

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 Drug 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 Who Are Part of a Cancer Care Team

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
- <u>Seeking a Second Opinion</u>

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-ofthe 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.

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.

<u>Clinical Trials</u>

Considering complementary and alternative methods

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

Complementary methods are treatments that are used **along with** your regular medical care. **Alternative** treatments are used **instead of** standard 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.

<u>Complementary and Integrative Medicine</u>

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

- Palliative Care
- Programs & Services

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 as 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

Surgery for Bile Duct Cancer

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. It's very important to understand how the surgery is likely to affect your quality of life.

Surgery for resectable bile duct cancers

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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 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 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/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html</u>
- 2. www.cancer.org/cancer/managing-cancer/finding-care/where-to-find-cancercare.html

- 3. <u>www.cancer.org/cancer/types/bile-duct-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 4. www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html
- 5. www.cancer.org/cancer/managing-cancer/side-effects.html

References

Radiation Therapy for Bile Duct Cancer

- Proton beam therapy
- Brachytherapy (internal radiation therapy)
- More information about radiation therapy

How is radiation therapy used to treat bile duct cancer?

Although radiation therapy is not often used to reat bile duct cancer, it might be helpful in some situations. Here are some of the ways it might be used:

- 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.

There are different types of radiation therapy. External beam radiation therapy (EBRT) is the most common form of radiation used to treat bile duct cancer.

External beam radiation therapy (EBRT)

In this type of radiation therapy, a machtn a

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, 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 the radiationwork better. 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

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

Proton beam therapy

In people with bile duct cancer, especially if the cancer is unresectable, proton therapy may be an option. Proton therapy is a type of radiation that uses protons rather than x-rays. A proton is a positively charged particle, which can be targeted specifically to the tumor. Compared to x-rays, proton therapy beams are less likely to damage surrounding organs. This form of radiation therapy continues to be studied.

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 <u>Radiation 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. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 2. www.cancer.org/cancer/managing-cancer/side-effects.html

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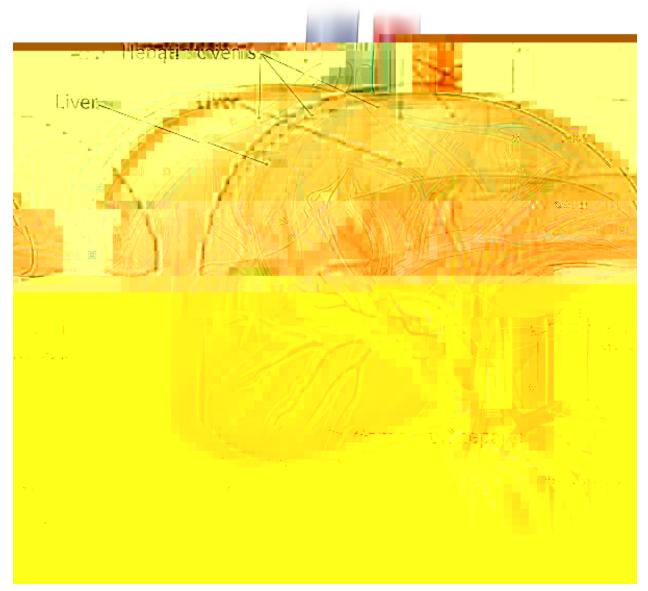
Chemotherapy for Bile Duct Cancer

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 people in poor health, but advanced age by itself is not a barrier to getting chemo.

Hepatic artery infusion (HAI)



Because giving chemo into a vein (IV) 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.

Drugs used to treat bile duct cancer

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

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

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)
- Organ dysfunction (can affect function of the kidney and liver)

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 cancer care team so that they can be treated right away. Most side effects can be treated. In some cases, the doses of the chemo drugs can be reduced or treatment can be delayed or stopped to keep the side effects from worsening.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see <u>Chemotherapy</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. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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Targeted Drug Therapy for Bile Duct Cancer

NTRK inhibitor

A very small number of bile duct cancers have changes in one of the *NTRK* genes, called *NTRK* gene fusions. Cells with these gene changes make abnormal TRK proteins, which can lead to abnormal cell growth and cancer.

Larotrectinib (Vitrakyi) or **entrectinib (Rozlytrek)** are NTRK inhibitors. TRK inhibitors target and disable the proteins made by the *NTRK* genes. This drug can be used in people with advanced bile duct cancer, who have not received prior systemic therapy.

These drugs are taken as pills, once or twice daily.

Possible side effects of NTRK inhibitors

Common side effects can include abnormal liver tests; decreased white blood cell and red blood cells; muscle and joint pain; tiredness; diarrhea or constipation; nausea and vomiting; and stomach pain.

Less common but more serious side effects can include mental changes, such as confusion, changes in mood, and changes in sleep; liver damage; changes in heart rhythm and/or function; vision changes; and harm to a fetus.

RET inhibitor

In a small percentage of bile duct cancers, the tumor cells have rearrangement in the *RET* gene that cause them to make an abnormal form of the RET protein. This abnormal protein helps the tumor cells grow.

Selpercatinib (Retevmo) or **pralsetinib (Gayreto)** are RET inhibitors and can be used to treat advanced bile duct cancers with the RET rearrangement.

These drugs are taken by mouth as capsules, typically once or twice a day.

Possible side effects of RET inhibitors

Common side effects can include dry mouth, diarrhea or constipation, high blood pressure, tiredness, swelling in hands and/or feet, skin rash, muscle and joint pain, low blood cell counts or changes in other blood tests.

Less common but more serous side effects can include liver damage, lung damage, allergic reactions, changes in heart rhythm, bleeding easily, and problems with wound

healing.

cough, decreased white blood cell and red blood cell counts, and changes in other blood tests.

Less common but more serious side effects can include kidney damage, liver damage,

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 types of immunotherapy are being tested in <u>clinical trials</u>¹, and some are used to treat bile duct cancer.

- Immune checkpoint inhibitors
- More information about immunotherapy

Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking the body's normal cells. To do this, it uses "checkpoint" proteins on immune cells, which act like switches that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to avoid being attacked by the immune system.

Drugs that target these checkpoints (called immune checkpoint inhibitors) can bcells. To do this, ij (

These drugs are given as an intravenous (IV) infusion, typically every 2 to 6 weeks.

PD-L1 inhibitor

Durvalumab (Imfinzi) is a drug that targets PD-L1, a protein related to PD-1 that is found on some tumor cells and immune cells. Blocking this protein can help boost the immune response against cancer cells.

This drug can be used along with the chemotherapy drugs gemcitabine and cisplatin to treat bile duct cancer that can't be removed by surgery or that has spread to other parts of the body.

This drug is given as an intravenous (IV) infusion, typically every 2 to 4 weeks.

CTLA-4 inhibitor

Ipilimumab (Yervoy) is another checkpoint inhibitor, but it has a different target. It blocks CTLA-4, another protein on T cells that normally helps keep them in check.

It can be given with Nivolumab (Opdivo) to people with bile duct tumors that have a high mutational burden (TMB-H).

This drug is given as an intravenous (IV) infusion, usually once every 3 weeks.

Possible side effects of immune checkpoint inhibitors

Some of the more common side effects of these drugs can include fatigue, cough, nausea, skin rash, poor appetite, constipation, joint pain, and diarrhea.

Other, more serious side effects occur less often.

Infusion reactions: Some people might have an infusion reaction while getting these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your doctor or nurse right away if you have any of these symptoms while getting these drugs.

Autoimmune reactions: These drugs remove one of the safeguards on the body's immune system. Sometimes the immune system responds by attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

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Palliative Therapy for Bile Duct Cancer

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

- When are palliative treatments used?
- Biliary stent or biliary catheter
- Biliary bypass
- Tumor ablation (radiofrequency ablation, cryosurgery, or alcohol ablation)
- Photodynamic therapy (PDT)
- More information about palliative care

When are palliative treatments used?

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>¹ and <u>drugs to control nausea</u>² 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:

Hyperlinks

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

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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
- Unresectable bile duct cancers
- Palliative care
- Recurrent bile duct cancer

Resectable bile duct cancers

Most <u>stage</u>¹ 0, I, and II cancers and possibly some stage III cancers are potentially resectable -- that is, it might be possible to remove them completely 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 Cancer²</u>.)

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 a person 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**.

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 might 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 resectable. Surgery could then be done to try to remove the cancer.

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 might 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 Theseshomghg113ve s0 canceblo73ead farther than was 60ed con

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

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