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Treating Pancreatic Cancer

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

How is pancreatic cancer treated?

Depending on the type and stage of the cancer and other factors, treatment options for people with pancreatic cancer can include:

- Surgery for Pancreatic Cancer
- Ablation or Embolization Treatments for Pancreatic Cancer
- Radiation Therapy for Pancreatic Cancer
- Chemotherapy for Pancreatic Cancer
- Targeted Therapy for Pancreatic Cancer
- Immunotherapy for Pancreatic Cancer
- Pain Control for Pancreatic Cancer

Common treatment approaches

Sometimes, the best option for treating pancreatic cancer might include more than one type of treatment.

Treating Pancreatic Cancer, Based on Extent of the Cancer

Who treats pancreatic cancer?

The doctors on your cancer treatment team might include:

- A **surgical oncologist:** a doctor who specializes in treating cancer with surgery
- A radiation oncologist: a doctor who specializes in treating cancer with radiation therapy
- A **medical oncologist:** a doctor who specializes in treating cancer with chemotherapy, immunotherapy, and targeted therapy
- A gastroenterologist: a doctor who specializes in diagnosing and treating diseases of the digestive system.

Many other specialists may be involved in your care as well, including nurse practitioners, nurses, psychologists, social workers, rehabilitation specialists, and other health professionals.

• Health Professionals Associated with Cancer Care

Making treatment decisions

It's important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. Some important things to consider include:

- Your age and expected life span
- Any other serious health conditions you have
- The stage (extent) of your cancer
- Whether or not surgery can remove (resect) the cancer
- The likelihood that treatment will cure the cancer (or help in some other way)
- Your feelings about the possible side effects from treatment

You may feel that you must make a decision quickly, but it's important to give yourself time to absorb the information you have just learned. Ask questions if there is anything you're not sure about.

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

- Questions to Ask About Pancreatic Cancer
- Seeking a Second Opinion

Thinking about taking part in a clinical trial

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

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

Clinical Trials

Considering complementary and alternative methods

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

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

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

Complementary and Integrative Medicine

Help getting through cancer treatment

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

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

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

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

- Palliative Care
- Find Support Programs and Services in Your Area

Choosing to stop treatment or choosing no treatment at all

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

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

• If Cancer Treatments Stop Working

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

Surgery for Pancreatic Cancer

Two general types of surgery can be used for pancreatic cancer:

- **Potentially curative surgery** is used when the results of exams and tests suggest that it's possible to remove (resect) all the cancer.
- Palliative surgery may be done if tests show that the cancer is too widespread to be removed completely. This surgery is done to relieve symptoms or to prevent certain complications like a blocked bile duct or intestine, but the goal is not to cure the cancer.

Staging Iaparoscopy

To determine which type of surgery might be best, it's important to know the stage¹ (extent) of the cancer. But it can be hard to stage pancreatic cancer accurately just using imaging tests². Sometimes laparoscopy is done first to help determine the extent of the cancer and if it can be resected.

For this procedure, the surgeon makes a few small incisions (cuts) in the abdomen (belly) and inserts long, thin instruments. One of these has a small video camera on the end so the surgeon can see inside the abdomen and look at the pancreas and other organs. Biopsy³ samples of tumors and other abnormal areas can show how far the cancer has spread.

Potentially curative surgery

Studies have shown that removing only part of a pancreatic cancer doesn't help patients live longer, so potentially curative surgery is only done if the surgeon thinks all of the cancer can be removed.

This is a very complex surgery and it can be very hard for patients. It can cause complications and might take weeks or months to recover from fully. If you're thinking about having this type of surgery, it's important to weigh the potential benefits and risks carefully.

Fewer than 1 in 5 pancreatic cancers appear to be confined to the pancreas at the time they are found. Even then, not all of these cancers turn out to be truly resectable (able to be completely removed). Sometimes after the surgeon starts the operation it becomes clear that the cancer has grown too far to be completely taken out. If this happens, the operation may be stopped, or the surgeon might continue with a smaller operation with a goal of relieving or preventing symptoms (see "Palliative surgery"

below). This is because the planned operation would be very unlikely to cure the cancer and could still lead to major side effects. It would also lengthen the recovery time, which could delay other treatments.

Surgery offers the only realistic chance to cure pancreatic cancer, but it doesn't always lead to a cure. Even if all visible cancer is removed, often some cancer cells have already spread to other parts of the body. These cells can grow into new tumors over time, which can be hard to treat.

Curative surgery is done mainly to treat cancers in the head of the pancreas. Because these cancers are near the bile duct, they often cause jaundice, which sometimes allows them to be found early enough to be removed completely. Surgeries for other parts of the pancreas are described below, and are done if it's possible to remove all of the cancer.

Whipple procedure (pancreaticoduodenectomy)

This is the most common operation to remove a cancer in the head of the pancreas.

During this operation, the surgeon removes the head of the pancreas and sometimes the body of the pancreas as well. Nearby structures such as part of the small intestine, part of the bile duct, the gallbladder, lymph nodes near the pancreas, and sometimes part of the stomach are also removed. The remaining bile duct and pancreas are then attached to the small intestine so that bile and digestive enzymes can still go into the small intestine. The end pieces of the small intestine (or the stomach and small intestine) are then reattached so that food can pass through the digestive tract (gut).

Most often, this operation is done through a large incision (cut) down the middle of the belly. Some doctors at major cancer centers also do the operation laparoscopically, which is sometimes known as <u>keyhole surgery</u>⁴ (see <u>What's New in Pancreatic Cancer Research?</u>⁵).

A Whipple procedure is a very complex operation that requires a surgeon with a lot of skill and experience. It carries a relatively high risk of complications that can be life threatening. When the operation is done in small hospitals or by doctors with less experience, as many as 15% of patients may die as a result of surgical complications. In contrast, when the operation is done in cancer centers by surgeons experienced in the procedure, fewer than 5% of patients die as a direct result of surgery.

To have the best outcome, it's important to be treated by a surgeon who does many of these operations and to have the surgery at a hospital where many of them are done. In general, people having this type of surgery do better when it's done at a hospital that does at least 15 to 20 Whipple procedures per year.

Still, even under the best circumstances, many patients have complications from the surgery. These can include:

- Leaking from the various connections between organs that the surgeon has to join
- Infections
- Bleeding
- Trouble with the stomach emptying after eating
- Trouble digesting some foods (which might require taking some pills to help with digestion)
- Weight loss
- Changes in bowel habits
- Diabetes

Distal pancreatectomy

In this operation, the surgeon removes only the tail of the pancreas or the tail and a portion of the body of the pancreas. The spleen is usually removed as well. The spleen helps the body fight infections, so if it's removed you'll be at increased risk of infection with certain bacteria. To help with this, doctors recommend that patients get certain vaccines before this surgery.

This surgery is used to treat cancers found in the tail and body of the pancreas. Unfortunately, many of these tumors have usually already spread by the time they are found and surgery is not always an option.

Total pancreatectomy

This operation removes the entire pancreas, as well as the gallbladder, part of the stomach and small intestine, and the spleen. This surgery might be an option if the cancer has spread throughout the pancreas but can still be removed. But this type of surgery is used less often than the other operations because there doesn't seem to be a major advantage in removing the whole pancreas, and it can have major side effects.

It's possible to live without a pancreas. But when the entire pancreas is removed, people are left without the cells that make insulin and other hormones that help maintain safe blood sugar levels. These people develop diabetes, which can be hard to manage because they are totally dependent on insulin shots. People who have had this surgery

also need to take pancreatic enzyme pills to help them digest certain foods.

Before you have this operation, your doctor will recommend that you get certain vaccines because the spleen will be removed.

Palliative surgery

If the cancer has spread too far to be removed completely, any surgery being considered would be palliative (intended to relieve symptoms). Because pancreatic cancer can spread quickly, most doctors don't advise major surgery for palliation, especially for people who are in poor health.

Sometimes surgery might be started with the hope it will cure the patient, but once it begins the surgeon discovers this is not possible. In this case, the surgeon might do a less extensive, palliative operation known as *bypass surgery* to help relieve symptoms.

Cancers growing in the head of the pancreas can block the common bile duct as it passes through this part of the pancreas. This can cause pain and digestive problems because bile can't get into the intestine. The bile chemicals will also build up in the body, which can cause jaundice, nausea, vomiting, and other problems. There are two main options to relieve bile duct blockage in this situation:

Stent placement

The most common approach to relieving a blocked bile duct does not involve actual surgery. Instead, a stent (small tube, usually made of metal) is put inside the duct to keep it open. This is usually done through an endoscope (a long, flexible tube) while you are sedated. Often this is part of an endoscopic retrograde cholangiopancreatography (ERCP)⁶. The doctor passes the endoscope down the throat and all the way into the small intestine. Through the endoscope, the doctor can then put the stent into the bile duct. The stent can also be put in place through the skin during a percutaneous transhepatic cholangiography (PTC). (See Tests for Pancreatic Cancer⁷.)

The stent helps keep the bile duct open even if the surrounding cancer presses on it. But after several months, the stent may become clogged and may need to be cleared or replaced. Larger stents can also be used to keep parts of the small intestine open if they are in danger of being blocked by the cancer.

A bile duct stent can also be put in to help relieve jaundice before curative surgery is done (which would typically be a couple of weeks later). This can help lower the risk of complications from surgery.

Bypass surgery

In people who are healthy enough, another option for relieving a blocked bile duct is surgery to reroute the flow of bile from the common bile duct directly into the small intestine, bypassing the pancreas. This typically requires a large incision (cut) in the abdomen, and it can take weeks to recover from this. Sometimes surgery can be done through several small cuts in the abdomen using special long surgical tools. (This is known as <u>laparoscopic or keyhole surgery</u>⁸.)

Having a stent placed is often easier and the recovery is much shorter, which is why this is done more often than bypass surgery. But surgery can have some advantages, such as:

- It can often give longer-lasting relief than a stent, which might need to be cleaned out or replaced.
- It might be an option if a stent can't be placed for some reason.
- During surgery, the surgeon may be able to cut some of the nerves around the pancreas or inject them with alcohol. Because pancreatic cancer often causes pain if it reaches these nerves, this procedure may reduce or get rid of any pain caused by the cancer.

Sometimes, the end of the stomach is disconnected from the duodenum (the first part of the small intestine) and attached farther down the small intestine during this surgery as well. This is known as a *gastric bypass*. This is done because over time the cancer might grow large enough to block the duodenum, which can cause pain and vomiting and often requires urgent surgery. Bypassing the duodenum before this happens can sometimes help avoid this.

Bypass surgery can still be a major operation, so it's important that you are healthy enough to tolerate it and that you talk with your doctor about the possible benefits and risks before you have the surgery.

More information about Surgery

For more general information about surgery as a treatment for cancer, see <u>Cancer</u> <u>Surgery</u>⁹.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>¹⁰.

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Hyperlinks

- 1. www.cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging/staging.html
- 2. <u>www.cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 3. www.cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging/how-diagnosed.html
- 4. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/endoscopy/laparoscopy.html</u>
- 5. www.cancer.org/cancer/pancreatic-cancer/about/new-research.html
- 6. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/endoscopy/upper-endoscopy.html</u>
- 7. <u>www.cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 8. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/endoscopy/laparoscopy.html</u>
- 9. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/surgery.html</u>
- 10. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Ablation or Embolization Treatments for Pancreatic Cancer

Ablation and embolization treatments are different ways of destroying tumors, rather than removing them with surgery. They are used much less often for pancreatic cancers but can sometimes be used to help treat pancreatic cancer that has spread to other organs, especially the liver.

These treatments are very unlikely to cure cancers on their own. They are more likely to be used to help prevent or relieve symptoms, when there are only a few areas of spread, and are often used along with other types of treatment.

Ablative treatments

Ablation refers to treatments that destroy tumors, usually with extreme heat or cold. They are generally best for tumors no more than about 2 cm (a little less than an inch) across. Typically, with this type of treatment you will not need to stay in the hospital. There are different kinds of ablative treatments:

Radiofrequency ablation (RFA) uses high-energy radio waves for treatment. A thin, needle-like probe is put through the skin and into the tumor. Placement of the probe is guided by ultrasound or CT scans. The tip of the probe releases a high-frequency electric current which heats the tumor and destroys the cancer cells.

Microwave thermotherapy is similar to RFA, except it uses microwaves to heat and destroy the cancer cells.

Ethanol (alcohol) ablation (also known as *percutaneous ethanol injection*) kills the cancer cells by injecting concentrated alcohol directly into the tumor. This is usually done through the skin using a needle guided by ultrasound or CT scans.

Cryosurgery (also known as cryotherapy or cryoablation) destroys a tumor by freezing it with a thin metal probe. The probe is guided through the skin and into the tumor, using ultrasound. Then very cold gasses are passed through the probe to freeze the tumor, killing the cancer cells. This method may be used to treat larger tumors than the other ablation techniques, but it sometimes requires general anesthesia (where you are put into a deep sleep).

Side effects of ablation treatments

Possible <u>side effects</u>¹ after ablation therapy include abdominal pain, infection, and bleeding inside the body. Serious complications are uncommon, but they are possible.

Embolization

During embolization, substances are injected into an artery to try to block the blood flow to cancer cells, causing them to die. This may be used for larger tumors (up to about 5 cm or 2 inches across) in the liver.

There are 3 main types of embolization:

Arterial embolization (also known as *trans-arterial embolization* or *TAE*) involves putting a catheter (a thin, flexible tube) into an artery through a small cut in the inner thigh and threaded up into the hepatic artery feeding the tumor. Blood flow is blocked (or reduced) by injecting materials that plug up that artery. Most of the healthy liver cells will not be affected because they get their blood supply from a different blood vessel, the portal vein.

Chemoembolization (also known as *trans-arterial chemoembolization* or *TACE*) combines embolization with chemotherapy. Most often, this is done by using tiny beads that give off a chemotherapy drug during the embolization. TACE can also be done by giving chemotherapy through the catheter directly into the artery, then plugging up the artery.

Radioembolization combines embolization with radiation therapy. In the United States, this is done by injecting small radioactive beads (called *microspheres*) into the hepatic artery. The beads lodge in the blood vessels near the tumor, where they give off small amounts of radiation to the tumor site. Since the radiation travels a very short distance, its effects are limited mainly to the tumor.

Side effects of embolization

Possible <u>side effects</u>² after embolization include abdominal pain, fever, nausea, infection, and blood clots in nearby blood vessels. Serious complications are not common, but they can happen.

Hyperlinks

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

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Radiation Therapy for Pancreatic Cancer

Radiation therapy uses high-energy x-rays (or particles) to kill cancer cells. It can be helpful in treating some pancreatic cancers.

When might radiation therapy be used?

Radiation might be given after surgery (known as adjuvant treatment) to try to lower

the chance of the cancer coming back. The radiation is typically given along with chemotherapy, which is together known as *chemoradiation* or *chemoradiotherapy*.

- For borderline resectable tumors, radiation might be given along with chemotherapy before surgery (*neoadjuvant* treatment) to try to shrink the tumor and make it easier to remove completely.
- Radiation therapy combined with chemotherapy may be used as part of the main treatment in people whose cancers have grown beyond the pancreas and can't be removed by surgery (locally advanced/unresectable cancers).
- Radiation is sometimes used to help relieve symptoms (such as pain) in people
 with advanced cancers or in people who aren't healthy enough for other treatments
 like surgery.

How is radiation therapy given?

The type of radiation most often used to treat pancreatic cancer (known as <u>external</u> <u>beam radiation therapy</u>¹) focuses radiation from a source outside of the body on the cancer.

Getting radiation therapy is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer. Most often, radiation treatments are given 5 days a week for several weeks.

Possible side effects

Some of the more common side effects of radiation therapy include:

- Skin changes in areas getting radiation, ranging from redness to blistering and peeling
- Nausea and vomiting
- Diarrhea
- Fatigue
- · Loss of appetite
- Weight loss

Radiation can also lower blood counts, which can increase the risk of serious infection.

Usually these effects go away within a few weeks after the treatment is complete. Ask your doctor what side effects to expect and how to prevent or relieve them.

More information about radiation therapy

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

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

Hyperlinks

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

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Chemotherapy for Pancreatic Cancer

Chemotherapy (chemo) is an anti-cancer drug injected into a vein or taken by mouth. These drugs enter the bloodstream and reach almost all areas of the body, making this treatment potentially useful for cancers whether or not they have spread.

When might chemotherapy be used?

Chemo is often part of the treatment for pancreatic cancer and may be used at any stage:

- Before surgery (neoadjuvant chemotherapy): Chemo can be given before surgery (sometimes along with radiation) to try to shrink the tumor so it can be removed with less extensive surgery. Neoadjuvant chemo is often used to treat cancers that are too big to be removed by surgery at the time of diagnosis (called locally advanced cancers).
- After surgery (adjuvant chemotherapy): Chemo can be used after surgery (sometimes along with radiation) to try to kill any cancer cells that have been left behind or have spread but can't be seen, even on imaging tests. If these cells were allowed to grow, they could form new tumors in other places in the body. This type of treatment might lower the chance that the cancer will come back later.
- For advanced pancreatic cancer: Chemo can be used when the cancer is advanced and can't be removed completely with surgery, or if surgery isn't an option, or if the cancer has spread to other organs.

When chemo is given along with radiation, it is known as *chemoradiation*. It helps the radiation work better, but can also have more side effects.

Which chemo drugs are used for pancreatic cancer?

In most cases (especially as adjuvant or neoadjuvant treatment), chemo is most effective when combinations of drugs are used. For people who are healthy enough, 2 or more drugs are usually given together. For people who are not healthy enough for combined treatments, a single drug (usually gemcitabine, 5-FU, or capecitabine) can be used.

The most common drugs used for both adjuvant and neoadjuvant chemo include:

- Gemcitabine (Gemzar)
- 5-fluorouracil (5-FU)
- Oxaliplatin (Eloxatin)
- Albumin-bound paclitaxel (Abraxane)
- Capecitabine (Xeloda)
- Cisplatin
- Irinotecan (Camptosar)

Chemotherapy for advanced pancreatic cancer

- Gemcitabine (Gemzar)
- 5-fluorouracil (5-FU) or Capecitabine (Xeloda) (an oral 5FU drug)
- Irinotecan (Camptosar) or Liposomal Irinotecan (Onivyde)
- Platinum agents: Cisplatin and Oxaliplatin (Eloxatin)
- Taxanes: Paclitaxel (Taxol), Docetaxel (Taxotere), and Albumin-bound paclitaxel (Abraxane)

How is chemotherapy given?

Chemo drugs for pancreatic cancer can be given into a vein (IV) or by mouth as a pill. The infusion can be done in a doctor's office, chemotherapy clinic, or in a hospital setting.

Often, a slightly larger and sturdier IV is required in the vein system to give chemo. They are known as <u>central venous catheters</u>¹ (CVCs), central venous access devices (CVADs), or central lines. They are used to put medicines, blood products, nutrients, or fluids right into your blood. They can also be used to take out blood for testing.

Doctors give chemo in cycles, with each period of treatment followed by a rest period to give you time to recover from the effects of the drugs. Cycles are most often 2 or 3 weeks long. The schedule varies depending on the drugs used. For example, with some drugs, the chemo is given only on the first day of the cycle. With others, it is given for a few days in a row, or once a week. Then, at the end of the cycle, the chemo schedule repeats to start the next cycle.

Adjuvant and neoadjuvant chemo is often given for a total of 3 to 6 months, depending on the drugs used. The length of treatment for advanced pancreatic cancer is based on how well it is working and what side effects you may have.

Possible side effects

Chemo drugs can cause side effects. These depend on the type and dose of drugs given and how long treatment lasts. Common possible side effects include:

- Nausea and vomiting
- Loss of appetite
- Hair loss
- Mouth sores
- Diarrhea or constipation

Chemo can also affect the blood-forming cells of the bone marrow, which can lead to:

- Increased chance of infection (from low white blood cells)
- Bleeding or bruising (from low platelet counts)
- Fatigue or shortness of breath (from low red blood cells)

These side effects usually go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting.

Some chemo drugs can cause other side effects. For example:

 Drugs such as cisplatin, oxaliplatin, and paclitaxel can damage nerves, which can lead to symptoms of numbness, tingling, or even pain in the hands and feet (called peripheral neuropathy). For a day or so after treatment, oxaliplatin can cause nerve pain that gets worse with exposure to cold, including when swallowing cold foods or liquids.

- Cisplatin can damage the kidneys. Doctors try to prevent this by giving the patient lots of intravenous (IV) fluid before and after the drug is given.
- Cisplatin can affect hearing. Your doctor may ask if you have any ringing in the ears or hearing loss during treatment.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see Chemotherapy².

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

Hyperlinks

- 1. <u>www.cancer.org/treatment/treatments-and-side-effects/planning-managing/tubes-lines-ports-catheters.html</u>
- 2. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy.html</u>
- 3. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Targeted Therapy for Pancreatic Cancer

As researchers have learned more about the changes in pancreatic cancer cells that help them grow, they have developed newer drugs to specifically target these changes. These targeted drugs work differently from standard chemo drugs. Sometimes they work when standard chemo drugs don't, and they often have different side effects. (See What's New in Pancreatic Cancer Research?¹ for more information.)

EGFR inhibitor

Erlotinib (Tarceva) is a drug that targets a protein on cancer cells called *EGFR*, which normally helps the cells grow. In people with advanced pancreatic cancer, this drug can be given along with the chemo drug gemcitabine. Some people may benefit more from this combination than others.

This drug is taken as a pill, once a day.

Common **side effects** of erlotinib include an acne-like rash on the face and neck, diarrhea, loss of appetite, and feeling tired. Less common but more serious side effects can include serious lung, liver, or kidney damage; holes (perforations) forming in the stomach or intestines; serious skin conditions; and bleeding or blood clotting problems.

PARP inhibitor

In a small number of pancreatic cancers, the cells have changes in one of the *BRCA* genes (*BRCA1* or *BRCA2*). Changes in one of these genes can sometimes lead to cancer.

Olaparib (Lynparza) is a type of drug known as a *PARP inhibitor*. PARP enzymes are normally involved in a pathway that helps repair damaged DNA inside cells. The *BRCA* genes are normally involved in a different pathway of DNA repair, and mutations in one of these genes can block that pathway. By blocking the PARP pathway as well, this drug makes it very hard for tumor cells with a mutated *BRCA* gene to repair damaged DNA, which often leads to their death.

Olaparib can be used to treat advanced pancreatic cancer in people with a known or suspected *BRCA* gene mutation, whose cancer has not gotten worse after at least 4 months of chemo that included a platinum drug (such as oxaliplatin or cisplatin).

This drug has been shown to help shrink or slow the growth of some advanced pancreatic cancers, although so far it's not clear if it can help people live longer.

This drug is taken by mouth as pills, typically twice a day.

Side effects of this drug can include nausea, vomiting, diarrhea or constipation, fatigue, feeling dizzy, loss of appetite, taste changes, low red blood cell counts (anemia), low white blood cell counts (with an increased risk of infection), belly pain, and muscle and joint pain. Less common but more serious side effects can include inflammation in the lungs and the development of certain blood cancers, such as myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML).

NTRK inhibitors

A small number of pancreatic cancers have changes in one of the *NTRK* genes. These gene changes can sometimes lead to abnormal cell growth and cancer.

Larotrectinib (Vitrakvi) and **entrectinib (Rozlytrek)** target the proteins made by the *NTRK* genes. These drugs can be used in people with advanced pancreatic cancer that has been found to have an *NTRK* gene change, typically when the cancer is still growing despite other treatments.

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

Common **side effects** of these drugs can include dizziness, fatigue, nausea, vomiting, constipation, weight gain, and diarrhea. Less common but more serious side effects can include abnormal liver tests, heart problems, and confusion.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Cancer</u> <u>Therapy</u>².

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>³.

Hyperlinks

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

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Immunotherapy for Pancreatic Cancer

Immunotherapy is the use of medicines to stimulate a person's own immune system to

recognize and destroy cancer cells more effectively. Certain types of immunotherapy can be used to treat pancreatic cancer.

Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking the body's normal cells. To do this, it uses "checkpoint" proteins on immune cells, which act like switches that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to keep the immune system from attacking them. But drugs that target these checkpoints hold a lot of promise as cancer treatments.

Drugs called **checkpoint inhibitors** can be used for people whose pancreatic cancer cells have tested positive for specific gene changes, such as a high level of *microsatellite instability (MSI-H)*, or changes in one of the *mismatch repair (MMR)* genes. Changes in MSI or in MMR genes (or both) are often seen in people with <u>Lynch syndrome</u>¹.

The drugs are used for people whose cancer starts growing again after chemotherapy. They might also be used to treat people whose cancer can't be removed with surgery, has come back (recurred) after treatment, or has spread to other parts of the body (metastasized).

PD-1 inhibitor

Pembrolizumab (Keytruda) is a drug that targets PD-1, a checkpoint protein on immune system cells called *T cells*, that normally helps keep these cells from attacking normal cells in the body. By blocking PD-1, this drug boosts the immune response against pancreatic cancer cells and can often shrink tumors.

This drug is given as an intravenous (IV) infusion every 2 or 3 weeks.

Side effects can include fatigue, cough, nausea, itching, skin rash, decreased appetite, constipation, joint pain, and diarrhea.

Other, more serious side effects occur less often. This drug works by basically removing the brakes from the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your health care team promptly. If serious side effects do occur, treatment may need to be stopped and you may get high doses of corticosteroids to suppress your immune system.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see <u>Cancer Immunotherapy</u>².

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>³.

Hyperlinks

- 1. <u>www.cancer.org/cancer/cancer-causes/genetics/family-cancer-syndromes.html</u>
- 2. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html</u>
- 3. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Pain Control for Pancreatic Cancer

Pain can be a major problem for people with pancreatic cancer. These cancers can

invade and press on nerves near the pancreas, which can cause pain in the abdomen (belly) or back.

Treatment is available to help relieve this pain. If you are having any pain, please be sure to tell your doctor or nurse. Pain is easier to control if the treatment is started when you first have it. You and your doctor or nurse can talk about the best ways to treat your pain. A pain specialist can also help develop a treatment plan.

Some proven ways to relieve pain from pancreatic cancer include:

Pain medicines

For most patients, morphine or similar drugs (opioids) can help control the pain. Many people are worried about these drugs because they fear becoming addicted, but studies have shown that the risk of this is low if the patient takes the drug for pain as directed by the doctor.

Pain medicines work best when they are taken on a regular schedule. They do not work as well if they are only used when the pain becomes severe. Several long-acting forms of morphine and other opioids are in pill form and only need be taken once or twice a day. There is even a long-acting form of the drug fentanyl that is applied as a patch every 3 days.

Common side effects of these drugs are nausea and feeling sleepy, which often get better over time. Constipation is a common side effect that does not get better on its own, so it needs to be treated. Most people need to take stool softeners and/or laxatives daily.

Other treatments

Sometimes certain procedures might be needed to treat pain. For example, cutting or injecting alcohol into some of the nerves (that carry pain sensations) near the pancreas can often improve pain and may allow you to use lower doses of pain medicines. If you are having surgery for some reason (such as to remove the cancer or relieve bile duct blockage), this can usually be done as part of the same operation.

This can also be done as a separate procedure. The doctor might do a nerve block by injecting the nerves near the pancreas with either an anesthetic or a medicine that destroys the nerves.

This can be done with the help of an ultrasound or CT scan either by:

- passing a needle through the skin or
- by using an endoscope¹ (a long, flexible tube that is passed down the throat and past the stomach) that guides a needle to the nerves.

Treating the cancer with chemotherapy and/or radiation therapy can also sometimes relieve pain by shrinking the size of the cancer.

For more information on pain and what can be done about it, see Cancer Pain².

Hyperlinks

- 1. <u>www.cancer.org/treatment/understanding-your-diagnosis/tests/endoscopy/upper-endoscopy.html</u>
- 2. <u>www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/pain.html</u>

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Treating Pancreatic Cancer, Based on Extent of the Cancer

This information is about treating exocrine pancreatic cancer, the most common type of pancreatic cancer. See <u>Pancreatic Neuroendocrine Tumor (NET)</u>¹ for information about how that type is typically treated.

Most of the time, pancreatic cancer is treated based on its <u>stage</u>² – how far it has spread in the body. But other factors, such as your overall health, can also affect treatment options. Talk to your doctor if you have any questions about the treatment plan they recommend.

It can be hard to stage pancreatic cancer accurately using <u>imaging tests</u>³. Doctors do their best to figure out before treatment if there is a good chance the cancer is resectable – that is, if it can be removed completely. But sometimes cancers turn out to have spread farther than was first thought.

Treating resectable cancer

Surgeons usually consider pancreatic cancer to be resectableif it looks like it is still just in the pancreas or doesn't extend far beyond the pancreas, and has not grown into nearby large blood vessels. A person must also be healthy enough to withstand surgery to remove the cancer, which is a major operation.

If imaging tests show a reasonable chance of removing the cancer completely, surgery is the preferred treatment if possible, as it offers the only realistic chance for cure. Based on where the cancer started, usually either a Whipple procedure (pancreaticoduodenectomy) or a distal pancreatectomy is used.

Sometimes even when a cancer is thought to be resectable, it becomes clear during the surgery that not all of it can be removed. If this happens, continuing the operation might do more harm than good. The surgery might be stopped, or the surgeon might continue with a smaller operation with a goal of relieving or preventing problems such as bile duct blockage.

Adjuvant treatment (treatment after surgery)

Even when the surgeon thinks all of the cancer has been removed, the cancer might still come back. Giving chemotherapy (chemo), either alone or with radiation therapy

(chemoradiation), *after* surgery (known as **adjuvant treatment**) might help some patients live longer. The chemo drugs most often used are gemcitabine (Gemzar) or 5-FU.

Neoadjuvant treatment (treatment before surgery)

Sometimes, if the tumor is thought to be resectable but is very large, has many nearby large lymph nodes, or is causing significant pain, chemotherapy or chemoradiation may be given *before* surgery to shrink the tumor (known as **neoadjuvant treatment)**. This may make it easier to remove all the cancer at the time of surgery. Additional chemo may still be recommended after surgery.

Treating borderline resectable cancer

A small number of pancreatic cancers have reached nearby blood vessels but have not grown deeply into them or surrounded them. These cancers might still be removable by surgery, but the odds of removing all of the cancer are lower, so they are considered borderline resectable.

These cancers are often treated first with neoadjuvant chemotherapy (sometimes along with radiation therapy) to try to shrink the cancer and make it easier to remove. Imaging tests⁴ (and sometimes laparoscopy) are then done to make sure the cancer hasn't grown too much to be removed. As long as it hasn't, surgery is then done to remove it. This might be followed by more chemotherapy.

Another option might be to have surgery first, followed by adjuvant chemotherapy (and possibly radiation). If, during the surgery, it becomes clear that not all of the cancer can be removed, continuing the operation might do more harm than good. The surgery might be stopped, or the surgeon might continue with a smaller operation with a goal of relieving or preventing problems such as bile duct blockage.

Treating locally advanced (unresectable) cancer

Locally advanced cancers have grown too far into nearby blood vessels or other tissues to be removed completely by surgery, but have not spread to the liver or distant organs and tissues. Surgery to try to remove these cancers does not help people live longer. Therefore, if surgery is done, it is to relieve bile duct blockage or to bypass a blocked intestine caused by the cancer pressing on other organs.

Chemotherapy, sometimes followed by chemoradiation, is the standard treatment option

for locally advanced cancers. This may help some people live longer even if the cancer doesn't shrink. Giving chemo and radiation therapy together may work better to shrink the cancer, but this combination has more side effects and can be harder on patients than either treatment alone. Sometimes, targeted therapy may be added to chemotherapy before chemoradiation is given.

Other times, immunotherapy given alone may also be an option.

Surgery might be done after chemo or chemoradiation, if imaging shows the cancer has become smaller and can be removed completely by surgery.

Treating metastatic (widespread) cancer

Pancreatic cancers often first spread within the abdomen (belly) and to the liver. They can also spread to the lungs, bone, brain, and other organs.

These cancers have spread too much to be removed by surgery. Even when imaging tests show that the spread is only to one other part of the body, it is often assumed that small groups of cancer cells (too small to be seen on imaging tests) have already reached other organs of the body.

Chemotherapy is typically the main treatment for these cancers. It can sometimes shrink or slow the growth of these cancers for a time and might help people live longer, but it is not expected to cure the cancer.

Gemcitabine is one of the drugs used most often. It can be used alone (especially for people in poor health), or it can be combined with other drugs like albumin-bound paclitaxel (Abraxane), capecitabine (Xeloda), or the targeted drug erlotinib (Tarceva).

Another option, especially for people who are otherwise in good health, is a combination of chemo drugs called FOLFIRINOX. This consists of 4 drugs: 5-FU, leucovorin, irinotecan (Camptosar), and oxaliplatin (Eloxatin). This treatment might help people live longer than getting gemcitabine alone, but it can also have more severe side effects.

In certain cases, immunotherapy or targeted therapy may be options for people whose cancer cells have certain gene changes.

Other treatments might also be used to help prevent or relieve symptoms from these cancers. For example, radiation therapy or some type of nerve block might be used to help relieve cancer pain, or a stent might be placed during an endoscopy to help keep the bile duct open.

Because the treatments now available don't work well for many people, you may want to think about taking part in a clinical trial⁵ of new drugs or combinations of drugs.

Treating pancreatic cancer that progresses or recurs

If cancer continues to grow during treatment (progresses) or comes back (recurs), your treatment options will depend on:

- Where and how much the cancer has spread
- · What treatments you have already had
- Your health and desire for more treatment

It's important that you understand the goal of any further treatment, as well as the likelihood of benefits and risks.

When pancreatic cancer recurs, it most often shows up first in the liver, but it may also spread to the lungs, bone, or other organs. This is usually treated with chemotherapy if you are healthy enough to get it. If you have had chemo before and it kept the cancer away for some time, the same chemo might be helpful again. Otherwise, different chemo drugs might be tried, sometimes along with targeted therapy. Immunotherapy may also be helpful in some cases of recurrent pancreatic cancer. Other treatments such as radiation therapy or stent placement might be used to help prevent or relieve symptoms from the cancer.

If the cancer progresses while you are getting chemotherapy, another type of chemotherapy might be tried if you are healthy enough.

At some point, it might become clear that standard treatments are no longer controlling the cancer. If you want to continue getting treatment, you might think about taking part in a <u>clinical trial</u>⁶ of a newer pancreatic cancer treatment. While these are not always the best option for every person, they may benefit you, as well as future patients.

Treating cancer of the ampulla of Vater

The ampulla of Vater is the area where the pancreatic duct and the common bile duct empty into the duodenum (the first part of the small intestine). Cancer at this site (known as *ampullary cancer*) can start in the pancreatic duct, the duodenum, or the common bile duct. In many patients, ampullary cancer can't be distinguished from pancreatic cancer until surgery has been done.

These cancers often cause early symptoms such as jaundice, so they are often found while they are still resectable. Surgery with the Whipple procedure is often successful in treating these early stage cancers. Adjuvant chemoradiotherapy is often recommended after surgery.

More advanced ampullary cancers are treated like pancreatic cancer.

Hyperlinks

- 1. www.cancer.org/cancer/pancreatic-neuroendocrine-tumor.html
- 2. <u>www.cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging/staging.html</u>
- 3. <u>www.cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 4. <u>www.cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 5. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
- 6. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html

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