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#Reference From NCCN Guidelines

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Pancreatic cancer basics

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Pancreatic cancer is one of the most common cancers. It is a challenging cancer to treat, but treatment is improving. Experts are studying the best ways to treat pancreatic cancer and are developing new treatments. Read this chapter to learn the answers to some common questions about pancreatic cancer.

What is pancreatic cancer?

Pancreatic cancer starts in a large gland called the pancreas. The pancreas is part of the digestive system. It makes enzymes that break down proteins, fats, sugars, and starches in

food. It also makes hormones called insulin and glucagon that control blood sugar levels.

Pancreatic cancer affects cell growth. Pancreatic cancer cells make many new cancer cells and do not die when they should. The overgrowth of pancreatic cancer cells becomes a mass called a tumor. Pancreatic cancer cells also don't stay in place and may grow into nearby body tissue. They may break away from a tumor, spread to other areas, and form more tumors.

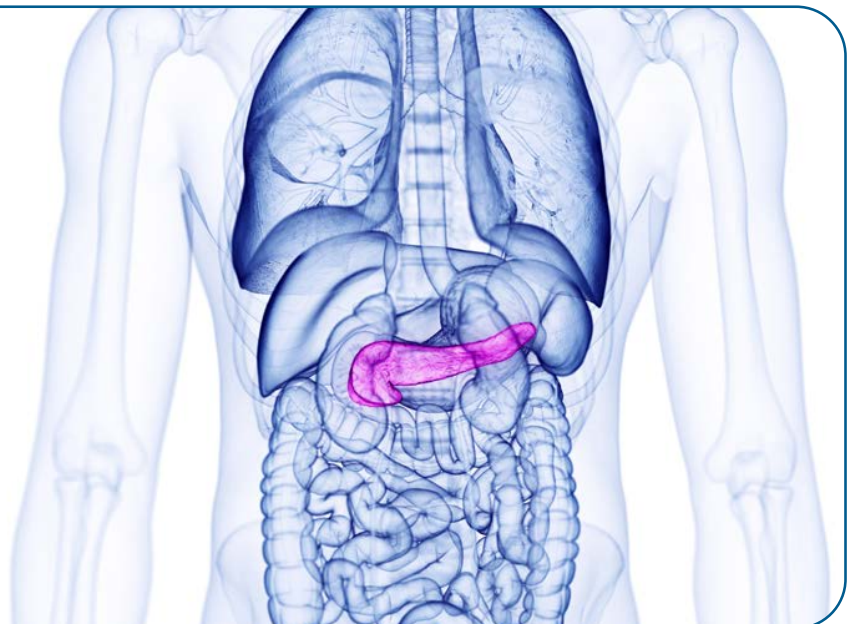
There are 2 main types of pancreatic cancer

The more common type of pancreatic cancer forms from exocrine cells. Exocrine cells make and move digestive enzymes. Pancreatic adenocarcinomas form from exocrine cells that line the tube-like ducts of the pancreas. They are also called pancreatic ductal adenocarcinoma (PDAC) and are the focus of this book.

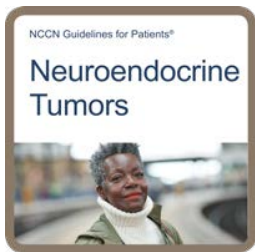
Pancreas

Sounds like PAN-kree-us.

The pancreas is deep inside the body. It sits just below the liver and behind the stomach. In adults, the pancreas is about 6 inches long.



Less often, pancreatic cancer forms from endocrine cells. Endocrine cells make hormones. Pancreatic cancer that forms from endocrine cells is called a neuroendocrine tumor. Information on pancreatic neuroendocrine tumors can be found at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the app [NCCN Patient Guides for Cancer](#).



What causes pancreatic cancer?

Many people with cancer wonder how they got it. Experts don't know exactly what causes pancreatic cells to become cancer cells. But they do know several factors that increase the chance of developing pancreatic cancer. Such risk factors include:

- Lifestyle factors, such as smoking tobacco, heavy alcohol use, and a less healthy diet
- Major contact with cancer-causing chemicals, such as pesticides
- Health conditions, such as diabetes and chronic inflammation of the pancreas
- Close blood relatives with pancreatic, breast, ovarian, or colorectal cancers or melanoma

About 1 in 10 pancreatic cancers are hereditary. This means that a higher risk was passed down to you by your parents through

your genes. The genetic cause of hereditary pancreatic cancer is unknown in most families. Hereditary health conditions that are known to increase risk of pancreatic cancer include:

- Hereditary breast-ovarian cancer syndrome (HBOC)
- Peutz-Jeghers syndrome, Lynch syndrome, and Li-Fraumeni syndrome
- Familial malignant melanoma syndrome, also known as melanoma-pancreatic cancer syndrome or familial atypical multiple mole melanoma (FAMMM) syndrome
- Hereditary pancreatitis

Genetic tests detect the genes that have been linked to these hereditary conditions and are discussed in Chapter 2.

What are the stages of pancreatic cancer?

The stages of pancreatic cancer range from stage 0 to stage 4. Often, stages 1 through 4 are written with Roman numerals—stages I, II, III, and IV. The cancer stages are based on the size of the pancreatic tumor and how far the cancer has spread.

- **Stage 0** pancreatic cancer is only in the innermost layer of the duct wall.
- **Stage 1** pancreatic cancer consists of a tumor that is 4 centimeters or smaller and has not spread outside the pancreas. For comparison, a golf ball is 4.3 centimeters.
- **Stage 2** pancreatic cancer consists of a tumor that is larger than 4 centimeters or the cancer has spread to 1 to 3 nearby

lymph nodes, which are small structures that help the body fight disease.

- **Stage 3** pancreatic cancer has grown through the pancreas to nearby major arteries or has spread to 4 or more lymph nodes.
- **Stage 4** pancreatic cancer has spread far and commonly involves the liver, lungs, or lining of the abdomen.

What stage is metastatic cancer?

Stage 4 pancreatic cancer is metastatic cancer, but other stages may become metastatic cancer over time. Metastatic pancreatic cancer has spread far from the pancreas.

Is staging used to plan treatment for pancreatic cancer?

Unlike other cancers, experts do not plan initial treatment mainly based on the five pancreatic

cancer stages. Instead, they use a different system to decide treatment for cancers that are not metastatic. This system is described in Chapter 5.

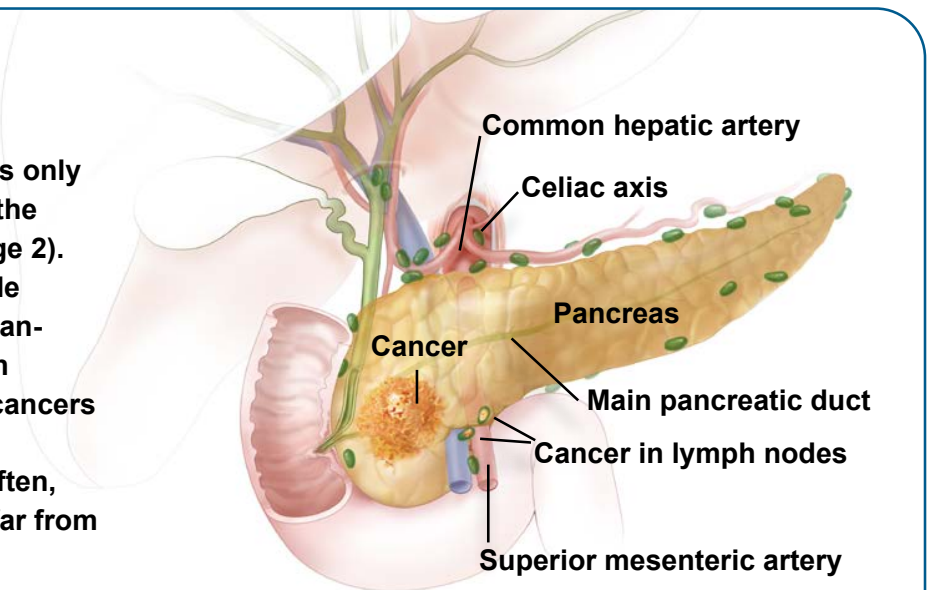
What is the best treatment for pancreatic cancer?

There's no treatment for pancreatic cancer that's best for everyone. The best treatment is the treatment that's right for you. Your treatment plan should follow best practices—cancer care based on science and expert consensus. The following chapters explain the best practices of testing for and treating pancreatic cancer.

Some people with stage 1, 2, or 3 pancreatic cancer have surgery to remove cancer from the body. Surgery is an option for more people now than in the past due to medical advances. Other types of cancer treatment are used with

Pancreatic cancer stages

Very rarely, pancreatic cancer is only in the duct (stage 0) or only in the pancreas (stage 1 or some stage 2). Stage 2 and stage 3 also include cancers that have spread to bean-shaped structures called lymph nodes (shown). Other stage 3 cancers have grown to nearby arteries, such as the celiac axis. Most often, pancreatic cancer has spread far from the pancreas, which is stage 4.



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surgery to improve results. Ongoing research is assessing whether it is better to receive these other treatments before or after surgery. Read Chapter 5 to learn more about treatment with surgery.

For most people with pancreatic cancer, surgery is not the best treatment. Instead, drug treatment is most often used to control cancer's growth and reduce symptoms. Research has compared current cancer drugs to identify the best ones. In recent years, drug regimens based on cancer markers have been used to improve results. Treatment without surgery is discussed in Chapter 6.

Clinical trials offer hope to all people with pancreatic cancer. Clinical trials are a type of health research that tests new ways of fighting cancer. Ask your care team if there is a clinical trial that is a good fit for you.

Key points

- The pancreas is a gland that helps digest food and control blood sugar.
- Pancreatic adenocarcinomas form from exocrine cells that line the ducts of the pancreas and are the focus of this book.
- Some families share genes that increase the risk of pancreatic cancer.
- There are five stages of pancreatic cancer that range from stage 0 to stage 4.
- Your cancer care team will make a treatment plan that is specific to you. Talk with your team about options for treatment and supportive care.



Advocate for yourself

Take steps to get the best care for you. Here are 3 ways to advocate for yourself:

- ✓ Read this book to learn about pancreatic cancer and its treatment. Use the questions in the back of the book to discuss and decide with your care team which care options are right for you.
- ✓ Choose a multidisciplinary team. It takes a team of experts to treat pancreatic cancer. Read this book to learn which care providers are part of the team. You choose your team by deciding where to get care. Getting a second opinion on treatment may help you decide which treatment to receive.
- ✓ Be an active team member. When discussing treatment, share your goals with your team. Ask questions when you don't understand. Supportive care is part of cancer care, so tell your team about symptoms and other challenges you have. Key parts of supportive care are explained in this book.

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Tests for pancreatic cancer

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A series of tests is needed to identify pancreatic cancer and make a treatment plan. Imaging is key to staging the cancer and deciding if surgery is a treatment option. Testing can also show if the cancer has unique features for which there is specific treatment.

Multidisciplinary consult

There is no tell-tale sign of pancreatic cancer, especially in early stages. Signs of pancreatic cancer may also be caused by other health conditions. Health care providers may suspect pancreatic cancer based on symptoms, such as yellowed skin or eyes called jaundice. Signs of pancreatic cancer on x-rays include wider-than-normal pancreatic ducts or an inflamed pancreas. If your provider suspects pancreatic cancer, testing will be needed.

Care team

Because pancreatic cancer is complex, it takes a team of experts to decide the best course to diagnose and treat pancreatic cancer. This team of experts should:

- **Be multidisciplinary** – Consist of health care providers from different fields of medicine
- **Work at a high-volume center** – Be very experienced with pancreatic cancer



Care team

A care team may include many multidisciplinary members, including a:

- ✓ Diagnostic radiologist
- ✓ Interventional radiologist
- ✓ Pathologist
- ✓ Gastroenterologist
- ✓ Medical oncologist
- ✓ Surgical oncologist
- ✓ Radiation oncologist
- ✓ Geriatrician
- ✓ Registered dietitian
- ✓ Genetic counselor
- ✓ Palliative care provider
- ✓ Mental health provider

Many of these experts are supported by nurses, technicians, or assistants who are often on the frontline of cancer care.

Look for descriptions of team members throughout this book.

Consult meeting

When your care team meets to consult with one another, they will review your health records and the tests done prior to your visit.

- Expect to be asked questions about your past and current health. This is called a medical history. You will also be asked about the health history of your close blood relatives.
- A team member will perform a physical exam of your body to check for signs of disease and to assess your physical ability.
- You will likely have at least one imaging scan and some of the other tests listed in **Guide 1**.

The team will discuss the diagnosis with you and if you need more tests. They will also discuss your treatment options. One of the main goals of the team is to decide if surgery is an option. The team will work with you to make a care plan that is specific to you.



Stay positive, seek happiness and joy, surround yourself with love, and connect to a higher power. "

Guide 1

Tests for pancreatic cancer

Tests for diagnosis and staging

Imaging

- Pancreatic protocol CT or MRI scan of the abdomen
- Possible CT of the chest and pelvis, MRI of the liver, or PET/CT if metastatic cancer was not found with the pancreatic protocol

Endoscopic tests

- EUS or laparoscopy may be done for staging

Biopsy to confirm there is cancer

- EUS-guided biopsy or imaging-guided biopsy

Blood tests

- Liver function tests and CA 19-9 marker

Tests for personalized treatment

- Genetic tests for inherited mutations
- Biomarker tests to obtain a molecular profile of the cancer

Imaging

Imaging takes pictures of the inside of the body. It can show cancer deep inside the body. Imaging of the pancreas is very important and is often the first test for pancreatic cancer. It is used to assess the cancer stage and plan treatment.

Imaging of the pancreas

Radiologists have identified which methods best show cancer in and near the pancreas. These methods are known as pancreatic protocols. There are pancreatic protocols for computed tomography (CT) and magnetic resonance imaging (MRI).

You'll receive contrast if it's safe for you to receive. Contrast makes images clearer. You will be injected with contrast. If undergoing CT, you will also drink a liquid contrast. Contrast travels in the bloodstream and is flushed out in urine.

A CT scan is a more detailed kind of x-ray. It takes many pictures from different angles. A computer combines the images to make 3-D pictures. A **pancreatic protocol CT** takes pictures before contrast and multiple times after contrast. The scan is finished in several minutes.

Imaging of the pancreas is most often done with CT, but you may undergo MRI instead. MRI uses strong magnetic fields and radio waves to make images. A **pancreatic protocol MRI** may show small tumors and metastases not seen on CT. The scan is completed in 30 to 90 minutes.

A magnetic resonance cholangiopancreatography (MRCP) is a type of MRI that is usually part of the MRI pancreatic protocol. It makes very clear pictures of the pancreas and bile ducts. No contrast is used because bile and other fluids act as contrast.

Imaging

Imaging is used to make pictures of the insides of your body. You will lie on a table that will move into the tunnel of the machine. You will need to lie still during the scan. You may be asked to hold your breath. A radiologist will view the pictures on a computer and look for signs of cancer.



Imaging of other areas

Pancreatic cancer has often spread far by the time cancer is diagnosed. Distant cancer spread is called metastatic cancer. Stage 4 means there is metastatic cancer at diagnosis. If the pancreatic protocol did not show distant spread, you may undergo more imaging:

- A CT scan with contrast of the chest and pelvis when getting the pancreatic scan or at a later time
- MRI to look for cancer spread to the liver if CT scan doesn't clearly show spread
- Positron emission tomography combined with CT (called a PET/CT scan) is not a routine test but may be helpful for some people

A PET scan highlights tissue in your body that may be cancerous. About an hour before the scan, you will be injected with a radioactive substance called a tracer. Cancer cells take in more of the tracer than normal cells and show up as bright spots on the scan. The tracer will pass out of your body in your urine.

A diagnostic radiologist is a doctor who's an expert in identifying health conditions through imaging. This doctor will review your scans, write a report, and discuss the findings with the multidisciplinary team.



As a 22-year survivor of pancreatic cancer, I can say from experience that if you have received a diagnosis that seemingly gives you little hope, the doctors may be expressing their own limitations. Hard-fought scientific breakthroughs administered through the healing hands and hearts of untold doctors, nurses, scientists and technicians make increasingly common, though still miraculous, outcomes possible. You need only seek them out."

Endoscopic tests

An endoscope is a medical device that allows doctors to see and work inside the body. It causes less trauma to the body than open surgery. Your care team will decide if endoscopic staging is needed, though this is not commonly done.

An endoscope is a device with a long, flexible tube. The endoscopist will guide the tube into your body. At the tip of the device is a light, a camera, and sometimes other tools. The endoscopist will view the images on a screen.

An **endoscopic ultrasound (EUS)** may be done to confirm where the pancreatic tumor has grown. An endoscope tube will be inserted into your mouth and guided down to the first part of the small intestine called the duodenum. The ultrasound probe on the endoscope makes images of the pancreas and nearby structures. Your doctor will look for

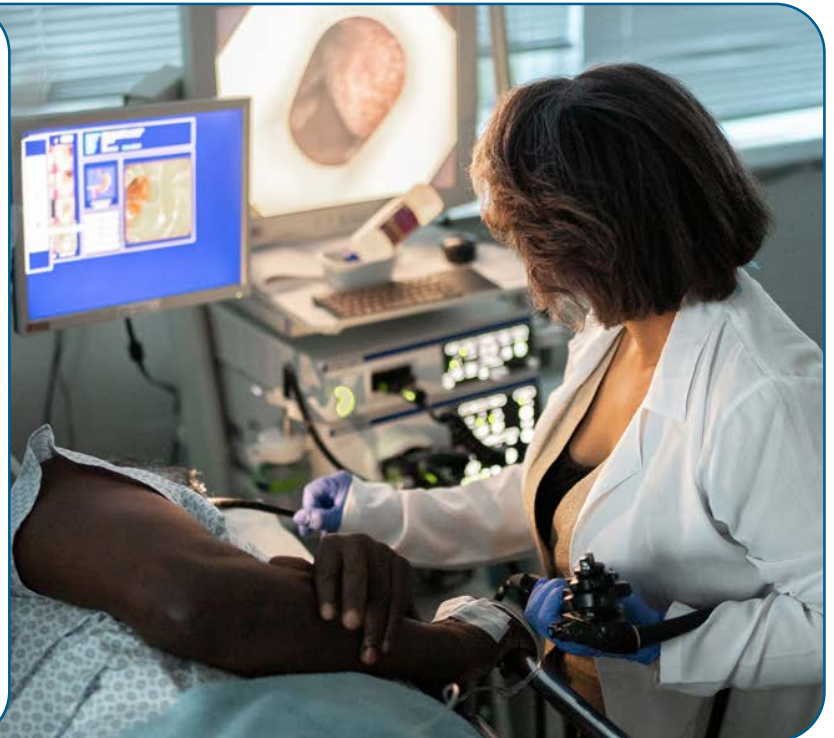
areas of cancer growth and may obtain tissue samples for testing.

Endoscopic retrograde cholangiopancreatography (ERCP) is mostly used to treat health conditions, such as a blocked bile duct. It may be used to look for areas of cancer growth. ERCP used for supportive care is described in Chapter 3.

A **laparoscopy** may be done if your care team suspects metastatic cancer but none was seen with imaging. First, your care team will give you general anesthesia to put you in a sleep-like state. Next, a surgeon will make small cuts in your abdomen. Through the cuts, gas will be pumped into your inner abdomen for a better view and a laparoscope will be inserted. Endoscopes designed for laparoscopy are referred to as laparoscopes. The surgeon will look for signs of cancer outside the pancreas.

Endoscopic ultrasound

For some people, an endoscopic ultrasound (EUS) may help stage pancreatic cancer. EUS can show where the tumor has grown in and around the pancreas. You will need to fast since the endoscope (shown) will be guided through your mouth down to your stomach. You will be given medicine to help you relax or sleep during the procedure. The scope may be fitted with a hollow needle to collect biopsy samples.



Tissue or fluid samples may be removed and tested for cancer.

Biopsy

A biopsy is a procedure that removes tissue or fluid samples from the body. Samples are sent to a lab and examined by a pathologist for cancer cells. This is the only way to confirm (diagnose) cancer.

Not everyone needs a biopsy before treatment. If you have surgery first, the diagnosis may be confirmed on the day of surgery to spare you from having another complex procedure. On the other hand, a biopsy is needed to confirm the diagnosis before drug treatment, such as chemotherapy.

Types of biopsy

The type of biopsy you will receive partly depends on where cancer may be and the treatment plan. The body part that likely has cancer and would provide the highest cancer stage will be sampled. Several samples should be removed for diagnosis as well as biomarker testing.

A biopsy for pancreatic cancer is often done with a needle. This is called a needle biopsy. The preferred method of performing a needle biopsy is with EUS. An **EUS-guided biopsy** obtains better samples and has less serious risks than other biopsies. If you undergo ERCP, the EUS-guided biopsy can be done before the stent is placed.

Another method of performing a needle biopsy is to go through the skin. This method is usually done if your team suspects pancreatic

cancer spread to the liver. A CT scan or ultrasound will be used to guide the needle to the right spot. **Imaging-guided biopsy** is the preferred method to remove small pieces of tumor.

A second biopsy may be needed

If no cancer cells are found, a second biopsy will likely be done if your care team believes there is cancer. Tissue from another area may be removed or a different type of biopsy may be done. You might need to go to a cancer center that treats many people with pancreatic cancer.

A pathologist is a doctor who's an expert in testing cells and tissue and diagnosing cancer. This doctor records the results of lab tests used for diagnosis in a pathology report. Ask your care team for a copy of the report and to review the results with you. Take notes and ask questions.

Blood tests

If metastatic cancer was not detected with imaging, two types of blood tests will be done to help with cancer staging. Blood samples will be removed by a needle placed into your vein. Blocked bile ducts can affect test results, so blood samples must be drawn only when your bile ducts are clear. A symptom of blocked ducts is jaundice.

Liver function tests

Liver function tests measure levels of proteins and enzymes made or processed by the liver. They also measure a chemical called bilirubin that makes bile yellow. Abnormal levels may be caused by pancreatic cancer that is blocking bile ducts or is in the liver.

CA 19-9 marker

Pancreatic cancer cells make a protein called carbohydrate antigen 19-9 (CA 19-9). High CA 19-9 levels in blood are a tumor marker of pancreatic cancer; however, CA 19-9 can't be used alone for diagnosis for two reasons:

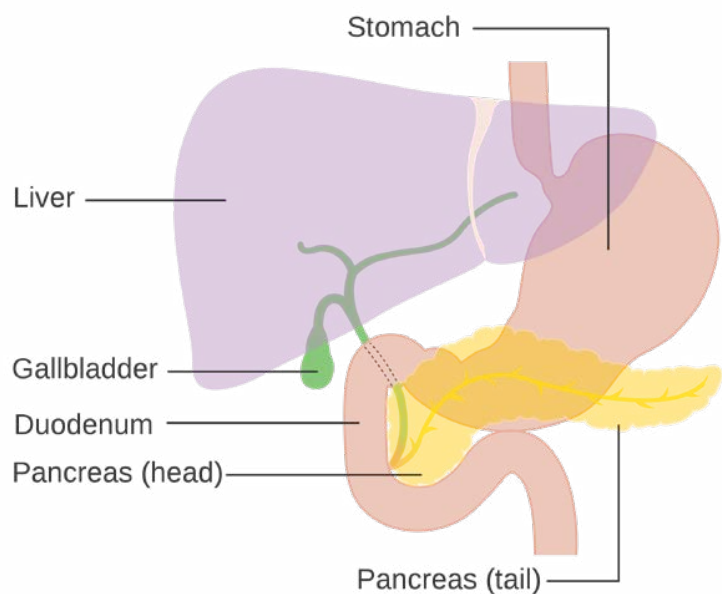
- High levels can be caused by other health conditions, including a blocked bile duct.
- Some people with pancreatic cancer have normal levels of CA 19-9.

When caused by pancreatic cancer, high CA 19-9 levels often mean a high cancer stage. Your care team will take CA 19-9 levels into account when planning treatment. This test may be repeated after treatment to check if levels are dropping or rising.

Liver function tests

The liver is the largest organ and sits below the right rib cage and above the pancreas. Liver function tests measure substances made or processed by the liver. Tumors in the head of the pancreas may block the common bile duct, which can cause high test results. Pancreatic cancer that has spread to the liver may also affect test results.

Credit: commons.wikimedia.org/wiki/File:Diagram_showing_the_position_of_the_pancreas_CRUK_356.svg



Genetic tests for inherited mutations

Some people with pancreatic cancer inherited a risk for the cancer from a birth parent. In these cases, the cancer is called hereditary pancreatic cancer. The cancer risk was passed down through abnormal genes called germline mutations. Genes tell cells how to build your body and make it work. Germline mutations are in every cell of the body that has DNA.

Genetic tests are used to look for germline mutations. **All people with pancreatic cancer should get genetic tests, which are used for treatment planning.** Either a sample of blood or spit (saliva) is tested. For a list of germline mutations related to pancreatic cancer, see **Guide 2**.

Genetic tests look for but will not find germline mutations in most people with pancreatic cancer. That's because most people don't have hereditary pancreatic cancer. Also, the

Guide 2

Inherited gene mutations that increase risk of pancreatic cancer

| Inherited mutations in these genes increase risk of pancreatic cancer | What does this gene or group of genes do? | What other cancers are related to mutations in these genes? |
|--|--|---|
| <i>ATM</i> | Helps repair damaged DNA and kill damaged cells | Breast and bladder cancers and melanoma |
| <i>BRCA1, BRCA2</i> (known as the breast cancer genes) | Helps repair damaged DNA | Breast, ovarian, prostate, bile duct, and colon cancers |
| <i>CDKN2A</i> | Helps control the number of new cells being made | Breast, bladder, head and neck, and lung cancers and melanoma |
| <i>MLH1, MSH2, MSH6, and PMS2</i> (known as the mismatch repair genes) | Helps repair damaged DNA | Brain, colon, gallbladder duct, ovarian, rectal, stomach, small intestine, upper urinary tract, and uterine cancers |
| <i>STK11</i> | Helps control the number of new cells being made | Breast, colon, lung, ovarian, and rectal cancers |
| <i>TP53</i> | Helps stop cell growth for DNA repair and helps kill damaged cells | Breast, bladder, bile duct, head and neck, kidney, lung, and ovarian cancers and melanoma |

genetic cause of hereditary pancreatic cancer is unknown in most families.

Talking to a genetic counselor may be helpful for people with pancreatic cancer who have either a:

- Cancer-causing germline mutation or
- Family history of cancer, especially pancreatic cancer.

Genetic counselors can help explain what the results of genetic tests mean. You may learn that you have a hereditary health condition. You and your counselor can discuss sharing your test results with your family.

Genetic testing is helpful for treatment planning. Some types of treatment work well for certain inherited mutations. An example is the drug olaparib (Lynparza) used to treat pancreatic cancer with germline *BRCA* mutations.

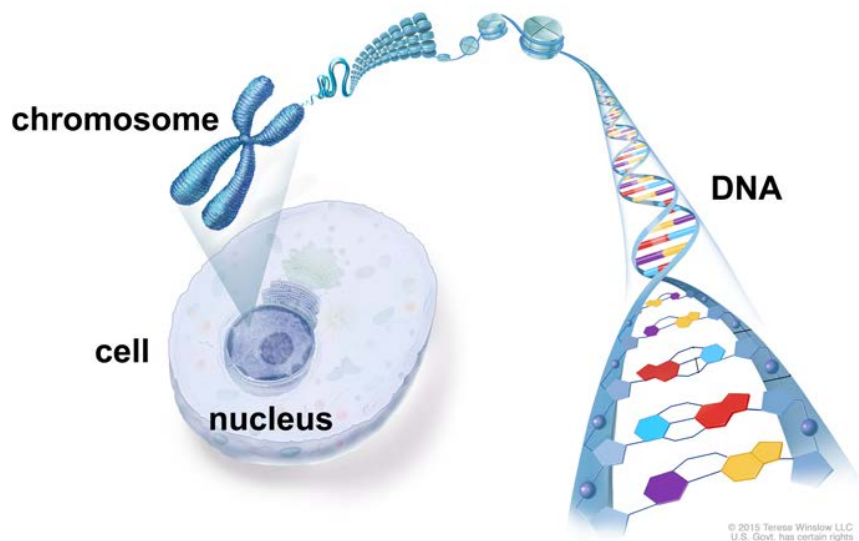
Biomarker tests for profiling

Biomarker tests look for biological clues, or markers, of cancer that differ between people. Such clues can help with diagnosis, such as the CA 19-9 marker, and with treatment. Biomarker testing is not the same as genetic testing that assesses what a person inherited from their birth parents.

Not all pancreatic cancers are the same. Biomarker tests for pancreatic cancer provide a molecular profile—small yet important features—of the cancer. They detect abnormal changes in cancer cells' genes that occurred during your lifetime. Some of these acquired changes are listed in **Guide 3**.

Genes and cancer

Genes are small segments of DNA that tell cells how to build your body and make it work. Some people are born with inherited changes in genes called germline mutations. Abnormal genes can develop during a lifetime, including gene mutations, fusions, and amplifications. Experts have developed treatments for some of the abnormal genes that promote the growth of pancreatic cancer.



At this time, molecular biomarker tests are done only on advanced and metastatic pancreatic cancer. A sample of the tumor is preferred for testing. Since fragments of DNA from cancer cells are in blood, a blood sample is also an option for some people.

Because of molecular biomarkers, a treatment that helps one person might not help you. Examples of treatment based on molecular biomarkers are listed in Guide 3. Who may receive these treatments and at what timepoint are explained in Chapter 6.

Guide 3

Biomarker profiling for advanced and metastatic pancreatic cancer

| Type of marker | Lab testing method | Examples of treatment for marker |
|--|----------------------------|---|
| A fusion is a joining of a piece of gene to a piece of another gene | Next-generation sequencing | <ul style="list-style-type: none"> • Entrectinib (Rozlytrek) and larotrectinib (Vitrakvi) for <i>NTRK</i> fusion • Selpercatinib (Retevmo) for <i>RET</i> fusion |
| A mutation is a change in a gene's DNA | Next-generation sequencing | <ul style="list-style-type: none"> • Dabrafenib (Tafinlar) and trametinib (Mekinist) for <i>BRAF</i> V600 mutation • Rucaparib (Rubraca) for <i>BRCA1</i>, <i>BRCA2</i>, and <i>PALB2</i> mutations |
| An amplification is extra copies of a gene | Next-generation sequencing | <ul style="list-style-type: none"> • Therapy for <i>HER2</i> amplifications is used to treat some cancers but needs to be tested in people with pancreatic cancer |
| Microsatellite instability is when errors are made in small DNA parts when DNA is being copied to make new cells | Next-generation sequencing | <ul style="list-style-type: none"> • Pembrolizumab (Keytruda); dostarlimab-gxly (Jemperli) |
| Mismatch repair deficiency is an inability to correct microsatellite instability due to an impaired repair system | Immunohistochemistry | <ul style="list-style-type: none"> • Pembrolizumab (Keytruda); dostarlimab-gxly (Jemperli) |
| Tumor mutational burden is the total number of DNA changes in cancer cells | Next-generation sequencing | <ul style="list-style-type: none"> • Pembrolizumab (Keytruda); nivolumab (Opdivo) plus ipilimumab (Yervoy) |

Key points

- A highly experienced team of experts should manage your care if pancreatic cancer is suspected or diagnosed. They will decide what treatments are options for you.
- When pancreatic cancer is suspected, a CT or MRI scan done according to a pancreatic protocol can best show if there is a mass and where it has grown. Additional imaging and endoscopic tests may be done to help stage the cancer.
- Liver function tests and a CA 19-9 test are needed for treatment planning.
- A biopsy to collect cell samples for cancer testing is needed before starting medical treatment, such as chemotherapy. If surgery will be your first treatment, a biopsy sample can be collected on the day of surgery.
- After diagnosis, genetic tests will be done to assess if you have an inherited risk of pancreatic cancer.
- Biomarker tests provide a molecular profile of the cancer. There are treatments for some markers.



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[NCCN.org/patients/feedback](https://www.nccn.org/patients/feedback)

3

Supportive care

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Supportive care is cancer care that improves your quality of life. One of its main goals is to relieve symptoms caused by cancer or its treatment. Supportive care for people with pancreatic cancer should be started as soon as possible.

About supportive care

Supportive care is a key part of treatment for everyone with pancreatic cancer. It is not just for people at the end of life who need hospice. Many people with pancreatic cancer need relief from symptoms starting at diagnosis.

Supportive care is sometimes called palliative care since symptom relief is a main goal. But supportive care addresses many other needs. You can get help with making treatment decisions and coordination of care between health providers. You can get emotional or spiritual support, financial aid, or family counseling.

This chapter describes some of the unique needs of people with pancreatic cancer. Pancreatic cancer and its treatment often cause poor nutrition and other health issues. This chapter also lists NCCN resources on supportive care. Tell your care team about your symptoms and other needs to get the best supportive care for you.

Blocked bile duct

A bile duct is a small tube-shaped structure that drains fluid called bile from the liver. The common bile duct runs through the head of the pancreas where most pancreatic tumors grow. Pancreatic tumors often grow large enough to block a bile duct.

A blocked bile duct can cause a range of symptoms. You may have pain or a fever. Stools (poop) may be lighter in color and float. Urine (pee) may be dark. Your eyes and skin may have a yellow tint called jaundice. Jaundice of the skin may cause itchiness.

There are three ways to treat a blocked duct:

- The most common is placement of a small, expandable tube, called a stent, in the bile duct during a procedure called endoscopic retrograde cholangiopancreatography (ERCP). Stenting will not be performed if you'll be having pancreatic surgery soon.
- Bile can be drained from the duct through a long, soft tube, called a catheter, to a bag outside your body then possibly later into your intestine.
- A surgery called a biliary bypass can be performed, which connects the small intestine to the common bile duct above the pancreas.

The preferred method to unblock a bile duct is a stent inserted during ERCP. In general, metal stents should be used instead of plastic stents. Sometimes it is not possible to place a metal stent right away, and a plastic stent will be used first.

Stents that are completely covered in material can be removed. Partially covered or bare

metal stents should be used if pancreatic cancer has been confirmed by a pathologist.

Blocked stomach

A pancreatic tumor may grow large enough to block food from leaving your stomach. The blockage may be where the stomach empties into the small intestine called the gastric outlet or pylorus. Blockages may also occur in the first part of the small intestine called the duodenum. These blockages can cause pain, vomiting, and weight loss. Treatments for a blocked stomach include:

- Bypassing the blockage with a surgery called gastrojejunostomy, which connects the bottom of the stomach to the middle of the small intestine
- Opening the blockage with a stent that is placed during an endoscopy

- Relieving stomach pressure with a venting percutaneous endoscopic gastrostomy tube (PEG or G-tube) that is inserted through the skin into the stomach

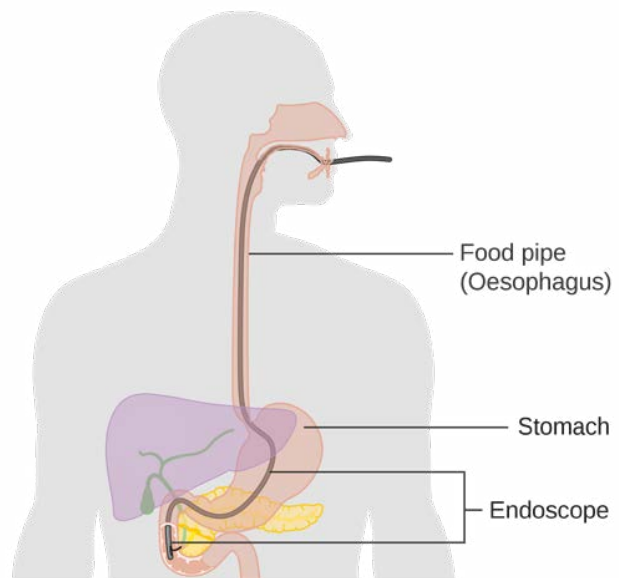
In addition to a gastrojejunostomy, you may receive a feeding tube. A PEG tube can be used as a feeding tube. A jejunostomy tube (J-tube) is also a feeding tube that is inserted through the skin into the small intestine.

Pancreatic cancer can make it hard to eat or digest food. A registered dietitian is an expert in nutrition and diet. They can recommend ways to get enough nutrition.

Blocked bile duct

An endoscopic retrograde cholangiopancreatography (ERCP) may be used to open a blocked bile duct. The endoscopist will guide an endoscope tube down your throat to the small intestine. An x-ray video will show the endoscope moving inside your body. Next, the doctor will insert a stent into the blocked duct.

Credit: commons.wikimedia.org/wiki/File:Diagram_showing_an_endoscopic_retrograde_cholangio_pancreatography_(ERCP)_CRUK_097.svg



Pancreatic insufficiency and diabetes

The pancreas makes two types of chemicals—enzymes and hormones. The enzymes break down proteins, fats, sugars, and starches in food. The hormones control blood sugar levels. People with pancreatic cancer may have abnormal levels of these chemicals.

Low pancreatic enzymes

Pancreatic cancer or its treatment may cause the pancreas to make fewer enzymes. This is called exocrine pancreatic insufficiency (EPI). Many people have EPI after surgery that removes pancreatic cancer.

You may have trouble digesting food without enough pancreatic enzymes. Symptoms include stomach cramps, gas, weight loss, and lack of proper nutrition. Stools (poop) may be especially smelly, light in color, and float.

Pancreatic enzyme replacement gives you the digestive enzymes you lack. You will need to take several capsules while you eat. The dose differs between people, so your care team will give you specific instructions. If the cost of enzyme replacement is high, ask your care team about how to obtain financial help.

Low pancreatic hormones

Insulin and glucagon are pancreatic hormones that control blood sugar levels. People with pancreatic cancer may not have enough of these hormones. The result may be abnormal levels of blood sugar.

The causes of abnormal blood sugar levels in people with pancreatic cancer are:

- Unrelated to cancer, the pancreas stopped making insulin (type 1 diabetes)

- Unrelated to cancer, the pancreas doesn't produce more insulin to unlock cells that are resistant to it (type 2 diabetes)
- Pancreatic cancer may stop pancreatic cells from making hormones (type 3c diabetes)
- Surgery that removes part of or your entire pancreas will reduce the amount of hormones made by your pancreas (type 3c diabetes)

Pancreatic cancer can change how diabetes is managed. Ask your care team what the best treatment is for you. Each type of diabetes is different and treated differently.

Pain

Most people with advanced pancreatic cancer have cancer-related pain. A large tumor can cause pain by pressing on nearby organs. Pancreatic cancer can also spread to nearby nerves and cause severe pain. Pain is most often felt in the belly area (abdomen) or the middle of the back.

There are many ways to manage pain. Your care team will develop a plan that works best for you. Working with a palliative care specialist or a pain specialist soon after the cancer diagnosis may be helpful. Pain from pancreatic cancer may be managed with:

- Pain medicine using opioids that are given around the clock since this schedule works better than taking these medicines as needed
- Injection of a nerve block into a nerve bundle called the celiac plexus during endoscopic ultrasound (EUS-guided celiac plexus neurolysis) or through the skin guided by imaging

If pain medicine doesn't control the pain well or has troublesome side effects, there are three other options:

- High-intensity focused ultrasound
- Tumor-directed radiation therapy with or without chemotherapy if it's not part of your cancer treatment
- A pain pump to give medicine directly to the spinal cord (also called intrathecal drug delivery)



The benefits of adding alternative therapies to conventional cancer treatments are great. For example, massage therapy and acupuncture can help with pain and anxiety. Meditation, yoga, and other exercises address the mind-body-spirit connection. Using these complementary treatments to ease side effects may just make the difference between tolerating treatment and feeling stronger. Be sure and check with your doctor when choosing alternative treatments."

A palliative care specialist has received specific training to provide additional support to you. Their care focuses on relieving symptoms and reducing stress. A palliative care specialist may be a doctor, nurse, or other type of care provider. Some cancer centers have palliative care programs.



Blood clots and bleeding

Pancreatic cancer can cause blood to thicken and form blood clots. A blood clot is a gel-like clump of blood. Pancreatic cancer may also cause bleeding in the gastrointestinal (GI) tract. Your care team will be on the lookout for symptoms related to these effects of cancer.

Thromboembolic disease

Normally, blood clots develop to stop bleeding and then dissolve. But a blood clot can form inside a blood vessel when there is no bleeding. This type of clot is called a thrombus

or thrombi if referring to more than one. Loose blood clots that travel in the bloodstream are called emboli.

Pancreatic cancer increases the chance of getting blood clots (thromboembolic disease). As blood clots worsen, they can block enough blood flow to cause symptoms. Untreated blood clots may cause long-term problems or be deadly.

Many blood clots are safely treated with medication called anticoagulants. Anticoagulants are often called blood thinners, though they do not thin the blood. Rather, they

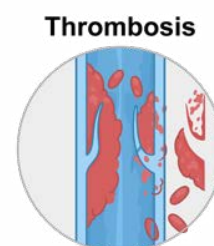
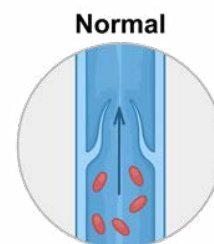
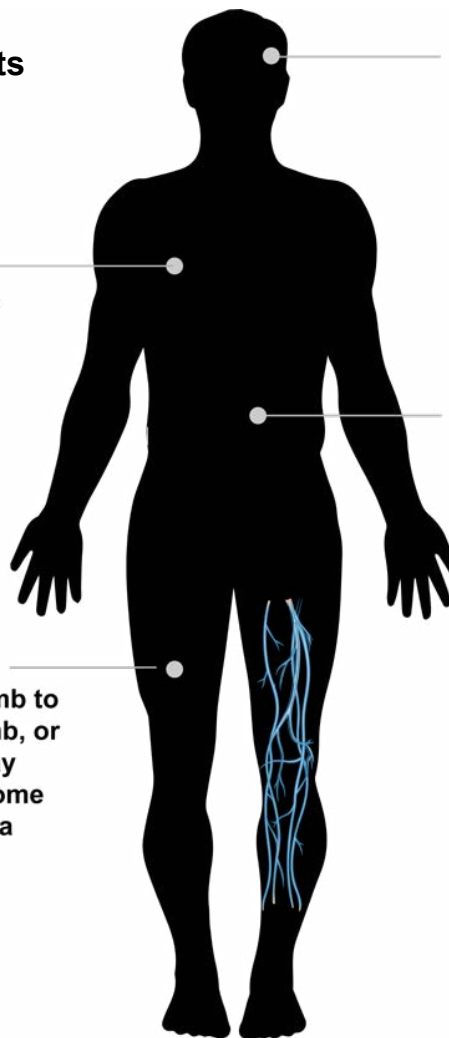
Warning signs of blood clots

Clots in the chest may cause sweating, breathing problems, and cough.

Clots in the legs and arms may cause a limb to feel heavy, cold, numb, or tingling. The limb may swell, cramp, or become weak. Skin may turn a bluish or red color.

Clots in the head may cause headaches, dizziness, slurred speech, and facial weakness.

Clots in the abdomen may cause nausea, vomiting, and loose or bloody stools.



slow down clotting time. Anticoagulants for blood clots include:

- Low-molecular-weight heparin (LMWH) – This medicine enhances the effect of a natural anticoagulant in your body. It is injected into the skin and can be taken at home.
- Vitamin K blockers – Among these medicines, warfarin (Coumadin, Jantoven) is most often used. It is a pill taken at home. Warfarin stops the liver from using vitamin K, which is needed to make clotting proteins. LMWH is preferred over warfarin for treatment.
- Direct oral anticoagulants – These pills disable proteins that help the blood to clot. A direct oral anticoagulant may be used if the pancreatic tumor is not growing inside the stomach or intestine.

Anticoagulants increase the risk of bleeding due to slow clotting time. The risk is even

higher when taking aspirin. You may bruise easily or get nose bleeds when taking anticoagulants. Your doctor may ask you to stop taking aspirin while you're on an anticoagulant.

Bleeding in the GI tract

GI bleeding may occur due to cancer-related ulcers or high blood pressure in the liver vein. If bleeding happens, you may have bloody stools or vomit blood. There are three treatments for bleeding:

- Treatment applied during an endoscopy
- Treatment with radiation if you haven't had radiation therapy in that area
- Blocking a blood vessel (embolization) that is bleeding with materials inserted through a long catheter tube that can be seen with an x-ray video (angiography)



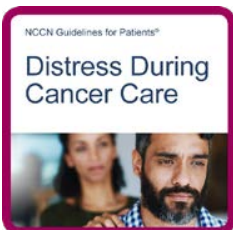
As a former caregiver, the best advice I can give is: don't give up. Don't give up hope, don't give up on the tasks that lie ahead, and don't give up on yourself or your loved one. Whether you have been a caregiver for months or years, you know there is a heaviness to it at times; some days feel like an uphill battle. However, what you are doing matters, every moment. Caregiving for my mom in her final years is an experience that I wouldn't trade for anything. But during those years, I still had to remind myself every day to not give up. It's easier said than done, but I encourage anyone caregiving today to try and do the same. "

Supportive care guidelines

The library of NCCN Guidelines for Patients has books on supportive care. These books focus on common physical and emotional effects of many cancers and their treatment. NCCN has books for:

Distress

Everyone with cancer feels distress at some point. It is normal to be worried, sad, helpless, or angry. Distress can become severe and affect the way you live. Read about managing distress at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Immunotherapy side effects

Immunotherapy is a newer cancer treatment that is used for some pancreatic cancers. A type of immunotherapy called immune checkpoint inhibitors may cause your immune cells to attack your healthy cells. Immune-related side effects can occur during or after treatment. Read about immune-related side effects at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.

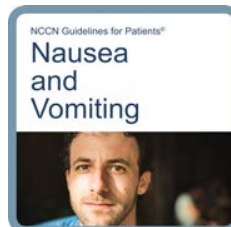


Chemotherapy and radiation effects

Chemotherapy and radiation therapy are cancer treatments that have been around for a long time. Chemotherapy causes side effects because it kills fast-growing normal cells as well as cancer cells. Likewise, radiation therapy may cause side effects by affecting fast-growing normal cells within the radiation beams.

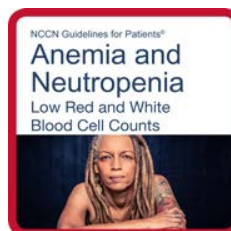
Nausea and vomiting

Both chemotherapy and radiation therapy can cause nausea and vomiting. Nausea is the feeling that you are going to throw up. Vomiting is forcefully throwing up what's in your stomach. Learn how to prevent and manage nausea and vomiting at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Anemia and neutropenia

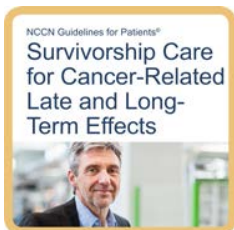
Chemotherapy often causes a drop in red and white blood cells. You are more likely to get infections when white blood cells counts are low (neutropenia). A low number of red blood cells (anemia) may cause severe tiredness



called fatigue. Learn about treatments for low blood cell counts at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.

Late and long-term effects

Cancer and its treatment can cause long-term and late effects. Long-term effects start during treatment and persist after treatment is done. Less often, effects start long after treatment has ended. Late and long-term effects include fatigue, poor sleep, pain, and depression. Read about treatment for these effects at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Advance care planning

When diagnosed with cancer, it may be time to consider what lies ahead. The pursuit of identifying what health care is important to you is called advance care planning. Advance care planning is for everyone, not just for those who are very sick.

Advance care planning involves making medical decisions now in case you become unable to do so. It's about making sure that your wishes are understood and respected. You should get the care you want and prevent care that you don't want. Making an advance care plan now will lessen future stress.

The planning process starts with a candid talk with your care team. Ask about the likely course of the cancer, which is called the prognosis. Having a general idea will help with planning. Learn what care options relieve symptoms and will give you the best quality of life. Invite close family and friends to take part in your advance care planning. They should know your wishes.

When you're ready to make decisions, you'll fill out a legal document that explains your wishes for health care. This document is called an advance directive. Health care providers follow an advance directive when you can't make your wishes known.

Give a copy of your advance directive to your care team. Also give a copy to anyone you've authorized to make decisions on your behalf.

You can change your advance care plan at any time. Frequent conversations with your care team can help. If you make changes, give everyone the new advance directive.

Key points

- Supportive care is not cancer treatment. It is cancer care that improves quality of life. Starting supportive care early can be helpful, especially for symptom relief.
- Pancreatic cancer often grows large enough to block a bile duct or the stomach. Small, short tubes called stents may be used to open the blockage. Surgery to bypass the blockage is another option.
- You may have trouble digesting food due to low digestive enzyme levels. Pancreatic enzyme replacement therapy gives you the digestive enzymes you need. A registered dietitian can also help you get enough nutrition.
- People with pancreatic cancer commonly have diabetes. The cause of diabetes varies between people and may affect how diabetes is managed.
- Pancreatic cancer may cause pain when it presses against other organs or spreads to nerves. Pain may be first treated with medication, a nerve block, or both. The next options are ultrasound treatment, palliative radiation, and a pain pump.
- Pancreatic cancer increases the chance of blood clots, which are treated with medicine called anticoagulants. Pancreatic cancer very rarely causes bleeding in the gastrointestinal tract. Bleeding may be stopped by locally applied treatment, radiation, or blocking the blood vessel.
- The library of NCCN Guidelines for Patients includes books on supportive care. These books focus on common

effects of cancer and its treatment, such as distress, nausea and vomiting, poor sleep, and fatigue.

- Advance care planning is done to ensure that your health care wishes are understood and respected.
- An advance directive is a legal document of your wishes that your care team follows if you're too ill to speak for yourself.



share with us.

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

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

4

Clinical trials

- 32 About clinical trials
- 32 Phases of clinical trials
- 32 Enrolling in a trial
- 33 Frequently asked questions
- 33 Key points

Advances in the treatment of pancreatic cancer were made possible by clinical trials. Yet better treatment is still needed. Read this chapter to learn what clinical trials are and how they can help you.

About clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases of clinical trials

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

Phase 1 trials study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.

Phase 2 trials study how well the drug or approach works against a specific type of cancer.

Phase 3 trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.

Phase 4 trials study the long-term safety and benefit of an FDA-approved treatment.

Enrolling in a trial

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment, you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.

Key points

- A clinical trial tests new ways of stopping cancer in people.
- Testing of new drugs or procedures has four phases. After the first 3 phases, the new treatment may become tomorrow's standard of care.
- Not everyone can enroll in a clinical trial. You must meet the criteria for the study.
- The consent form explains all the details of a clinical trial. Take your time to read

the form. Ask questions if you don't understand.

- Advocate for yourself. Ask your care team if there are clinical trials that are a good fit for you.
- Learn the truth about clinical trials. There is a lot of misinformation about them. Ask your care team questions.



Finding a clinical trial

In the United States

NCCN Cancer Centers

[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

The National Cancer Institute (NCI)

[cancer.gov/about-cancer/treatment/clinical-trials/search](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search)

Worldwide

The U.S. National Library of Medicine (NLM)

clinicaltrials.gov

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)

1.800.4.CANCER (1.800.422.6237)

[cancer.gov/contact](https://www.cancer.gov/contact)

5

Treatment with surgery

- 35 Making the decision for surgery
- 38 Stopping cancer growth before surgery
- 41 Pancreatic surgery
- 43 Decisions during surgery
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Surgery is the only current treatment that may cure pancreatic cancer. With advances in medicine, more people with pancreatic cancer are having surgery than in the past. Read this chapter to learn how care teams decide for whom surgery is safe and helpful.

Making the decision for surgery

Surgery may be an option if tests don't find clear signs of distant cancer spread. Distant spread is called metastases or stage 4. If the cancer is not stage 4, your care team will decide if surgery is an option. They will discuss your health history and test results, such as the CA 19-9 tumor marker and imaging. The team will look at two key factors:

- Your physical well-being, which is measured by performance status
- How much contact the cancer has with nearby blood vessels

Performance status

Performance status is your ability to do day-to-day activities. Cancer and other diseases can limit what you can do. Early-stage pancreatic cancer often doesn't affect performance status (stages 1 and 2), but late stages might (stages 3 and 4). If your performance status is limited,



I was diagnosed with pancreatic cancer in 2012.

I asked, 'Why me?' I waited 15 seconds for an answer and then asked, 'What's the plan? When do we start? What's my job?'

I had a Whipple and then we tried a new thing called a liquid biopsy, which pointed my oncologists to a therapy that saved my life.

After 7 years as a survivor, the Canopy Cancer Collective called and asked me to be on their Patient Advisory Council, and we were able to start a virtual peer-to-peer support group for pancreatic cancer patients.

Everything that I experienced brought me to this opportunity to help others. The most common comment I hear is, 'I didn't know anyone survived pancreatic cancer. Now, I'm hopeful. I don't feel alone anymore.' "

some cancer treatments may cause serious health problems.

The Eastern Cooperative Oncology Group (ECOG) Performance Status is a common scoring system. It consists of five scores ranging from 0 to 4. Lower scores represent a better ability to do self-care.

Cancer growth to blood vessels

The goals of surgery are to safely remove all the cancer to prolong life and to improve quality of life. These goals may be reached if the cancer hasn't grown much outside the pancreas. Larger pancreatic cancers are harder or impossible to remove. Most often, local pancreatic cancer can't be removed because of major growth to nearby blood vessels.

In recent years, more local cancers have been treated with surgery due to advances in medicine. Improved imaging shows more clearly where the cancer has grown. Newer surgical approaches can remove cancer that couldn't be removed before. Treatment that shrinks the cancer may make surgery possible.

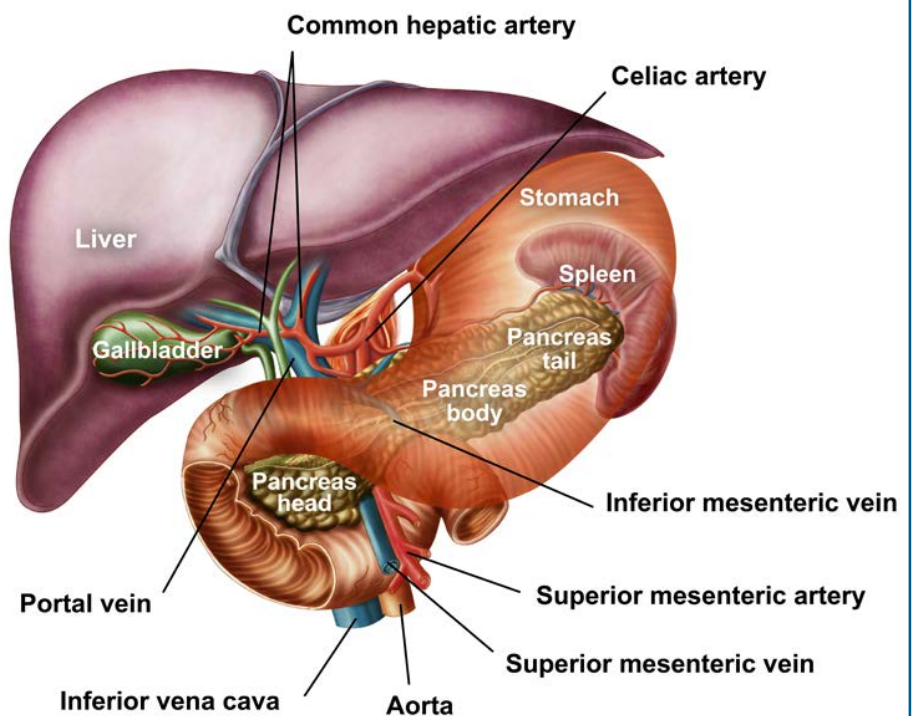
NCCN keeps track of medical advances and updates the criteria for surgery. Currently, surgery is based on how much the cancer has grown to nearby blood vessels and which blood vessels are involved.

Based on this information, pancreatic cancers are divided into three surgery groups:

- **Resectable** means all the cancer can be removed. To improve outcomes, you

Major blood vessels near the pancreas

There are several major blood vessels near the pancreas (shown). Treatment of pancreatic cancer with surgery is based on cancer growth to nearby blood vessels. Arteries carry blood away from the heart, and veins return blood to the heart. Surgery is more often done when the cancer has no contact with blood vessels.



will receive other types of treatment before or after surgery.

- **Borderline resectable** means that it would be hard to safely remove all the cancer, so treatment to shrink the cancer should be received first.
- **Locally advanced** means that the cancer can't be removed or the blood

vessel repaired afterward, though some people have surgery after treatment as described in Chapter 6.

See Guide 4 to learn about the criteria for the three surgery groups.

Guide 4

Criteria for deciding if pancreatic cancer can be treated with surgery

Resectable

A surgeon can remove the cancer because:

- There is no contact with nearby major veins and arteries or
- The cancer has limited contact with the superior mesenteric vein or portal vein that doesn't alter the vessel's shape

Borderline resectable

A surgeon would have a hard time safely removing all the cancer due to limited growth to blood vessels, such as in the following instances:

- Cancer in the head of the pancreas has grown to only the common hepatic artery, wraps less than halfway around the superior mesenteric artery, or has grown to a small artery that branches off a larger artery in an unusual spot
- Cancer in the body or tail of the pancreas wraps less than halfway around the celiac artery
- The cancer has grown to the superior mesenteric vein or portal vein and the vein can be repaired
- The cancer has grown to the inferior vena cava

Locally advanced

A surgeon can't remove the cancer because of major growth to blood vessels:

- The cancer wraps more than halfway around the superior mesenteric artery or celiac artery
- Cancer in the body or tail of the pancreas has grown to the celiac artery or aorta
- The superior mesenteric vein or portal vein cannot be repaired due to cancer growth or blockage of the vein

Stopping cancer growth before surgery

Neoadjuvant therapy is cancer treatment that's given before the main treatment, in this case, surgery. Borderline resectable pancreatic cancer must first be treated with neoadjuvant therapy to reduce its size for surgery. Resectable cancer may first be treated with surgery, but neoadjuvant therapy before

surgery is becoming more common for these cancers.

Chemotherapy is used for neoadjuvant therapy. Chemoradiation after chemotherapy is sometimes part of treatment. **See Guide 5** for neoadjuvant therapy options.

Chemotherapy

Chemotherapy kills fast-growing cells like cancer. It is given as a slow drip or injection

Guide 5 Neoadjuvant therapy of pancreatic cancer

Neoadjuvant therapy may shrink cancer and have other benefits. NCCN recommends that neoadjuvant treatment be received at or managed by a high-volume center. Ask your care team if there is a clinical trial on neoadjuvant therapy that's a good fit for you.

Option 1: FOLFIRINOX with or without chemoradiation

FOLFIRINOX is an intense chemotherapy used to treat people with a performance score of 0 or 1. It may shrink the pancreatic tumor, especially if there is a *BRCA1*, *BRCA2*, or *PALB2* mutation. FOLFIRINOX is a short name for these cancer drugs:

- FOL = leucovorin
- F = fluorouracil (also called 5-FU)
- IRI = irinotecan
- OX = oxaliplatin

The modified FOLFIRINOX regimen may be received. This regimen includes only a slow drip of 5-FU and not the faster injection. Chemoradiation may be received after chemotherapy.

Option 2: Gemcitabine combination with or without chemoradiation

Gemcitabine is used with another chemotherapy for better results. The gemcitabine combination used for most pancreatic cancers is:

- Gemcitabine plus albumin-bound paclitaxel

Since platinum chemotherapy works better for pancreatic cancers with *BRCA1*, *BRCA2*, or *PALB2* mutations, the option for these cancers is:

- Gemcitabine plus cisplatin

Chemoradiation may be received after chemotherapy.

into a vein. It travels in the bloodstream and can treat cancer in many places and in hard-to-reach places. Research on which chemotherapy drugs work best for neoadjuvant therapy is ongoing.

Chemotherapy is given in cycles of treatment days followed by days of rest. The cycles vary in length depending on which drugs are used. Chemotherapy is usually given for up to 6 months.

Ask your medical oncologist how many cycles you will have and how many days of treatment there are within a cycle. Also ask about health problems, called side effects, caused by treatment. Each chemotherapy drug has its own set of side effects.

Chemoradiation

Chemoradiation is treatment with both chemotherapy and radiation therapy. Chemotherapy makes radiation therapy work better. The two preferred chemotherapy drugs are capecitabine and fluorouracil (5-FU). Another option is gemcitabine.

Radiation therapy uses high-energy x-rays to treat pancreatic cancer. The cancer cells either die or can't make more cancer cells. External beam radiation therapy is used to treat pancreatic cancer. A large machine makes radiation beams shaped to the form of the tumor. The machine aims the highest radiation dose at the cancer. Nearby healthy tissue may receive some radiation in the process.

Side effects of radiation therapy are cumulative. This means they build up slowly and are worse at the end of treatment. Common effects are feeling fatigued and skin changes. Often, people describe skin changes as like a sunburn.

Possible benefits of neoadjuvant therapy

There are several promising reasons to have neoadjuvant therapy, but more research is needed. Your care team may recommend neoadjuvant therapy because:

- ✓ More people are able to start and complete chemotherapy or chemoradiation if received before surgery rather than after surgery
- ✓ Metastatic cancer that can't be detected is treated early when treatment might work better
- ✓ Some people are spared the hardship of surgery if the cancer is growing too fast or treatment doesn't work
- ✓ Some cancers shrink enough so that surgery becomes an option
- ✓ The risk of cancer spread during surgery is lower
- ✓ Overall treatment time is shorter
- ✓ The chance of cancer returning after surgery is lower
- ✓ Radiation therapy may work better before blood vessels are altered by surgery
- ✓ Most of the body tissue that is treated with radiation is removed, and new tissue connections from surgery are spared from radiation

Assessing treatment results

After neoadjuvant therapy, you will have some tests that you had before. Tests that will be repeated are:

- Pancreatic protocol computed tomography (CT) or magnetic resonance imaging (MRI)
- CT scan of the chest and pelvis
- CA 19-9 test

The cancer may have grown or spread during treatment. Imaging may show a larger tumor. The CA 19-9 level may be higher. In this case, the cancer may be treated with a different neoadjuvant therapy if surgery still seems possible. If surgery is not an option, read Chapter 6 for options.

If there are no signs of cancer growth, your next treatment will likely be surgery. Surgery should be scheduled no more than 4 weeks after imaging.

A medical oncologist is an expert in chemotherapy. They will prescribe a neoadjuvant regimen and monitor its effects. If your care involves radiation therapy, they will coordinate care with the radiation oncologist, who's an expert in treating cancer with radiation.



To be a survivor of pancreatic cancer means I've been given a very special gift, the precious gift of life, the gift to love more deeply, the gift to inspire someone, to make a difference, to give back, to do better, to be better, to take a leap of faith. "

Pancreatic surgery

Surgery will be scheduled if there's a good chance that all the cancer will be removed. There must be no clear signs of distant metastases. Your surgeon must see a way to remove the tumor with enough normal-looking tissue at its edge, which is called the surgical margin. The goal is to have no cancer cells in the margin, so a cure is likely. Treatment used to cure cancer is called definitive therapy.

Experience is important

Pancreatic surgery is complex. It is a long surgery with multiple steps. Here's a few examples of what happens during surgery:

- Right before surgery, you will be given general anesthesia. These drugs will put you in a sleep-like state, so you won't feel pain. One or more cuts called incisions will be made in your abdomen.
- Organs will be detached from other tissues, so they can be moved. This is called mobilization. Often, the common bile duct and blood vessels are tied off (ligated). Many structures will be divided to remove the tumor.
- After removing the tumor, your surgeon will rebuild cut tissues. This is called reconstruction. New connections between body parts will be made (anastomoses). Sometimes, blood vessels will be repaired with vessels from other areas of the body (grafts).

You want an experienced surgeon to do this complex surgery. Choose a care center that does at least 15 to 20 pancreatic cancer surgeries every year. This is considered a high-volume center.

A surgical oncologist is an expert in performing cancer operations. They remove cancer and connect body tissue together. Choose a surgeon who is very experienced in treating pancreatic cancer.

Types of surgery

The type of surgery you will have depends on where the tumor is in the pancreas.

A tumor in the pancreas head is treated with a pancreaticoduodenectomy (also called a Whipple procedure). This surgery removes these body parts:

- Some of the pancreas, common bile duct, and small intestine
- Gallbladder
- Nearby lymph nodes
- At times, some of the stomach and parts of blood vessels

A classic Whipple procedure removes part of the stomach, but a pylorus-preserving procedure does not.

Reconstruction starts with attaching the pancreas and bile duct to the mid-small intestine called the jejunum. Then either the stomach or duodenum is attached farther down on the jejunum. Blood vessels may need reconstruction.

A tumor in the pancreas body or tail is treated with a distal pancreatectomy and splenectomy. A distal pancreatectomy removes

the body and tail of the pancreas, and a splenectomy removes the entire spleen. The left adrenal gland might also be removed.

A tumor in the pancreas neck may be treated with either a Whipple procedure, distal pancreatectomy, or total pancreatectomy. An extended Whipple procedure and extended distal pancreatectomy remove more tissue than standard surgeries. A total pancreatectomy removes these body parts:

- Pancreas, spleen, and gallbladder
- Some of the stomach, small intestine, and common bile duct

- Nearby lymph nodes
- At times, parts of blood vessels

Reconstruction involves attaching the bile duct and stomach to the jejunum. Blood vessels may need reconstruction.

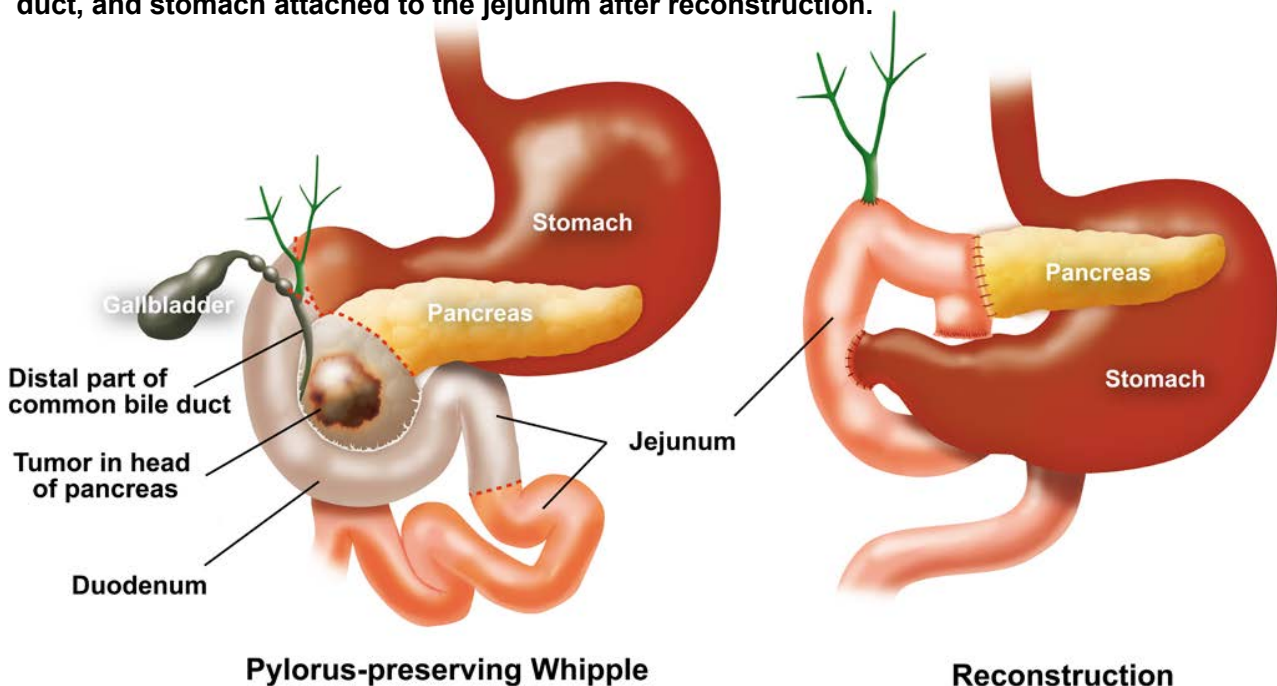
Methods of surgery

Pancreatic surgery is done with one of two methods.

The classic method is called **open surgery** or laparotomy. Your surgeon will remove tissue through one large cut in the middle of your body. The cut starts between the ribs and

Whipple procedure

A Whipple procedure is a type of pancreatic surgery. It is also called a pancreaticoduodenectomy. This surgery removes at least the gallbladder and some of the pancreas, common bile duct, and small intestine (gray-colored parts in left image). The image on the right shows the pancreas, bile duct, and stomach attached to the jejunum after reconstruction.



extends down to the belly button. Through the cut, your surgeon can see and access the pancreatic tumor.

The newer method is called **minimally invasive surgery or laparoscopic surgery**. Your surgeon will use surgical tools inserted through several small cuts made in your abdomen. One of the tools is a laparoscope, which has a small video camera. The video of your inner abdomen will be displayed on a screen.

Your surgeon may perform laparoscopic surgery using robotic arms to control the surgical tools. This is called robot-assisted laparoscopic surgery.

Side effects of surgery

Common side effects of surgery are pain, swelling, and scars. Pain and swelling often fade away in the weeks after surgery. Numbness near the surgical area may be long-lasting. There is a chance of infection. If part of your pancreas remains, it may leak digestive enzymes. An opening between the pancreas and other organs, called fistulas, may develop.

Decisions during surgery

Sometimes pancreatic surgeries are not completed. Your surgeon will explore your inner abdomen to see if the cancer has spread far. Metastatic cancer may not be seen in imaging scans but then will be found during surgery. If metastatic cancer is found, pancreatic surgery should not be done.

Pancreatic surgeries are also not completed if the tumor can't be safely removed. Your surgeon has a better view of the tumor during surgery. They may see that the tumor has grown so much around blood vessels that it can't be removed.

If pancreatic surgery isn't completed, your surgeon may perform other procedures while you're still under anesthesia:

- Celiac plexus neurolysis is an injection of a nerve block into a nerve bundle called the celiac plexus to reduce pain
- Gastrojejunostomy is a surgery that connects the bottom of the stomach to the jejunum so that food doesn't get blocked by the tumor
- A biliary bypass is a surgery that connects the small intestine to the common bile duct above the pancreas to treat jaundice
- Instead of a bypass, placement a small, metal, expandable tube (stent) into the bile duct may be done to treat jaundice

When surgery isn't completed, the cancer will be treated by other methods to try to control its growth. Read Chapter 6 to learn about treatment options.

Killing cancer after surgery

Adjuvant therapy is cancer treatment that follows the main treatment. It kills cancer cells that weren't removed during surgery because they couldn't be seen.

Before adjuvant therapy, two tests are needed. You will have a CT scan with contrast of the chest, pelvis, and abdomen and a CA 19-9 test. These tests check for metastases and serve as a baseline for future tests. If tests

show metastases, read Chapter 6 to learn about treatment options.

Adjuvant therapy can start when you've recovered enough from surgery. It's ideal to start within 12 weeks after surgery. **See Guide 6** for adjuvant therapy options based on whether you had neoadjuvant therapy or did not receive it.

If you did not have neoadjuvant therapy, treatment within a clinical trial is

Guide 6

Adjuvant therapy of pancreatic cancer

Adjuvant therapy treats cancer cells that may be in your body after surgery. It lowers the chance of cancer returning. Treatment options are based on whether you had neoadjuvant therapy.

You did not have neoadjuvant therapy

There are three options:

- Treatment within a clinical trial (preferred option)
- Treatment with a recommended chemotherapy regimen
 - Preferred regimens are modified FOLFIRINOX or gemcitabine plus capecitabine
 - Other regimens that may be used are bolus 5-FU plus leucovorin, continuous infusion 5-FU, gemcitabine, or capecitabine
- Treatment with chemotherapy then chemoradiation then possibly more chemotherapy
 - Gemcitabine, bolus 5-FU plus leucovorin, or continuous infusion 5-FU may be used for chemotherapy
 - Capecitabine (preferred), continuous infusion 5-FU (preferred), or gemcitabine may be used for chemoradiation

You had neoadjuvant therapy

Adjuvant therapy may not be needed if there are no signs of cancer. Your care team will discuss whether more treatment may be helpful.

- Your team may recommend chemotherapy
- If a pathologist finds cancer cells in the removed tissue that surrounds the tumor, your team may recommend chemotherapy followed by chemoradiation if you did not have chemoradiation before

preferred. Clinical trials are explained in Chapter 4. Besides clinical trials, chemotherapy or chemoradiation are options. Some chemotherapy regimens are preferred because the results are better.

If you did have neoadjuvant therapy, your team will decide if more treatment may be helpful. Adjuvant therapy options are based on the results of neoadjuvant therapy and other factors. Your team will take into account that chemotherapy is usually received for up to 6 months.

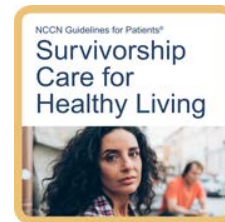
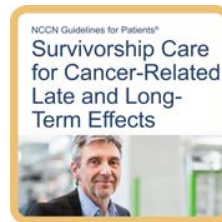
Follow-up care

While pancreatic cancer can sometimes be cured, it is very important to monitor the return of the cancer. The return of cancer is called a recurrence. Routine testing for a recurrence is called surveillance.

You will have the following tests every 3 to 6 months for 2 years, then every 6 to 12 months if needed:

- Medical history and physical exam to assess symptoms
- CA 19-9 level
- CT scan of chest
- CT or MRI scan with contrast of abdomen and pelvis

During health visits, your care team will assess for side effects. They will also help you prevent other diseases. Information about treatment of common side effects and healthy living is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Chemoradiation

Radiation therapy combined with chemotherapy is called chemoradiation. It may be part of neoadjuvant or adjuvant therapy. During radiation therapy, you will lie on a table during treatment (shown), and devices that limit your movement will be used. To spare normal tissue from radiation, intensity-modulated radiation therapy (IMRT) or three-dimensional conformal radiation therapy (3D-CRT) should be used.



When cancer comes back

Follow-up tests may find signs of pancreatic cancer. In this case, your care team may want a biopsy to confirm there is cancer. If not done before, genetic and biomarker tests are needed to help plan treatment.

Treatment of a recurrence is based on where the recurrence is located. **See Guide 7** to learn the treatment options for a recurrence.

Surgery

If cancer is only in the pancreas, surgery may be an option. You will need a surgical consult and a multidisciplinary team review of your test results.

Clinical trial

Enrolling in a clinical trial may be an option. Ask your care team if there is a clinical trial that is a good fit for you. Read Chapter 4 to learn more about clinical trials.

Systemic therapy

Systemic therapy treats cancer wherever it is in the body. Chemotherapy is a type of systemic therapy. Systemic therapy for recurrence is based on these timeframes:

- If you had chemotherapy less than 6 months ago, you'll be switched to a different type of chemotherapy (gemcitabine-based chemotherapy vs. fluoropyrimidine-based chemotherapy)

Guide 7

Treatment options for recurrent pancreatic cancer

The return of cancer after treatment is called a recurrence. Treatment options are based on where the cancer returned.

| | |
|--|--|
| The cancer returned in the pancreas | Surgery may be an option |
| The cancer returned in the body tissue that was next to the removed tissue called the operative bed | <p>There are five options:</p> <ul style="list-style-type: none"> • Treatment within a clinical trial (preferred option) • Systemic therapy (See Guide 12) • Systemic therapy followed by either chemoradiation or stereotactic body radiation therapy (SBRT) • SBRT • Supportive care |
| The cancer returned far from where the pancreatic is or was | <p>There are three options.</p> <ul style="list-style-type: none"> • Receive treatment in a clinical trial (preferred option) • Systemic therapy (See Guide 12) • Supportive care |

- If you had chemotherapy 6 or more months ago, you may repeat the same regimen or start a new systemic therapy

There are many options for systemic therapy. The regimens used for recurrence are the same as those used for second-line therapy listed in Chapter 6.

Radiation therapy

For a recurrence near to where the tumor was, treatment may involve radiation therapy. Stereotactic body radiation therapy (SBRT) treats small tumors with very precise, high-dose x-ray beams and is finished in 5 or fewer sessions. SBRT may be used for treatment without systemic therapy.

If you had systemic therapy, you may have chemoradiation or SBRT afterward. The two preferred regimens are capecitabine and fluorouracil (5-FU). Another option is gemcitabine.

Supportive care

Cancer treatment is too intense for some people. In this case, NCCN experts advise receiving supportive care. Supportive care aims to improve your quality of life. One of its aims is to treat symptoms caused by cancer. Talk with your doctor about supportive care to get the best care plan for you. More information on supportive care is in Chapter 3.

Key points

- Pancreatic cancer may be treated with surgery if there are no clear signs of metastases. Also, it must be very likely that all the cancer can be safely removed.
- Resectable pancreatic cancer can be surgically removed but first may be treated with chemotherapy. Borderline resectable pancreatic cancer first must be treated with chemotherapy to shrink it for surgery. Some people receive chemoradiation after chemotherapy.
- Pancreatic surgery is complex. Choose a care center that does at least 15 to 20 pancreatic cancer surgeries every year.
- There are three main types of pancreatic surgery. A pancreaticoduodenectomy (Whipple) and distal pancreatectomy remove part of the pancreas. A total pancreatectomy removes the entire pancreas. Which surgery you will receive depends on where the cancer is in the pancreas.
- Pancreatic surgery can be performed by one of two methods. During open surgery, body tissue is removed through one large cut. Minimally invasive surgery is performed through several small cuts.
- If your surgeon is unable to remove the tumor, procedures to prevent or relieve symptoms may be done instead.
- After pancreatic surgery, you may receive more treatment to kill any cancer cells that remain in your body. Chemotherapy and chemoradiation are options.
- When cancer treatment is finished, follow-up care is started. Your care team will check for signs of the cancer returning.

You will also receive care for side effects and help to live a healthy life.

- If cancer returns after surgery, treatment will be based on where the cancer is located. Cancer in the pancreas may be treated with surgery. Treatment for cancer outside the pancreas may consist of cancer drugs, radiation therapy, or both. Supportive care can help relieve symptoms of the cancer and its treatment.



They tell me to take a day at a time, dealing with pancreatic cancer, treatments, and side effects. It's more like a moment at a time. Ultimately those moments become days and then weeks. One day, you'll look back and recognize the challenges you've overcome and the milestones you've surpassed. "

6

Treatment without surgery

- 50 Treatment goals
- 51 First-line therapy
- 54 Tests during treatment
- 56 Second-line therapy
- 58 Key points

Systemic therapy treats pancreatic cancer anywhere in the body. It is the main treatment for most pancreatic cancers, and there are many options. Read this chapter to learn which drug regimens are preferred and other options for cancer care.

Treatment goals

Surgery is not an option for most pancreatic cancers. It won't control the growth of the cancer or extend life. It may even be harmful. Surgery can't treat these common pancreatic cancers:

- **Locally advanced cancer** – There is major cancer growth to blood vessels, which can't be safely removed by surgery
- **Metastatic cancer** – The cancer has spread far from the pancreas and is in too many places for it to be removed by surgery

Systemic therapy is the main treatment of locally advanced and metastatic cancer. It treats cancer anywhere it is in the body. The goal of treatment is to control cancer and prolong life. You will also receive supportive care to improve your quality of life.

A medical oncologist is an expert in systemic therapy. They will choose a regimen for you based on your health history and test results. The two of you will meet often, so the effects of treatment can be assessed.



As a patient advocate, I speak with many pancreatic cancer patients and families each week. I share with each one that there are extraordinary responders to this disease. I want everyone to say to themselves, 'Why not me? I too can be one of the extraordinary responders.'

It's important to choose an experienced pancreas medical team within a high-volume medical center for the best outcome. Have a dietician and palliative care doctor on your team as well. Get involved with the pancreatic cancer community so this doesn't feel like a solitary experience. You are not alone!"

First-line therapy

The first treatment given is referred to as first-line therapy. Treatment options are based on your ability to do day-to-day activities. This ability is called performance status. Cancer and other diseases can limit what you can do. If your ability is limited, some treatments may cause serious health problems.

The Eastern Cooperative Oncology Group (ECOG) Performance Status is a common scoring system. It consists of five scores ranging from 0 to 4. Lower scores represent a better ability to do self-care. **See Guide 8** for a list of treatment options based on performance status.

Supportive care

All people with pancreatic cancer should receive supportive care. Supportive care

provides relief from symptoms of cancer and its treatment. It also helps with mental, social, and spiritual issues. Supportive care involves the whole person, not just their cancer. More information on supportive care is in Chapter 3.

Clinical trial

A clinical trial is a type of health research that tests new ways of fighting cancer. Enrolling in a clinical trial may be an option. Ask your care team if there is a clinical trial that's a good fit for you. Clinical trials are discussed in more detail in Chapter 4.

Systemic therapy

Systemic therapy is whole-body treatment with cancer drugs. A regimen consists of one or more drugs that are taken at a specific dose, schedule, and length of time. Preferred

Guide 8

First-line therapy for locally advanced and metastatic pancreatic cancer

Cancer care must be safe. When cancer affects your physical ability, some treatments may not be safe. A high performance status reflects poorer health and a need for a different type of care.

Performance status 0, 1, or 2

Options for both locally advanced and metastatic cancer are:

- Treatment within a clinical trial (preferred option)
- Systemic therapy

There are two more options for locally advanced cancer:

- Systemic therapy (chemotherapy) followed by either chemoradiation or stereotactic body radiation therapy (SBRT)
- Chemoradiation or SBRT

Performance status 3 or 4

There are two options:

- One chemotherapy drug or targeted therapy
- Supportive care including radiation therapy for symptom relief

regimens work better, are safer, or cost less than other options.

Chemotherapy is a classic systemic therapy. It kills fast-growing cells including cancer. Preferred regimens for first-line systemic therapy consist only of chemotherapy. **See Guide 9** for a list of preferred regimens.

All chemotherapy regimens for pancreatic cancer include a drug called an antimetabolite. These drugs include fluorouracil (also called 5-FU), gemcitabine (Gemzar, Infugem), and capecitabine (Xeloda). People with better health may receive more than one antimetabolite or a combination of drug types:

- Antimetabolites plus platinum chemotherapy, such as oxaliplatin (Eloxatin) or cisplatin, which works better for pancreatic cancers with *BRCA1*,

BRCA2, or *PALB2* mutations than taxane chemotherapy

- Antimetabolites plus taxane chemotherapy, such as paclitaxel with human albumin (Abraxane) and docetaxel (Taxotere)
- Antimetabolites plus a targeted therapy called erlotinib

Targeted therapy stops chemical signals that tell pancreatic cancer cells to grow. These drugs are pills that you can take at home. First-line targeted therapies for pancreatic cancer are:

- Erlotinib (Tarceva) stops growth signals from a protein called EGFR
- Larotrectinib (Vitrakvi) and entrectinib (Rozlytrek) stop TRK signals

Guide 9

Preferred regimens for first-line systemic therapy

Preferred regimens for locally advanced and metastatic pancreatic cancer consist of chemotherapy. Treatment options are based on performance status. Regimens with one chemotherapy drug have less serious effects than combined regimens.

| | |
|--------------------------------------|--|
| Performance status 0 or 1 | <p>There are two options for all cancers:</p> <ul style="list-style-type: none"> • First option is FOLFIRINOX or modified FOLFIRINOX, which consists of fluorouracil (5-FU), leucovorin, irinotecan, and oxaliplatin • Second option is a gemcitabine combination with either: <ul style="list-style-type: none"> ▪ Gemcitabine plus albumin-bound paclitaxel or ▪ Gemcitabine plus cisplatin if the cancer has <i>BRCA1</i>, <i>BRCA2</i>, or <i>PALB2</i> mutations |
| Performance status 2 | <ul style="list-style-type: none"> • Capecitabine • Gemcitabine • Gemcitabine with albumin-bound paclitaxel |
| Performance status 3 or 4 | <ul style="list-style-type: none"> • Capecitabine • Gemcitabine • Continuous infusion 5-FU |

- Dabrafenib (Tafinlar) stops BRAF signals
- Trametinib (Mekinist) stops BRAF signals by stopping MEK signals

Your medical oncologist may prescribe larotrectinib, entrectinib, or dabrafenib plus trametinib if the cancer cells have specific biomarkers. Biomarker tests are explained in Chapter 2.

Immunotherapy uses the immune system to kill cancer cells. Some pancreatic cancers stop immune cells called T cells from killing them. Pembrolizumab (Keytruda) restores the killing ability of T cells. It is an option for metastatic pancreatic cancers with specific biomarkers. Pembrolizumab is slowly injected into a vein for up to an hour. **See Guide 10** for a list of immunotherapy, targeted therapy, and other

Guide 10

Other regimens for first-line systemic therapy

Your medical oncologist may not prescribe a preferred regimen. Ask why since there are different reasons for this decision. The regimens listed below have benefits for people with pancreatic cancer. They may extend life, delay cancer growth, or reduce symptoms.

| | |
|---|---|
| <p>Performance status 0 or 1</p> | <p>Options for both locally advanced and metastatic cancer are:</p> <ul style="list-style-type: none"> • Gemcitabine • Gemcitabine plus erlotinib • Gemcitabine plus capecitabine • Capecitabine plus oxaliplatin (CapeOx) • Fluorouracil (5-FU), leucovorin, and oxaliplatin (OFF) • Gemcitabine, albumin-bound paclitaxel, and cisplatin • Fixed-dose-rate gemcitabine, docetaxel, and capecitabine (GTX) • Liposomal irinotecan, 5-FU, leucovorin, and oxaliplatin (NALIRIFOX) • Capecitabine (additional option for locally advanced) • Continuous infusion 5-FU (additional option for locally advanced) • Dabrafenib plus trametinib if <i>BRAF</i> V600E biomarker (additional option for metastatic cancer) • Pembrolizumab (additional option for metastatic cancer) |
| <p>Performance status 2</p> | <ul style="list-style-type: none"> • NALIRIFOX |
| <p>Performance status 3 or 4</p> | <p>Only preferred regimens are recommended for locally advanced cancer, but options for metastatic cancer are:</p> <ul style="list-style-type: none"> • Pembrolizumab (MSI-H, dMMR, or TMB-H biomarker) • Larotrectinib (<i>NTRK</i> biomarker) • Entrectinib (<i>NTRK</i> biomarker) • Dabrafenib plus trametinib (<i>BRAF</i> V600E biomarker) |

chemotherapy regimens used for first-line therapy.

Radiation therapy

Radiation therapy uses high-energy x-rays to kill or damage pancreatic cancer cells. The most common method is called external beam radiation therapy (EBRT). EBRT involves a large machine that makes radiation beams. Modern machines precisely target tumors.

A radiation oncologist is an expert in treating cancer with radiation. They will lead a team that designs your treatment plan and gives radiation therapy.

Locally advanced cancer may be treated with EBRT called **stereotactic body radiation therapy (SBRT)**. SBRT is very precise, delivers high doses each session, and is finished in 5 or fewer sessions. If you undergo chemotherapy, you may have SBRT afterward. If chemotherapy isn't an option for you, SBRT by itself may be used for treatment.

Palliative radiation therapy may be part of supportive care. It can help relieve pain and stop bleeding. It may shrink the tumor so that it is not blocking other body structures.

Chemoradiation

Chemoradiation is treatment with both chemotherapy and radiation therapy. Locally advanced cancer that is treated with chemotherapy for 4 to 6 months may later be treated with chemoradiation.

For chemoradiation, radiation sessions occur on weekdays for about 5 to 6 weeks. During these weeks, you will also receive chemotherapy. Preferred regimens are capecitabine and 5-FU. Another option is gemcitabine.

Tests during treatment

During cancer treatment you will get tests so your care team can assess if treatment is working.

- You will have a series of imaging scans. Imaging may be done with computed tomography (CT) or magnetic resonance imaging (MRI). Contrast is needed. If surgery becomes an option for locally advanced cancer, a pancreatic protocol should be followed as explained in Chapter 2.
- Your care team will also look at other signs of health. A team member will ask if you're having symptoms and check your performance status. A CA 19-9 test will be done.
- If the cancer is locally advanced, you may have a laparoscopy to look for metastases before surgery, chemoradiation, or SBRT.

During first-line therapy, the cancer may have gotten smaller, stayed the same, or grew more. Based on the results of treatment, your care team will provide you with treatment options.

No signs of cancer growth

If locally advanced cancer did not grow during treatment and your performance status is 0, 1, or 2, options are:

- Surgery, if possible, followed by adjuvant therapy (See *Pancreatic surgery* in Chapter 5)
- Continue with chemotherapy
- Ongoing testing to watch for cancer growth
- Clinical trial

If metastatic cancer did not grow during systemic therapy, options are:

- Maintenance therapy listed in **Guide 11**
- Treatment within a clinical trial
- Take a break from therapy (treatment holiday)

Signs of cancer growth

During treatment, the cancer may have continued to grow. Your performance status may have declined. In this case, read the *Second-line therapy* section to learn what your options are.

Guide 11

Maintenance therapy for metastatic pancreatic cancer

The goal of maintenance therapy is to extend the time until the cancer worsens. Treatment options are based on the regimen you had.

If you had FOLFIRINOX

There are 7 options:

- Olaparib for people with inherited *BCRA1* or *BCRA2* mutation (preferred)
- Clinical trial
- Capecitabine
- Fluorouracil (5-FU) and leucovorin
- 5-FU, leucovorin, and irinotecan (FOLFIRI)
- 5-FU, leucovorin, and oxaliplatin (FOLFOX)
- Rucaparib for people with inherited or acquired *BCRA1*, *BCRA2*, or *PALB2* mutation

If you had a regimen with cisplatin or oxaliplatin

There are 3 options:

- Olaparib for people with inherited *BCRA1* or *BCRA2* mutation (preferred)
- Clinical trial
- Rucaparib for people with inherited or acquired *BCRA1*, *BCRA2*, or *PALB2* mutation

If you had gemcitabine and albumin-bound paclitaxel

There are 3 options:

- Clinical trial
- Gemcitabine plus albumin-bound paclitaxel modified schedule
- Gemcitabine

Second-line therapy

Pancreatic cancer may be treated with multiple lines of therapy. Second-line therapy is the second treatment used for cancer care. If more lines of therapy are needed, the options mentioned in this section may be tried.

Care options

If cancer treatment is an option, your care team will suggest a different treatment than used for first-line therapy and continue to provide supportive care.

- Treatment within a clinical trial is preferred. In a clinical trial, you'll receive standard treatment or a new cancer drug.
- In addition to clinical trials, standard systemic therapy is an option.
- Locally advanced cancer may be treated with chemoradiation or SBRT if you haven't had radiation therapy before.

- If cancer treatment would be too harsh on your body, supportive care is recommended. Your care team may prescribe radiation therapy or single-agent chemotherapy to relieve symptoms.

Systemic therapy

There are many options for second-line systemic therapy. Some first-line regimens are also options for second-line therapy, and there are new options, too. **See Guide 12** for a complete list.

Second-line regimens consist of targeted therapy, immunotherapy, or chemotherapy. Biomarker tests are needed to know if you may benefit from targeted therapy or immunotherapy.

Chemotherapy

Chemotherapy for pancreatic cancer is often a liquid that is injected into a vein. Some injections are done in the arm or hand while others are done through an implanted device called a port. An infusion is a slow drip controlled by a pump that may take hours. A continuous infusion may last for days. A bolus and a push are faster injections.



Guide 12

Second-line systemic therapy based on performance status (PS)

| Regimens | PS 0 or 1 | PS 2 | PS 3 or 4 |
|---|-------------|------------------|-----------|
| Options after any type of first-line systemic therapy: | | | |
| Entrectinib (<i>NTRK</i> biomarker) | ● | | ● |
| Larotrectinib (<i>NTRK</i> biomarker) | ● | | ● |
| Pembrolizumab (MSI-H, dMMR, or TMB-H biomarker) | ● | | ● |
| Dostarlimab-gxly (MSI-H or dMMR biomarker) | ● | ● | ● |
| Nivolumab plus ipilimumab (TMB-H biomarker) | ● | ● | |
| Adagrasib (<i>KRAS</i> G12C biomarker) | ● | ● | ● |
| Sotorasib (<i>KRAS</i> G12C biomarker) | ● | ● | ● |
| Dabrafenib plus trametinib (<i>BRAF</i> V600E biomarker) | ● | | ● |
| Selpercatinib (<i>RET</i> biomarker) | ● | | |
| Capecitabine | | | ● |
| Continuous infusion 5-FU | | | ● |
| Gemcitabine standard or prolonged dose | | | ● |
| Options after fluoropyrimidine-based therapy: | | | |
| Fluorouracil (5-FU), leucovorin, and liposomal irinotecan | ● | ● | |
| Gemcitabine plus albumin-bound paclitaxel | ● | ● | |
| Gemcitabine | ● | | |
| Gemcitabine plus cisplatin (<i>BCRA1</i> or <i>BCRA2</i> mutation) | ● | | |
| Gemcitabine and erlotinib | ● | | |
| Gemcitabine, albumin-bound paclitaxel, and cisplatin | ● | | |
| Options after gemcitabine-based therapy: | | | |
| 5-FU, leucovorin, and liposomal irinotecan | ● | ● | |
| Capecitabine | ● | | |
| Capecitabine and oxaliplatin (CapeOx) | ● | | |
| Continuous infusion 5-FU | ● | | |
| 5-FU, leucovorin, and irinotecan (FOLFIRI) | ● | | |
| FOLFIRINOX or modified FOLFIRINOX | ● | | |
| Oxaliplatin, 5-FU, and leucovorin (OFF) | ● | | |
| 5-FU, leucovorin, and oxaliplatin (FOLFOX) | ● | | |
| | ● preferred | ● other regimens | |

Second-line targeted therapies that weren't recommended for first-line therapy are:

- Adagrasib (Krazati) and sotorasib (Lumakras), both of which stop KRAS growth signals
- Selpercatinib (Retevmo), which stops RET signals

Second-line immunotherapies that weren't recommended for first-line therapy are:

- Nivolumab (Opdivo) plus ipilimumab (Yervoy)
- Dostarlimab-gxly (Jemperli)

Chemotherapy is usually switched from one type to another:

- Regimens with fluoropyrimidine (5-FU, capecitabine) are used after regimens with gemcitabine
- Regimens with gemcitabine are used after fluoropyrimidine-based therapy

One exception is the 5-FU, leucovorin, and liposomal irinotecan regimen. This may be an option even if you had 5-FU before, but you must not have already had irinotecan.

Health visits

During second-line therapy, you'll continue to have imaging scans to watch for cancer growth. Your care team will ask about cancer symptoms at health visits. It's also important that they ask how you're feeling. It's common to feel anger, regret, despair, and uncertainty—even all at the same time. Share your feelings with your care team. They can connect you with resources during this challenging time.

Key points

- For most people with pancreatic cancer, surgery is not the best treatment. Whole-body treatment with cancer drugs, called systemic therapy, is most often used to treat advanced and metastatic pancreatic cancer.
- Treatment options are based on your ability to do daily activities called performance status.
- Everyone should have supportive care. It improves quality of life. It can help relieve symptoms as well as help with mental, social, and spiritual issues.
- If cancer treatment is an option, receiving treatment in a clinical trial is preferred.
- If you don't enroll in a clinical trial, the cancer will likely be treated with approved systemic therapy. Options include a range of chemotherapy regimens, and possibly targeted therapy or immunotherapy based on biomarker tests. Chemoradiation or SBRT is a third option if the cancer hasn't spread far.
- If cancer treatment would be too harsh on your body, cancer care will consist of supportive care. You may have systemic therapy or radiation therapy to relieve symptoms.
- Your care team will look for signs of cancer growth during treatment. When cancer grows, your care team will provide you with options.
- Tell your care team about any challenges you are having so they can connect you to helpful resources.

7

Making treatment decisions

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- 60 Questions to ask
- 68 Resources

It is important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

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

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

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

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

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor.

If you take the time to build a relationship with your team, it will help you feel supported when considering options and making treatment decisions.

Second opinion

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

Things you can do to prepare:

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

Support groups

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

Questions to ask

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

Questions about cancer testing

1. What tests will I have?
2. Do the tests have any risks?
3. Do I need to do anything to prepare for testing?
4. Should I bring someone with me to the appointments?
5. Where do I go for testing, and how long will it take?
6. If any of the tests will hurt, what will you do to make me comfortable?
7. How soon will I know the results and who will explain them to me?
8. How can I get a copy of the pathology report and other test results?
9. Is there an online portal with my test results?

Questions about treatment options

1. What are my treatment options?
2. Is a clinical trial an option for me?
3. What will happen if I do nothing?
4. Are you suggesting options other than what NCCN recommends? If yes, why?
5. How do my age, sex, overall health, and other factors affect my options?
6. What if I am pregnant, or planning to become pregnant?
7. Does any option offer a cure or long-term cancer control?
8. What are the side effects of the treatments?
9. How do I get a second opinion?
10. How long do I have to decide about treatment, and is there a social worker or someone who can help me decide?

Questions about what to expect

1. Does this hospital or cancer center offer the best treatment for me?
2. Do I have a choice of when to begin treatment?
3. How long will treatment last?
4. Whom should I contact with questions or concerns if the office is closed?
5. How will you know if treatment is working?
6. What are the chances of the cancer worsening or returning?
7. What follow-up care is needed after treatment?
8. What happens if treatment stops working?

Questions about side effects

1. What are the possible complications and side effects of treatment?
2. Does the cancer itself cause any side effects?
3. Which side effects are most common and how long do they usually last?
4. Which side effects are serious or life-threatening?
5. Are there any long-term or permanent side effects?
6. What symptoms should I report right away, and whom do I contact?
7. What can I do to prevent or relieve the side effects of treatment?
8. Do any medications worsen side effects?
9. Do any side effects lessen or worsen in severity over time?
10. Will you stop or change treatment if there are serious side effects?

Questions about clinical trials

1. Do you recommend that I consider a clinical trial for treatment?
2. How do I find clinical trials in which I can participate?
3. What are the treatments used in the clinical trial?
4. Has the treatment been used for other types of cancer?
5. What are the risks and benefits of this treatment?
6. What side effects should I expect and how will they be managed?
7. How long will I be in the clinical trial?
8. Will I be able to get other treatment if this doesn't work?
9. How will you know if the treatment is working?
10. Will the clinical trial cost me anything?

Questions about your care team’s experience

1. What is your experience as well as your team's experience with treating my type of cancer?
2. How many patients like me (of the same age, gender, race) have you treated?
3. Will you be consulting with experts to discuss my care? Whom will you consult?
4. Is this treatment (or procedure) a major part of your practice? How often have you done this treatment (or procedure) in the last year?
5. How many of your patients have had complications? What were the complications?

Questions about supportive care

1. What supportive care and services are available to me and my caregivers?
2. Are there any programs to help pay for out-of-pocket costs of cancer care?
3. Does this center provide transportation to and from appointments? What about child care during health care appointments?
4. Is there help for basic needs like food and housing?
5. Where can I get legal advice? Is my job legally protected if I take a leave from work?
6. Who can help me cope with stress? Is there a support group that would be a good fit for me?
7. Who can advise me and my family about end-of life concerns?

Resources

Cancer Hope Network

cancerhopenetwork.org

Hirshberg Foundation for Pancreatic Cancer Research

pancreatic.org

Lustgarten Foundation

lustgarten.org

National Cancer Institute (NCI)

cancer.gov/types/pancreatic/patient/pancreatic-treatment-pdq

Triage Cancer

triagecancer.org

U.S. National Library of Medicine Clinical Trials Database

clinicaltrials.gov



Remember having pancreatic cancer does not define you, the way you live your life is who you are. "



share with us.

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

NCCN.org/patients/comments



Words to know

adjuvant therapy

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

advance directive

A legal document of your wishes for health care should you become unable to make these wishes known.

anticoagulant

A drug that slows down the time it takes for blood to clot.

bile duct

A small tube-shaped structure that drains fluid called bile from the liver.

biliary bypass

Surgery that re-routes the flow of bile into the small intestine.

bilirubin

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

biomarker

Any molecule in your body that can be measured to assess your health.

biopsy

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

borderline resectable pancreatic cancer

Pancreatic cancer that has minor involvement with nearby blood vessels.

CA 19-9

A protein made by some types of cancer and found in blood.

cancer stage

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

celiac plexus neurolysis

Injection of a nerve block into a nerve bundle called the celiac plexus.

chemoradiation

Treatment that combines chemotherapy and radiation therapy.

chemotherapy

Treatment with cancer drugs that kill fast-growing cells.

common bile duct

A tiny tube that carries a fluid called bile from the liver into the intestine.

computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the inside of the body.

contrast

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

distal pancreatectomy

Surgery that removes the widest part (body) and narrow end (tail) of the pancreas as well as other nearby organs.

ECOG

Eastern Cooperative Oncology Group

endoscopic retrograde cholangiopancreatography (ERCP)

A procedure that uses x-rays and a medical device that is guided down the throat.

Words to know

endoscopic ultrasound (EUS)

A procedure that takes detailed pictures inside the body with a device guided down the throat.

EPI

exocrine pancreatic insufficiency

EUS-guided biopsy

A procedure to remove a tissue sample using a medical device guided down your throat.

FAMMM

familial atypical multiple mole melanoma syndrome

FDA

Food and Drug Administration

first-line therapy

The first treatment given to treat a disease. Might be followed by second-line or more lines of treatment.

gastroenterologist

A doctor who's an expert in diseases of the digestive system.

gastrojejunostomy

Surgery to bypass a blocked stomach.

GI

gastrointestinal

HBOC

Hereditary breast-ovarian cancer syndrome

hereditary pancreatic cancer

Cancer in a person who had an inherited high risk of getting the cancer.

immunotherapy

A drug treatment that helps the body's immune system find and destroy cancer cells.

IMRT

intensity-modulated radiation therapy

interventional radiologist

A doctor who is an expert in imaging and procedures using scoping tools.

jaundice

Yellowing of the skin and eyes due to a buildup of bilirubin in the body.

jejunostomy tube (J-tube)

A feeding tube that is inserted through the skin into the small intestine.

laparoscopy

A procedure that inserts thin tools through small cuts to do work inside the belly area.

liver function test

A lab test on a blood sample that measures chemicals made or processed by the liver.

locally advanced pancreatic cancer

Pancreatic cancer that has major involvement with nearby blood vessels.

LMWH

Low-molecular-weight heparin

magnetic resonance

cholangiopancreatography (MRCP)

A test that uses radio waves and powerful magnets to make very clear pictures of the pancreas and bile ducts.

magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

medical oncologist

A doctor who is an expert in cancer drugs.

metastasis

The spread of cancer from the place where it started to another part of the body.

neoadjuvant therapy

A treatment that is given before the main treatment to reduce cancer.

Words to know

pancreatic protocol

Methods of imaging that improve pictures of the pancreas.

pancreatoduodenectomy

Surgery to remove the widest part (head) of the pancreas and parts of other nearby organs. Also called Whipple procedure.

pathologist

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

PDAC

pancreatic ductal adenocarcinoma

percutaneous endoscopic gastrostomy (PEG) tube

A feeding tube that is inserted through a cut in the abdomen and into the stomach. Also called gastrostomy tube (G-tube).

performance status

A rating of a person's ability to do daily activities.

positron emission tomography (PET)

A test that uses radioactive material to show the shape and function of tissue.

radiation therapy

The use of high-energy rays to destroy cancer cells.

recurrence

The return of cancer after treatment.

resectable pancreatic cancer

Cancer that can be completely removed with surgery.

stent

A small tube-shaped, expandable device.

stereotactic body radiation therapy (SBRT)

Treatment with high-dose radiation to smaller areas over 1 to 5 sessions.

supportive care

Cancer care given to improve quality of life. Also called palliative care.

surgical margin

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

surveillance

Ongoing testing to watch for cancer growth when not receiving cancer treatment.

3D-CRT

three-dimensional conformal radiation therapy

total pancreatectomy

Surgery to remove the entire pancreas and other nearby organs and tissues.

Whipple procedure

Surgery to remove the head of the pancreas and parts of other nearby organs. Also called pancreaticoduodenectomy.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma, Version 2.2023. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • pennmedicine.org/cancer

**Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute**
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

**Dana-Farber/Brigham and Women's Cancer Center |
Massachusetts General Hospital Cancer Center**
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
800.824.2073 • huntsmancancer.org

**Indiana University Melvin and Bren Simon
Comprehensive Cancer Center**
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

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Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

**Robert H. Lurie Comprehensive Cancer Center
of Northwestern University**
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

**Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine**
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

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

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

**The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute**
Columbus, Ohio
800.293.5066 • cancer.osu.edu

**The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins**
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

NCCN Cancer Centers

UC San Diego Moores Cancer Center

La Jolla, California

858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center

Los Angeles, California

310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family Comprehensive Cancer Center

San Francisco, California

800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center

Aurora, Colorado

720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center

Ann Arbor, Michigan

800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center

Madison, Wisconsin

608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons Comprehensive Cancer Center

Dallas, Texas

214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center

Nashville, Tennessee

877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital

New Haven, Connecticut

855.4.SMILOW • yalecancercenter.org

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BSES MG Hospital (Andheri):

9 am to 10 am (Monday to Friday)

Nanavati Max Hospital (Vile Parle):

10 am to 12 pm (Monday to Saturday)

S. L. Raheja Hospital (Mahim):

12 pm to 4 pm (Monday to Saturday)

Suvarna Hospital (Borivali):

5 pm to 6 pm (Monday and Friday)

Sushrut Hospital (Chembur):

By appointment

Hinduja Hospital (Khar): By

appointment

Galaxy Healthcare (Borivali): By

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