoscopy can also help plan the operation to remove it.

Surgery to remove bile duct cancer can have serious side effects and, depending on how extensive it is, you may need many weeks to recover. If your cancer is very unlikely to be curable, be sure to carefully weigh the pros and cons of surgery or other treatments that will need a lot of recovery time. It's very important to understand the goal of any surgery for bile duct cancer, what the possible benefits and risks are, and how the surgery is likely to affect your quality of life.

Surgery for resectable bile duct cancers

For resectable cancers, the type of operation depends on where the cancer is.

Intrahepatic bile duct cancers are in bile ducts that are inside the liver. To treat
these cancers, the surgeon cuts out the part of the liver containing the cancer.
Removing part of the liver is called a partial hepatectomy. Sometimes this means
that a whole lobe (right or left part) of the liver must be removed. This is called
hepatic lobectomy and is a complicated operation that requires an experienced
surgical team. If the amount of liver removed is not too great, the liver will still work
normally because it has some ability to grow back.

- Perihilar bile duct cancer develops where the branches of the bile ducts first leave the liver. Surgery for these cancers is complicated and requires great skill. Usually part of the liver is removed, along with the bile duct, gallbladder, nearby lymph nodes, and sometimes part of the pancreas and small intestine. Then the surgeon connects the remaining ducts to the small intestine. This is a complex operation that can lead to life-threatening complications for some people.
- Distal bile duct cancers are further down the bile duct near the pancreas and small intestine. Along with the bile duct and nearby lymph nodes, the surgeon often has to remove part of the pancreas and small intestine. This operation is called a Whipple procedure. Like the other operations, this is a complex procedure that requires an experienced surgical team.

Surgery for unresectable bile duct cancers

Surgery is less likely to be done for unresectable cancers, but there are some instances where it might be helpful.

Liver transplant

For some people with early stage, unresectable intrahepatic or perihilar bile duct cancers, removing the liver and bile ducts and then transplanting a donor liver may be an option. In some cases it might even cure the cancer. But getting a new liver may not be easy. Not many centers accept patients with bile duct cancer into their transplant programs. Also, few livers are available for patients with cancer because they tend to be used for more curable diseases. People needing a transplant must wait until a liver is available, which can take too long for some people with bile duct cancer.

One option might be having a living donor (often a close relative) give a part of their liver for transplant. This can be successful, but it carries risks for the donor. Another option might be to treat the cancer first with chemotherapy and radiation. Then a transplant is done when a liver becomes available. Clinical trial results using this approach have been promising.

Like other surgeries for bile duct cancer, a liver transplant is a major operation with potential risks (bleeding, infection, complications from anesthesia, etc.). But there are also some additional risks after this surgery. After liver transplant, drugs have to be taken to help suppress the patient's immune system to keep it from rejecting the new liver. These drugs have their own risks and side effects, especially the risk of getting serious infections. Some of the drugs used to prevent rejection can cause high blood

pressure, high cholesterol, and diabetes. They can also weaken the bones and kidneys and can lead to the development of another cancer. After a liver transplant, regular blood tests are needed to check for signs of rejection. Sometimes liver biopsies are also done to see if rejection is occurring and if the anti-rejection medicines need to be changed.

Palliative surgery for bile duct cancer

Palliative surgery is done to relieve symptoms or treat (or even prevent) complications, such as blockage of the bile ducts. This type of surgery is done when the cancer is too widespread to be removed completely. Palliative surgery is not expected to cure the cancer, but it can sometimes help a person feel better and sometimes can even help them live longer.

In some cases the doctor might think the cancer can be removed (is resectable) based on the information available (imaging tests, laparoscopy, etc.), but then once surgery is started it becomes clear that the cancer is too advanced to be removed completely. In these cases, the surgeon might still try to prevent or relieve symptoms using a different approach.

Biliary bypass

The surgeon creates a bypass around the tumor blocking the bile duct by connecting part of the bile duct before the blockage with a part of the duct that lies past the blockage The bile duct may also be connected to the intestine itself. Often, the gallbladder is used to provide some of the bypass. Different types of biliary bypass operations may be done, based on where the blockage is. The bypass allows the bile to flow into the intestines and can help reduce symptoms such as jaundice or itching.

Stent placement

If a bypass can't be done, the surgeon may put a plastic or expandable metal tube (called a stent) inside the bile duct to keep it open and allow bile to flow.

Palliative surgery is described in more detail in the section Palliative Therapy for Bile Duct Cancer.

Possible risks and side effects of bile duct surgery

The risks and side effects of surgery depend on the extent of the operation and a

person's overall health before surgery. Another key factor is how well the liver is working. All surgery carries some risk, including the possibility of bleeding, blood clots, infections, complications from anesthesia, pneumonia, and even death in rare cases.

People will have some pain from the incision for some time after surgery, but this can usually be controlled with medicines.

Surgery for bile duct cancer is a major operation that might mean removing parts of other organs. This can have a major effect on a person's recovery and health after the surgery. Serious problems soon after surgery can include bile leakage into the abdomen, infections, and liver failure. Because most of the organs removed are involved in digestion, eating and nutrition problems may be a concern after surgery.

More information about Surgery

For more general information about surgery as a treatment for cancer, see <u>Cancer</u> <u>Surgery</u>⁴.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁵.

Hyperlinks

- 1. <u>www.cancer.org/treatment/finding-and-paying-for-treatment/choosing-your-treatment-team/seeking-a-second-opinion.html</u>
- 2. <u>www.cancer.org/treatment/finding-and-paying-for-treatment/choosing-your-treatment-team/nci-cancer-center-programs.html</u>
- 3. <u>www.cancer.org/cancer/bile-duct-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 4. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/surgery.html</u>
- 5. <u>www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html</u>

References

Abou-Alfa GK, Jarnagin W, Lowery M, D'Angelica M, Brown K, Ludwig E, Covey A, Kemeny N, Goodman KA, Shia J, O'Reilly EM. Liver and bile duct cancer. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier; 2014:1373-1395.

Hoyos S, Navas M-C, Restrepo J-C, Botero RC. Current controversies in cholangiosarcoma. *BBA - Molecular Basis of Dis.* 2108; 1864:1461-1467.

National Cancer Institute. Bile Duct Cancer (Cholangiocarcinoma) Treatment (PDQ®)—Patient Version. March 22, 2018. Accessed at www.cancer.gov/types/liver/patient/bile-duct-treatment-pdg on June 22, 2018.

National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Hepatobiliary Cancers, Version 2.2018 -- June 7, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf on June 22, 2018.

Patel T, Borad MJ. Carcinoma of the biliary tree. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2015:715-735.

Rizvi S, Khan SA, Hallemeier CL, Kellek RK, Gores GJ. Cholangiosarcoma -- evolving concepts and therapeutic strategies. *Nat Rev Clin Oncol.* 2018;15(2):95-111.

See all references for Bile Duct Cancer (www.cancer.org/cancer/bile-duct-cancer/references.html)

Last Revised: July 3, 2018

Radiation Therapy for Bile Duct Cancer

Radiation therapy uses high-energy rays or particles to destroy cancer cells. Radiation isn't often used to treat bile duct cancer, still, it might be used in these ways:

- After surgery to remove the cancer: This is called adjuvant therapy. It's used to kill any tiny deposits of cancer cells that are left after surgery but are too small to see. Not all doctors agree that adjuvant radiation therapy is helpful.
- Before surgery for cancers that might be able to be taken out: Some doctors may use radiation therapy before surgery for certain cancers that are thought to be resectable (removable). This is done to try to shrink the cancer and make it easier to take it out. This is called **neoadjuvant therapy**. It's not clear how helpful this is.
- As part of the main therapy for some advanced cancers: Radiation therapy can

also be used as a main therapy for some patients whose cancer has not spread widely throughout the body, but can't be removed with surgery. While treatment in this case does not offer a cure, it may help patients live longer.

• As palliative therapy: Radiation therapy is often used to ease symptoms when a cancer is too advanced to be cured. It can help relieve pain or other symptoms by shrinking tumors that block bile ducts or blood vessels, or press on nerves.

The 2 main types of radiation therapy are external beam radiation therapy (EBRT) and brachytherapy. EBRT is the most common form of radiation for bile duct cancer.

External beam radiation therapy (EBRT)

In this type of <u>radiation therapy</u>, a machine sends x-rays to a specific part of the patient's body to kill cancer cells.

Before your treatments start, the radiation team will take careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. The treatment is much like getting an x-ray, but the radiation is much stronger. The procedure itself is painless. Each treatment lasts only a few minutes, but the set-up time – getting you into place for treatment – usually takes longer. Most often, radiation treatments are given 5 days a week for many weeks. These are some of the ways EBRT might be given:

Three-dimensional conformal radiation therapy (3D-CRT) uses special computers to precisely map the location of the tumor(s). Radiation beams are then shaped and aimed at the tumor(s) from several directions, which makes it less likely to damage normal tissues. It may be used to treat localized intrahepatic bile duct cancers that can't be removed with surgery.

Intensity-modulated radiation therapy (IMRT) is an advanced form of 3D-CRT. It uses a computer-driven machine that moves around you as it delivers radiation. Along with shaping the beams and aiming them at the cancer from many angles, the intensity (strength) of the beams can be adjusted to limit the dose reaching the most sensitive normal tissues. This lets doctors deliver an even higher dose to the cancer.

Stereotactic body radiotherapy (SBRT) uses the techniques of 3D-CRT and IMRT, but gives a high dose of radiation over fewer sessions. A course of SBRT may take a week or 2, while a course of radiation using these other techniques often takes 3 to 6 weeks.

Chemoradiation is when chemotherapy (chemo) is given along with EBRT to help it work better. It may be tried in select patients with early stage perihilar bile duct cancer before a liver transplant is done. The main drawback of this approach is that the side effects tend to be worse than giving radiation alone.

EBRT side effects

Some common side effects of ERBT to treat bile duct cancer include:

- Skin changes, ranging from redness to blistering and peeling (in the area being treated)
- Nausea and vomiting
- Diarrhea
- Fatigue (tiredness)
- Hair loss (on the skin in the area being treated)
- · Low blood cell counts
- Liver damage

Side effects from radiation often start a week or 2 into treatment, and usually get better over time once treatment is over.

Brachytherapy (internal radiation therapy)

This type of treatment uses small pellets of radioactive material that are put next to or right into the tumor. The radiation travels a very short distance, so it affects the cancer without causing much harm to nearby healthy body tissues. For bile duct cancer, brachytherapy is sometimes done with a thin radioactive wire that's put into the bile duct for a short time. This may be called intrabiliary brachytherapy. Brachytherapy can be used alone, or it may be used along with EBRT. At this time it's mostly used as a palliative treatment.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see Radiation Therapy².

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects³.

Hyperlinks

- 1. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/x-rays-and-other-radiographic-tests.html</u>
- 2. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/radiation.html</u>
- 3. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

References

Abou-Alfa GK, Jarnagin W, Lowery M, D'Angelica M, Brown K, Ludwig E, Covey A, Kemeny N, Goodman KA, Shia J, O'Reilly EM. Liver and bile duct cancer. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier; 2014:1373-1395.

Labib PL, Davidson BR, Sharma RA, Pereira SP. Locoregional therapies in cholangiocarcinoma. *Hepat Oncol.* 2017;4(4):99-109.

Lischalk JW, Repka MC, Unger K. Radiation therapy for hepatobiliary malignancies. *J Gastrointest Oncol.* 2017;8(2):279-292.

National Cancer Institute. Bile Duct Cancer (Cholangiocarcinoma) Treatment (PDQ®)—Patient Version. March 22, 2018. Accessed at www.cancer.gov/types/liver/patient/bile-duct-treatment-pdg on June 22, 2018.

National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Hepatobiliary Cancers, Version 2.2018 -- June 7, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf on June 22, 2018.

Patel T, Borad MJ. Carcinoma of the biliary tree. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2015:715-735.

Rizvi S, Khan SA, Hallemeier CL, Kelley RK, Gores GJ. Cholangiocarcinoma: Evolving concepts and therapeutic strategies. *Nat Rev Clin Oncol.* 2018;15(2):95-111.

See all references for Bile Duct Cancer (www.cancer.org/cancer/bile-duct-cancer/references.html)

Last Revised: July 3, 2018

Chemotherapy for Bile Duct Cancer

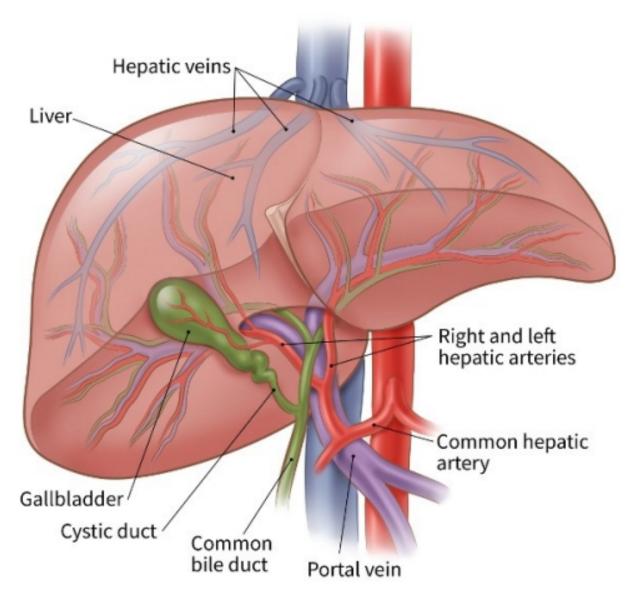
Chemotherapy (chemo) is treatment with cancer-killing drugs that are usually given into a vein (IV) or taken by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment useful for some cancers that have spread to organs beyond the bile duct. Because the drugs reach all the areas of the body, this is known as a **systemic**treatment.

Chemo can help some people with bile duct cancer, but so far it's not clear how useful it is for this type of cancer. Still, chemo might be used in these ways:

- After surgery to remove the cancer: Chemo may be given after surgery (often along with radiation therapy) to try to lower the risk that the cancer will come back. This is called adjuvant chemo.
- **Before surgery:** It may be given before surgery for cancers that might be able to be completely removed. Chemo might shrink the tumor enough to improve the odds that surgery will be successful. This is called **neoadjuvant treatment**.
- As part of the liver transplant process: Chemo may be used to keep bile duct cancer under control while waiting for a liver transplant.
- As part of the main treatment for some advanced cancers: Chemo can be used (sometimes with radiation therapy) for more advanced cancers that cannot be removed or have spread to other parts of the body. Chemo does not cure these cancers, but it might help people live longer.
- As palliative therapy: Chemo can help shrink tumors or slow their growth for a time. This can help relieve symptoms from the cancer, for instance, by shrinking tumors that are pressing on nerves and causing pain.

Doctors give chemo in cycles, with each period of treatment followed by a rest period to give the body time to recover. Chemo cycles generally last about 3 to 4 weeks. Chemo usually isn't recommended for patients in poor health, but advanced age by itself is not a barrier to getting chemotherapy.

Hepatic artery infusion (HAI)



Because giving chemo into a vein isn't always helpful for bile duct cancer, doctors have tried giving the drugs right into the main artery going into the liver, called the hepatic artery. The hepatic artery also supplies most bile duct tumors, so putting the chemo into this artery means more chemo goes to the tumor. The healthy liver then removes most of the remaining drug before it can reach the rest of the body. This can lessen chemo side effects. HAI may help some people whose cancer couldn't be removed by surgery live longer, but more research is needed. This technique often requires surgery to put a catheter into the hepatic artery, and many people with bile duct cancer are not well enough to have this surgery.

Trans-arterial chemoembolization (TACE)

Embolization is a procedure where a substance is put into the blood vessels to help stop blood from getting to a tumor. TACE uses tiny beads of chemo to do this. A catheter is used to put the beads into the artery that "feeds" the tumor. The beads lodge there to block blood flow and give off the chemo. TACE may be used for tumors that can't be removed or to treat bile duct cancer that comes back after surgery.

Drugs used to treat bile duct cancer

The drugs used most often to treat bile duct cancer include:

- 5-fluorouracil (5-FU)
- Gemcitabine (Gemzar®)
- Cisplatin (Platinol®)
- Capecitabine (Xeloda[®])
- Oxaliplatin (Eloxatin[®])

In some cases, 2 or more of these drugs may be combined to try to make them more effective. For example, combining gemcitabine and cisplatin may help people live longer than getting just gemcitabine alone.

Possible side effects of chemotherapy

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells can be affected by chemo, which can lead to side effects.

The side effects of chemo depend on the type and dose of drugs given, how they're given, and the length of treatment. Side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- Nerve damage (neuropathy), which can lead to numbness, tingling, and even pain in the hands and feet
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)

Fatigue (from having too few red blood cells)

Ask your cancer care team what you should watch for. Most side effects are short-term and go away after treatment ends. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to ask your doctor or nurse about medicines to help reduce side effects.

Report any side effects you notice to your medical team so that they can be treated right away. Most side effects can be treated. In some cases, the doses of the chemo drugs may need to be reduced or treatment might need to be delayed or stopped to keep the effects from getting worse.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see Chemotherapy1.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>².

Hyperlinks

- 1. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy.html</u>
- 2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

References

Abou-Alfa GK, Jarnagin W, Lowery M, D'Angelica M, Brown K, Ludwig E, Covey A, Kemeny N, Goodman KA, Shia J, O'Reilly EM. Liver and bile duct cancer. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier; 2014:1373-1395.

Hoyos S, Navas M-C, Restrepo J-C, Botero RC. Current controversies in cholangiosarcoma. *BBA - Molecular Basis of Dis.* 2108;1864:1461-1467.

Labib PL, Davidson BR, Sharma RA, Pereira SP. Locoregional therapies in cholangiocarcinoma. *Hepat Oncol.* 2017;4(4):99-109.

National Cancer Institute. Bile Duct Cancer (Cholangiocarcinoma) Treatment (PDQ®)—Patient Version. March 22, 2018. Accessed at www.cancer.gov/types/liver/patient/bile-duct-treatment-pdq on June 25, 2018.

National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Hepatobiliary Cancers, Version 2.2018 -- June 7, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf on June 25, 2018.

Park HM, Yun SP, Lee EC, et al. Outcomes for Patients with Recurrent Intrahepatic Cholangiocarcinoma After Surgery. *Ann Surg Oncol.* 2016;23(13):4392-4400.

Patel T, Borad MJ. Carcinoma of the biliary tree. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2015:715-735.

Rizvi S, Khan SA, Hallemeier CL, Kelley RK, Gores GJ. Cholangiocarcinoma: Evolving concepts and therapeutic strategies. *Nat Rev Clin Oncol.* 2018;15(2):95-111.

Valle JW, Lamarca A, Goyal L, Barriuso J, Zhu AX. New Horizons for Precision Medicine in Biliary Tract Cancers. *Cancer Discov.* 2017;7(9):943-962.

See all references for Bile Duct Cancer (www.cancer.org/cancer/bile-duct-cancer/references.html)

Last Revised: July 3, 2018

Targeted Therapy for Bile Duct Cancer

As researchers learn more about the changes in cells that cause cancer, they've developed drugs to target some of these changes. These targeted drugs work differently from standard chemotherapy (chemo) drugs. They sometimes work when standard chemo drugs don't, and they often have different side effects.

FGFR2 inhibitor

FGFRs (fibroblast growth factor receptors) are proteins on cells that help them grow and divide normally. A small number (about 15%) of people with bile duct cancer within the

liver have changes in the genes that make FGFRs, which result in abnormal FGFR proteins that cause cells to grow out of control and turn into cancer.

Pemigatinib (Pemazyre), a FGFR2 inhibitor, blocks the abnormal FGFR2 protein in bile duct cancer cells and keeps them from growing and spreading to other places. It can be used to treat some advanced bile duct cancers that cannot be removed by surgery or have spread to distant areas after at least one previous chemotherapy treatment. For this drug to work, your cancer must have the abnormal FGFR2 gene, so your cancer will be tested before starting the drug.

This drug is given as a tablet by mouth once a day for 2 weeks, followed by one week off, then started again.

Possible side effects of a FGFR2 inhibitor

The most common side effects of pemigatinib are having too much or too little phosphate in the blood, hair loss, diarrhea, constipation, nail problems, fatigue, taste changes, nausea, vomiting, dry mouth or mouth sores, loss of appetite, dry skin, dry eye or other eye problems, and joint, abdominal, or back pain.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Therapy</u>¹.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>².

Hyperlinks

- 1. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/targeted-therapy.html</u>
- 2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

References

Abou-Alfa GK, Sahai V, Hollebecque A, Vaccaro G, Melisi D, Al-Rajabi R, et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study. *Lancet Oncol.* 2020 May;21(5):671-684. doi:

10.1016/S1470-2045(20)30109-1. Epub 2020 Mar 20.

DeLeon TT, Ahn DH, Bogenberger JM, et al. Novel targeted therapy strategies for biliary tract cancers and hepatocellular carcinoma. *Future Oncol.* 2018;14(6):553-566.

Hoyos S, Navas M-C, Restrepo J-C, Botero RC. Current controversies in cholangiosarcoma. *BBA - Molecular Basis of Dis.* 2108;1864:1461-1467.

Lombardi P, Marino D, Fenocchio E, et al. Emerging molecular target antagonists for the treatment of biliary tract cancer. *Expert Opinion on Emerging Drugs*. 2018;23(1):63-75.

National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Hepatobiliary Cancers, Version 2.2018 -- June 7, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf on June 26, 2018.

Rizvi S, Khan SA, Hallemeier CL, Kelley RK, Gores GJ. Cholangiocarcinoma: Evolving concepts and therapeutic strategies. *Nat Rev Clin Oncol.* 2018;15(2):95-111.

Valle JW, Lamarca A, Goyal L, Barriuso J, Zhu AX. New Horizons for Precision Medicine in Biliary Tract Cancers. *Cancer Discov.* 2017;7(9):943-962.

Last Revised: May 8, 2020

Immunotherapy for Bile Duct Cancer

Immunotherapy is the use of medicines to help a person's immune system better recognize and destroy cancer cells. Many of these drugs are being tested in <u>clinical trials</u>¹ to see if they might help treat bile duct cancer.

To learn more about how drugs that work on the immune system are used to treat cancer, see Cancer Immunotherapy².

Hyperlinks

- 1. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
- 2. www.cancer.org/treatment/treatments-and-side-effects/treatment-

types/immunotherapy.html

References

Abou-Alfa GK, Jarnagin W, Lowery M, D'Angelica M, Brown K, Ludwig E, Covey A, Kemeny N, Goodman KA, Shia J, O'Reilly EM. Liver and bile duct cancer. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier; 2014:1373-1395.

Blair AB, Murphy A. Immunotherapy as a treatment for biliary tract cancers: A review of approaches with an eye to the future. *Curr Probl Cancer*. 2017 Oct [Epub ahead of print].

National Cancer Institute. Physician Data Query (PDQ). *Bile Duct (Cholangiocarcinoma) Cancer Treatment*. 03/14/2018. Accessed at https://www.cancer.gov/types/liver/hp/bile-duct-treatment-pdq on March 29, 2018.

National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology: Hepatobiliary Cancers. v.1.2018.* Accessed at https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf on March 29, 2018.

Patel T, Borad MJ. Carcinoma of the biliary tree. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015:715-735.

Rizvi S, Khan SA, Hallemeier CL, Kelley RK, Gores GJ. Cholangiocarcinoma: Evolving concepts and therapeutic strategies. *Nat Rev Clin Oncol.* 2018 Mar;15(2):95-111.

Last Revised: July 3, 2018

Palliative Therapy for Bile Duct Cancer

<u>Palliative care</u>¹ is treatment used to help control or reduce symptoms caused by cancer. It's not meant to cure the cancer.

If bile duct cancer has spread too far to be removed by surgery, doctors may focus on palliative treatments. For instance, <u>pain medicines</u>² and <u>drugs to control nausea</u>³ or itching might be used to help you feel better. Chemotherapy and radiation can also be used to relieve problems caused by the tumor(s). Sometimes, surgery or other treatments are used to help you feel better or to help prevent possible problems the cancer might cause. Because bile duct cancers tend to grow and spread quickly, doctors try to use palliative therapies that are less likely to have unpleasant short-term side effects, whenever possible. Your cancer care team will talk with you about the pros and cons of all the treatments that might help you.

Here are some examples of procedures that might be used as part of palliative care for bile duct cancer:

Biliary stent or biliary catheter

If cancer is blocking a bile duct, it can lead to jaundice (yellowing of the skin and eyes) as well as other problems, like infection and liver failure. A small tube or a catheter can be put into the duct to help keep it open.

- A **stent** is a small metal or plastic tube that's put through the blockage in the duct. It keeps the duct open to allow bile to drain into the small intestine.
- A catheter is a thin, flexible tube that's put in through the skin over the abdomen (belly). One end of the tube is put into a bile duct and the other end is outside the body. This allows the bile to drain into a bag. The bag can be emptied when needed. If you have a catheter, your doctor or nurse will teach you how to care for it.

These procedures can be done as part of a cholangiography procedure such as ERCP or PTC (see <u>Tests for Bile Duct Cancer</u>⁴) or, in some cases, during surgery. They're often done to help prevent or relieve symptoms from more advanced cancers, but they can also be done to help relieve jaundice before <u>potentially curative surgery</u> is done. This helps lower the risk of complications from the surgery.

The stent or catheter might need to be replaced every few months to help reduce the risk of infection and gallbladder inflammation. It will also need to be replaced if it becomes clogged.

Biliary bypass

Another option to allow bile to go into the small intestine and not build up in the liver is a

surgery called biliary bypass. There are different biliary bypass operations. The decision on which one to use depends on where the blockage is. In these procedures, the surgeon creates a bypass around the tumor blocking the bile duct by connecting part of the bile duct before the blockage with a part of the duct that lies past the blockage, or with the intestine itself.

As mentioned in Surgery for Bile Duct Cancer, biliary bypass is more likely to be done if a patient is already having surgery to try to cure the cancer by taking it out, but it turns out the cancer cannot be totally removed. While a bypass is clearly more invasive than placing a stent or catheter, it has some advantages in that it may last longer and infection is less likely to be a problem.

Tumor ablation (radiofrequency ablation or cryosurgery)

Tumors in the liver that can't be resected can sometimes be destroyed (ablated) by putting a long metal probe through a small hole in the skin and into the tumor. A CT scan or ultrasound is used to guide it to the right place. The tip of the probe is then heated (in <u>radiofrequency ablation</u>⁵) or frozen (in cryotherapy) to kill the cancer cells.

Photodynamic therapy (PDT)

For PDT⁶, a light-activated drug is injected into a vein. Over time, the drug tends to collect in cancer cells more than in normal cells. A few days later, an endoscope (a long, flexible tube that can be used to look inside the body) is passed down the throat, through the stomach and intestine, and into the bile ducts. A special laser light on the end of the endoscope is aimed at the tumor. The light turns on the drug, causing the cells to die. The combination of PDT and stenting can be helpful for patients with bile duct cancer whose tumors can't be removed with surgery.

The drugs used for PDT can also collect in normal cells in the body, making a person very sensitive to sunlight or strong indoor lights. You'll need to stay out of any strong light for several weeks after the injection.

Alcohol injection

To relieve pain, doctors may deaden the nerves that carry pain signals from the bile duct and intestinal area to the brain by injecting these nerves with alcohol. This can be done during surgery or through a long, hollow needle that's guided into place with the help of a CT scan.

Hyperlinks

- 1. www.cancer.org/treatment/treatments-and-side-effects/palliative-care.html
- 2. <u>www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/pain.html</u>
- 3. <u>www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/nausea-and-vomiting/nausea-and-vomiting.html</u>
- 4. <u>www.cancer.org/cancer/bile-duct-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 5. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/hyperthermia.html</u>
- 6. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/radiation/photodynamic-therapy.html</u>

References

Abou-Alfa GK, Jarnagin W, Lowery M, D'Angelica M, Brown K, Ludwig E, Covey A, Kemeny N, Goodman KA, Shia J, O'Reilly EM. Liver and bile duct cancer. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier; 2014:1373-1395.

Labib PL, Davidson BR, Sharma RA, Pereira SP. Locoregional therapies in cholangiocarcinoma. *Hepat Oncol.* 2017;4(4):99-109.

National Cancer Institute. Bile Duct Cancer (Cholangiocarcinoma) Treatment (PDQ®)—Patient Version. March 22, 2018. Accessed at www.cancer.gov/types/liver/patient/bile-duct-treatment-pdq on June 26, 2018.

National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Hepatobiliary Cancers, Version 2.2018 -- June 7, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf on June 26, 2018.

Squadroni M, Tondulli L, Gatta G, et al. Cholangiocarcinoma. *Crit Rev Oncol Hematol.* 2017;116:11-31.

See all references for Bile Duct Cancer (www.cancer.org/cancer/bile-duct-cancer/references.html)

Last Revised: July 3, 2018

Treatment Options Based on the Extent of Bile Duct Cancer

The extent of bile duct cancer is an important factor in deciding on treatment options. Whenever possible, surgery is the main treatment for bile duct cancers. It offers the only realistic chance for a cure. Because of this, doctors generally divide bile duct cancers into:

- **Resectable cancers**, those that doctors believe can be removed completely by surgery, based on the results of imaging tests and other tests.
- **Unresectable cancers**, those that have spread too far or are in too difficult a place to be removed entirely by surgery.

Most bile duct cancers are unresectable by the time they're found.

Resectable bile duct cancers

Most stage 0, I, and II cancers and possibly some stage III cancers are potentially resectable -- it might be possible to completely take out the cancer with surgery. But other factors can impact whether this is a good option, such as where the cancer is and whether the patient is healthy enough to have major surgery.

Surgery to remove the cancer completely is the preferred treatment if it's possible. If surgery is being considered, a staging laparoscopy may be done first. This allows the doctor to look inside the abdomen (belly) for any spread of the cancer that could make it unresectable. (Laparoscopy is described in <u>Tests for Bile Duct Cancer</u>1)

Types of surgery

The type of surgery done to remove the cancer depends on the location and extent of the cancer. (See Surgery for bile duct cancer for more details.)

Other treatments that may be used with surgery

If the patient has jaundice (yellowing of the skin and eyes) before surgery, a stent or catheter may be put in the bile duct first. This allows the bile to flow the way it should. It can help relieve symptoms over a few days and might help make a person healthy enough to have the operation.

Radiation therapy and/or chemotherapy (chemo) may be given after surgery to try to lower the risk that the cancer will come back. This is called adjuvant therapy. Doctors aren't sure how helpful adjuvant therapy is. It's more likely to be used if there's a higher chance that the cancer wasn't removed completely (based on looking at and testing the tissue removed during surgery). If it's clear that some cancer was left behind, a second surgery to take out more tissue may also be an option in some cases.

Sometimes it isn't clear from imaging or other tests whether the cancer can be removed completely. These cancers may be called *borderline resectable* tumors. Some doctors may recommend treatment with radiation and/or chemo before surgery to try to shrink the tumor. (This is called neoadjuvant treatment.) Then, if the cancer shrinks, surgery can be done to try to remove all of it.

Unresectable bile duct cancers

These cancers cannot be removed with surgery, which includes most stage III and IV cancers. It may also include earlier stage cancers if a person isn't healthy enough for surgery.

Trying surgery

As noted above, in cases where it isn't clear if a cancer is resectable, chemotherapy and/or radiation therapy may be used first to try to shrink the cancer and make it able to be removed. Surgery could then be done to try to remove the cancer completely.

In some cases, the doctor might think that a cancer is resectable, but once the operation starts it becomes clear that it can't be removed completely. For example, the cancer may turn out to have spread farther than was seen on the imaging tests done before surgery. It doesn't help to remove only part of the cancer, and surgery could still cause major side effects, so this part of the operation is stopped. But while the doctor can see the area, a biliary bypass may be done to relieve any bile duct blockage or to try to keep it from happening in the future. Putting stents in the bile ducts to keep them open may also be an option.

Liver transplant

For some unresectable intrahepatic or perihilar bile duct cancers, a liver transplant (after complete removal of the liver and bile ducts) may be an option. Chemo and radiation may be given first. It's often hard to find a compatible liver donor, but a liver transplant can provide a chance for a cure.

Other options

For most bile duct cancers, it's clear from imaging tests and/or laparoscopy when they're not resectable. For these cancers, treatment is aimed at trying to control the growth of the cancer for as long as possible and to relieve any symptoms it's causing.

Radiation and/or chemo: Radiation therapy and/or chemo may shrink or slow the growth of the cancer for a time. When chemo is given alone (without radiation) the drugs cisplatin and gemcitabine (Gemzar) are often used. When chemo is given with radiation, 5-FU is the drug most often used.

Targeted therapy: For bile duct cancers within the liver that have the FGFR2 gene mutation (change) and have grown after at least one chemotherapy treatment, the targeted therapy drug Pemigatinib (Pemazyre) might be an option.

Ablation: For bile duct cancers within the liver, ablation using extreme heat (radiofrequency ablation) or cold (cryotherapy) may help control the tumors. But almost all of these cancers will start to grow again in the future.

Clinical trials: For people looking to continue to try to treat the cancer, taking part in <u>clinical trials</u>² of newer treatments may be an option. This way patients can get the best treatment available now and may also get the treatments that are thought to be even better.

Much of the focus of treating people with unresectable cancers is on relieving symptoms from the cancer. Two of the most important problems are bile duct blockage (which can lead to jaundice, itching, and other symptoms) and pain.

Palliative care

This is supportive care. It's aimed at preventing and treating symptoms or problems caused by the bile duct cancer. Palliative care is used with every type of cancer treatment at every stage of bile duct cancer. It includes things like medicines to prevent nausea, pain control, and maintaining the flow of bile where a tumor may block it.

Palliative care is focused on helping you feel better, it's not used to treat the cancer.

Maintaining your quality of life is an important goal. Please don't hesitate to discuss pain, other symptoms, or any quality-of-life concerns with your cancer care team.

See Palliative Therapy for Bile Duct Cancer for details on some of these treatments.

Recurrent bile duct cancer

Cancer is called recurrent when it come backs after treatment. Recurrence³ can be local (in or near the same place it started) or distant (it comes back in other parts of the body, like the lungs). If the cancer comes back, further treatment depends on where the cancer recurs, the kind of treatment used in the past, and the patient's overall health.

In most cases if the cancer comes back after initial treatment, it will not be resectable. Treatment will be aimed at controlling the cancer growth and relieving symptoms, as described above for unresectable cancers and palliative care. In rare cases, if the cancer comes back where it started, surgery to try to remove the cancer (and possibly adjuvant therapy afterwards) may be an option. Because most of these cancers are not curable, people might want to consider taking part in a clinical trial⁴ of newer treatments.

Hyperlinks

- www.cancer.org/cancer/bile-duct-cancer/detection-diagnosis-staging/howdiagnosed.html
- 2. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
- 3. <u>www.cancer.org/treatment/survivorship-during-and-after-treatment/understanding-recurrence.html</u>
- 4. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html

References

Abou-Alfa GK, Jarnagin W, Lowery M, D'Angelica M, Brown K, Ludwig E, Covey A, Kemeny N, Goodman KA, Shia J, O'Reilly EM. Liver and bile duct cancer. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier; 2014:1373-1395.

Abou-Alfa GK, Sahai V, Hollebecque A, Vaccaro G, Melisi D, Al-Rajabi R, et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma:

a multicentre, open-label, phase 2 study. *Lancet Oncol.* 2020 May;21(5):671-684. doi: 10.1016/S1470-2045(20)30109-1. Epub 2020 Mar 20.

American Society of Clinical Oncology. Bile Duct Cancer (Cholangiocarcinoma): Treatment Options. 11/2017. Accessed at www.cancer.net/cancer-types/bile-duct-cancer-cholangiocarcinoma/treatment-options on June 27, 2018.

Hoyos S, Navas M-C, Restrepo J-C, Botero RC. Current controversies in cholangiosarcoma. *BBA - Molecular Basis of Dis.* 2108;1864:1461-1467.

National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Hepatobiliary Cancers, Version 2.2018 -- June 7, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf on June XX, 2018.

Patel T, Borad MJ. Carcinoma of the biliary tree. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015:715-735.

See all references for Bile Duct Cancer (www.cancer.org/cancer/bile-duct-cancer/references.html)

Last Revised: May 8, 2020

Written by

The American Cancer Society medical and editorial content team (www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).

cancer.org | 1.800.227.2345