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Treating Pancreatic Neuroendocrine Tumors

If you've been diagnosed with a pancreatic neuroendocrine tumor (NET), 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 are pancreatic neuroendocrine tumors treated?

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

- Surgery for Pancreatic Neuroendocrine Tumor
- Ablation or Embolization Treatments for Pancreatic Neuroendocrine Tumor
- Radiation Therapy for Pancreatic Neuroendocrine Tumor
- Chemotherapy for Pancreatic Neuroendocrine Tumor
- Targeted Drug Therapy for Pancreatic Neuroendocrine Tumor
- Other Drugs for Pancreatic Neuroendocrine Tumors

Common treatment approaches

For pancreatic neuroendocrine tumors (NETs), treatment options might include surgery,

of doctors on your treatment team. The doctors on your cancer treatment team might include:

- A surgeon: a doctor who uses surgery to treat cancers or other problems
- An endocrinologist: a doctor who specializes in the diagnosis and treatment of diseases involving hormones
- A radiation oncologist: a doctor who specializes in treating cancer with radiation
- A **medical oncologist:** a doctor who specializes in treating cancer with chemotherapy, immunotherapy, targeted therapy and other medicines
- 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. Many other specialis9.48 r specil bk 0 g /F1 12 Tf 0 0 0 ragg4 doc64.72 Tm /F2 1

- Questions to Ask About Pancreatic Neuroendocrine Tumor
- 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.

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, integrative, and alternative methods

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

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

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

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 they 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 Cancer Knowledge Hub at 1-800-227-2345 and speak with one of our caring, trained cancer helpline specialists. Or, if you prefer, you can use our chat feature on cancer.org to connect with one of our specialists.

- Palliative Care
- Programs & Services

Choosing to stop treatment or choosing no treatment at all

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

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

People who have advanced cancer and who are expected to live less than 6 months may want to consider hospice care. Hospice care is designed to provide the best possible quality of life for people who are near the end of life. You and your family are encouraged to talk with your doctor or a member of your supportive care team about hospice care options, which include hospice care at home, a special hospice center, or other health care locations. Nursing care and special equipment can make staying at home a workable option for many families.

- If Cancer Treatments Stop Working
- Hospice Care

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 Neuroendocrine Tumor

Two general types of surgery can be used for pancreatic neuroendocrine tumors (NETs):

- **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 imaging tests show that the cancer is too
 widespread to be removed completely. This surgery is done to reduce tumor size
 to relieve symptoms from excess hormone production or to prevent certain
 complications like a blocked bile duct or intestine. The goal is not to try to cure the
 cancer.
- Potentially curative surgery
- Palliative surgery
- More information about surgery

To know if the cancer can be surgically removed, it is staged before the surgery, and sometimes, during the surgery.

• Staging before surgery: This uses <u>imaging tests</u>¹ such as CT scans, MRI scans, and/or radionuclide scans, to see if the cancer has spread beyond the pancreas, both locally and distantly. Exploratory <u>laparoscopy</u>²may also be done to help

determine if the cancer has spread 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 instrument has a small video camera on the end so the surgeon can see inside the abdomen. The surgeon can look at the pancreas and other organs for tumors and take biopsy³ samples of abnormal areas to learn how far the cancer has spread.

Staging during surgery: Even after imaging tests are completed, the pancreas may still need to be looked at closely to understand if the tumor can be removed safely. In these cases, intraoperative imaging, such as an intraoperative ultrasound, will need to be done. Intraoperative ultrasound is used during the surgery to better

specific kind of pancreatic NET (functioning or nonfunctioning).

Enucleation (removing just the tumor)

Sometimes if a pancreatic NET is small, just the tumor itself is removed. This is called **enucleation**. This operation may be done using a laparoscope, so that only a few small cuts on the belly are needed.

This operation may be an option for patients with an insulinoma or a gastrinoma that is smaller than 2 cm (less than 1 inch), since these PNETs are believed to be less aggressive. For PNETs that are located close to the common bile duct or pancreatic duct, are larger than 3 cm (a little more than an inch), and are suspected of having spread to nearby lymph nodes, enucleation is commonly not the first surgical approach.

Central pancreatectomy

A central pancreatectomy is a surgical option for small, low-grade PNETs that are located in the neck or upper body of the pancreas, if enucleation can not be safely done. During this operation, the surgeon removes only the neck and upper body of the pancreas, keeping the pancreatic head and tail intact. This helps keep most of the functions of the pancreas.

Distal pancreatectomy

A distal pancreatectomy is used to treat pancreatic NETs found in the tail and body of the pancreas. 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, but can be saved in certain situations. 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 having this surgery.

Whipple procedure (pancreaticoduodenectomy)

A Whipple procedure is used to treat pancreatic NETs found in the head of the pancreas that cannot be removed by enucleation. 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 (duodenum), 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 small intestine (or the stomach and small intestine) is then reattached so that food can pass through the digestive tract.

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 **keyhole surgery**.

This 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, less than 5% of patients die as a direct result of surgery.

In general, people having this type of surgery do better when it's done at a hospital where at least 15 to 20 Whipple procedures are done 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 joined
- Infections
- Bleeding
- Trouble with the stomach emptying after eating
- Trouble digesting some foods (which might require taking pancreatic enzymes in pill form to help with digestion)
- Weight loss
- Changes in bowel habits
- Diabetes

Total pancreatectomy

Total pancreatectomy might be an option if the cancer has spread throughout the pancreas but can still be removed. This operation removes the entire pancreas, as well as the gallbladder, part of the stomach and small intestine, and the spleen. 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 your 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 and improve your quality of life). This type of surgery may be considered in some people with pancreatic NETs whose tumor has recurred and is causing local problems or is making too many hormones that are causing symptoms.

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** instead to help prevent or 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 2 main options for relieving bile duct blockage: stent placement, and bypass surgery.

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) whilpc5a8se paiyae de

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.

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

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.

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 (laparoscopicsurgery).

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

- 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. This 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 withstand it and that you talk with your doctor about the possible benefits and risks before you have the surgery.

Surgery for cancer that has spread

Surgery may be used to remove metastases if a pancreatic NET has spread to the liver (the most common site of spread) or the lungs. Surgically removing metastases can improve symptoms and help patients with pancreatic NETs live longer.

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Ablation or Embolization Treatments for Pancreatic Neuroendocrine Tumor

Ablation refers to treatments that destroy tumors, usually with extreme heat or cold. They are generally best for tumors no more than about 3 cm across. There are different kinds of ablative treatments:

- Radiofrequency ablation (RFA) uses high-energy radio waves. A thin, needle-like probe is put through the skin and into the tumor. Placement of the probe is guided by an ultrasound or CT scan. 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 using a needle through the skin, guided by ultrasound or CT scans.
- Cryosurgery (also known as cryotherapyor cryoablation) destroys a tumor by freezing it with a thin metal probe. Using ultrasound, the probe is guided through the skin and into the tumor. 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 asleep).

Side effects of ablation treatments

Possible side effects 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 5 cm across; almost 2 inches) in the liver.

There are 3 main types of embolization:

Arterial embolization (also known as transarterial embolization or TAE) involves putting a catheter (a thin, flexible tube) into an artery through a small cut in the inner thigh69 gshan-0 1 72tub 3 toto the tuhepioncrtery thf0 0 rg 2Fs/GS486 gs (Embolization)Tj (

different blood vessel, the portal vein.

- Chemoembolization (also known as transarterial 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 (also known as transarterial radioembolization or TARE) combines embolization with radiation therapy. This is done by injecting small beads, called microspheres that are tagged with a radioactive substance (yttrium-90) 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 for several days. Since the radiation travels a very short distance, its effects are limited mainly to the tumor.

Side effects of embolization

Possible complications after embolization include abdominal <u>pain</u>¹, <u>fever</u>², <u>nausea</u>³, <u>infection</u>⁴, and blood clots in nearby blood vessels. Serious complications are not common, but they can happen.

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/side-effects/pain.html
- 2. www.cancer.org/cancer/managing-cancer/side-effects/infections/fever.html
- 3. <u>www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</u>
- 4. www.cancer.org/cancer/managing-cancer/side-effects/infections.html

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Radiation Therapy for Pancreatic Neuroendocrine Tumor

Radiation therapy uses high-energy rays (such as x-rays) or radioactive particles to kill cancer cells.

Surgery is the main treatment for most pancreatic neuroendocrine tumors (NETs), but radiation therapy may be an option for those who can't have surgery for some reason. It may also be given alone or with chemotherapy to reduce the size of the tumor and improve symptoms (for example, radiation to the bone to improve bone pain)

- External beam radiation therapy
- Radioactive drugs

specific part of the body. In general, radiation to the abdomen is avoided as it may cause severe side effects.

Before your treatment starts, the radiation team will determine the correct angles for aiming the radiation beams and the proper dose of radiation. The treatment is much like getting an x-ray, but the radiation is 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, but this can vary based on the reason it's being given.

Some common side effects of radiation therapy include:

- Skin changes in areas getting radiation, ranging from redness to blistering and peeling
- Nausea and vomiting
- Diarrhea
- Fatique
- Loss of appetite
- Weight loss
- Low blood counts, which can increase the risk of serious infection.

Usually these side 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.

Radioactive drugs

Radioembolization

Radioembolization (also known as transarterial radioembolization or TARE) combines embolization with radiation therapy and can be used to treat liver metastases. Small beads called microspheres are attached to a radioactive element called yttrium-90 (or 90Y) and then injected into an artery close to the liver. The beads travel in the liver blood vessels until they get stuck in small blood vessels near the tumor. There they give off radioactivity for a short while, killing nearby tumor cells. The radiation travels a very short distance, so its effects are limited mainly to the tumor.

Peptide receptor radionuclide therapy (PRRT)

People with <u>somatostatin receptor (SSTR)-positive</u>² neuroendocrine tumors who have been already treated with octreotide or lanreotide may be candidates for PRRT. In

PRRT, a radioactive element, called **lutetium-177**, is linked to a **somatostatin analog**, called **dotatate**, and injected into a vein in the arm. This drug, called **Lu-177 dotatate**, travels throughout the body, attaches to the somatostatin receptor (a protein) on the cancer cell, and gives off radiation to kill it. The radiation is delivered directly to the tumor, so there is less effect on healthy tissue.

If you are already taking octreotide or lanreotide, you will most likely need to stop taking these medicines for a certain time before you can be treated with PRRT.

Common side effects of PRRT include low levels of white blood cells, abnormal liver test results, nausea and vomiting, high levels of blood sugar, and pain.

Serious side effects include low levels of blood cells, development of certain blood or bone marrow cancers, kidney damage, liver damage, abnormal levels of hormones in the body, and infertility. Tell your cancer care team if you are pregnant or might become pregnant, because Lu-177 dotatate can harm the baby. There is not enough information regarding yttrium-90 in pregnant women so you should discuss this with your doctor.

Since these drugs expose you to radiation, people who might come into contact with you need to follow certain radiation safety practices to limit their exposure. See Systemic Radiation Therapy for more information.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see Radiation Therapy⁴.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁵.

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/external-beam-radiation-therapy.html</u>
- 2. www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/detection-diagnosis-staging/how-diagnosed.html
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/radiation/systemic-

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- 4. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 5. www.cancer.org/cancer/managing-cancer/side-effects.html

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Chemotherapy for Pancreatic

Neuroendocrine Tumor

Chemo is most often used to treat pancreatic neuroendocrine tumors (NETs) if they:

- Have not responded to other medicines (such as somatostatin drugs or targeted therapy)
- Have spread to other organs
- Are large or growing quickly
- Are causing severe symptoms, or
- Are high grade (grade 3)
- How is chemotherapy given?
- Possible side effects of chemotherapy
- More information about chemotherapy

Chemotherapy (chemo) uses anti-cancer drugs injected into a vein or taken by mouth to kill cancer cells. These drugs enter the bloodstream and reach almost all areas of the body, potentially making this treatment useful for cancers that have spread.

Chemo drugs can be given alone or combined with another chemo drug. The most commonly used drugs for pancreatic NETs include:

- Temozolomide (Temodar)
- Capecitabine (Xeloda)
- Oxaliplatin (Eloxatin)
- Fluorouracil (5-FU)
- Cisplatin or Carboplatin
- Etoposide (VePesid)
- Irinotecan (Camptosar)

How is chemotherapy given?

Chemo drugs may be given in a different ways, such as by mouth or by vein (intravenous, IV).

When chemo is a pill or capsule, usually you can take it at home. Your care team may give you a calendar showing which day to take the pills and how many to take. Your

doctor will want to see you frequently to make sure you are doing well while you take the treatment at home.

When the chemo is given by vein, it as an injection over a few minutes or infusion over a longer period of time. This can be done in a doctor's office, chemotherapy clinic, or in a hospital setting.

In general, chemo is given in cycles, which includes a period of treatment followed by a rest period to give you time to recover from the effects of the drugs. Each cycle of chemo can range from 2 to 6 weeks. 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.

The length of treatment for advanced pancreatic NETs is based on how well it is working and what side effects you have.

Possible side effects of chemotherapy

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

The side effects of chemo depend on the type and dose of drugs given and the length of time they are taken. Common side effects can include:

- Nausea and vomiting
- Diarrhea or constipation
- Loss of appetite
- Hair loss
- Mouth sores
- Skin rashes
- Fatigue (from having too few red blood cells)
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)

Most side effects go away after treatment is finished. Tell your cancer care team about any side effects or changes you notice while getting chemotherapy, so that they can be

treated promptly. Often medicines can help prevent or minimize many of the side effects. For example, your doctor can prescribe drugs to help prevent or reduce nausea and vomiting. In some cases, the doses of the chemo drugs might need to be lowered or treatment might need to be delayed or stopped to keep the effects from getting worse.

More information about chemotherapy

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Targeted Drug Therapy for Pancreatic Neuroendocrine Tumor

Targeted drugs work differently from standard chemotherapy (chemo) drugs. These drugs target specific parts of cancer cells.

The targeted drugs used to treat pancreatic neuroendocrine tumors (NETs) by blocking angiogenesis (the growth of new blood vessels that nourish cancers) or other important proteins in cancer cells that help them grow.

- Sunitinib (Sutent)
- Everolimus (Afinitor)
- Belzutifan (Welireg)
- More information about targeted therapy

Sunitinib (Sutent)

Sunitinib blocks several tyrosine kinases and attacks new blood vessel growth. It has been shown to help slow tumor growth. This drug is a pill taken once a day.

The most common side effects are tiredness (fatigue), nausea, vomiting, diarrhea, constipation, abdominal pain, mouth sores, problems breathing, cough, and changes in skin or hair color. Other possible effects include high blood pressure, heart problems, bleeding, hand-foot syndrome (redness, pain, and skin peeling of the palms of the hands and the soles of the feet), and low thyroid hormone levels.

Everolimus (Afinitor)

Everolimus blocks a protein known as *mTOR*, which normally helps cells grow and divide. Everolimus has been shown to help treat advanced pancreatic NETs. Everolimus is a pill taken once a day.

Common side effects of this drug include mouth sores, infections, loss of appetite, diarrhea, tiredness, cough, and increases in blood sugar and cholesterol levels. A less common but serious side effect is damage to the lungs, which can cause shortness of breath (dyspnea) or other problems.

Belzutifan (Welireg)

Belzutifan is a type of drug known as a HIF inhibitor

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Other Drugs for Pancreatic Neuroendocrine Tumors

Several medicines can help control symptoms and tumor growth in people with advanced pancreatic neuroendocrine tumors (NETs). These drugs are used mainly when the tumor can't be removed with surgery.

- Somatostatin analogs
- Pembrolizumab (Keytruda)
- Other drugs used for specific pancreatic NETs

Somatostatin analogs

Somatostatin analogs are compounds similar to somatostatin, a natural hormone in the body. They can help slow the growth of neuroendocrine tumor cells. They can be very helpful for patients with pancreatic NETs that have somatostatin receptors. When somatostatin analogs bind to the somatostatin receptors on cancer cells, they may stop the cancer cells from releasing hormones into the bloodstream, which can often relieve symptoms and help patients feel better. These analogs also seem to help slow the growth of some tumors, but cannot cure them.

These drugs can help reduce side effects, such as diarrhea in patients with VIPomas and help the skin rash of glucagonomas. They, however, may not be as effective in treating low blood sugar in patients with insulinomas or treating increased stomach acid production in patients with gastrinomas.

They are very useful in people who have <u>carcinoid syndrome</u>¹ (facial flushing, diarrhea, wheezing, rapid heart rate), although this syndrome is not as common with NETs in the pancreas as it is with NETs found in other places.

• Octreotide (Sandostatin): One version of octreotide is short-acting and is injected 2 to 4 times a day under the skin. There is also a long-acting form of the drug

(called **Sandostatin LAR Depot**) that only needs to be given once a month, by injection into a muscle. Depending on the severity of symptoms, some people are given injections every day when first starting treatment. Once symptoms are controlled, the longer-acting monthly injection may then be used. Other times, the long-acting drug may be started from the beginning.

• Lanreotide (Somatuline Depot): This is a long-acting somatostatin analog. It is given once a month, by injection under the skin.

Either drug may be given by your doctor or nurse, or you may learn how to give the injection at home.

Possible side effects of somatostatin analogs

The main side effects of these drugs are pain at the site of the injection, and rarely, stomach cramps, nausea, vomiting, headaches, dizziness, and fatigue. These drugs can also cause sludge to build up in the gallbladder, which can lead to gallstones that usually do not cause symptoms. They can also make the body resistant to the action of insulin, which can raise blood sugar levels and make pre-existing diabetes harder to control.

Other approved uses of this drug: Pembrolizumab can also be used to treat people with many other specific types of cancer, such as lung cancer and melanoma skin cancer.

Possible side effects of pembrolizumab

Common side effects include fatigue, muscle and joint pain, cough, rash, fever, nausea, abdominal (belly) pain, constipation, poor appetite, shortness of breath, low thyroid hormone levels, and diarrhea.

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

Autoimmune reactions: This drug basically removes one of the safeguards on the body's immune system. Sometimes this causes the immune system to attack other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, skin, or other organs.

It's very important to report any new side effects to your health care team right away. If you do have a serious side effect, treatment may need to be stopped and you may be given high doses of corticosteroids to suppress your immune system.

Other drugs used for specific pancreatic NETs

Other drugs may be used to treat specific symptoms or problems that are caused by the excess hormone being produced by pancreatic NETs. .

diet changes (higher carbohydrate intake or more frequent meals) may be started to raise glucose levels.

Diabetes drugs

Glucagonomas make too much glucagon, a hormone that increases blood glucose (sugar) levels. It works the opposite of insulin. These cancers may be treated with medicines for diabetes if somatostatin analogs alone are not enough to control the high glucose levels.

IV fluids

VIPomas make too much vasoactive intestinal peptide (VIP), a hormone that regulates water and mineral (such as potassium and magnesium) levels in the gut. Treatment may involve giving intravenous (IV) fluids to treat the dehydration from diarrhea as well as replace certain minerals that are low.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/detection-diagnosis-staging/signs-symptoms.html</u>
- 2. <u>www.cancer.org/cancer/understanding-cancer/anatomy-gallery/respiratory-</u> system.html

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Anatomy Gallery: Respiratory System²

Explore our 3D interactive tour of the respiratory system.

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Treating Pancreatic Neuroendocrine Tumor, Based on Extent of the Tumor

Treating unresectable tumors

Sometimes it can be hard to determine if cancer is resectable – that is, if it can be removed completely – using just <u>imaging tests</u>¹. A laparoscopy might be done before surgery to help determine if the tumor can be removed. But even then, cancers sometimes turn out to have spread farther than was first thought.

Pancreatic NETs are more likely to be resectable than <u>exocrine pancreas cancers</u>² (the most common type of pancreatic cancer). Most NETs that have not spread to distant parts of the body are resectable. Even some NETs that have spread might be resectable if they have not spread too far (such as only to a few spots in the liver).

Treating resectable tumors

If the tumor is resectable, <u>surgery</u> will be recommended. The procedure used depends on the type of tumor, its size, and its location in the pancreas. Surgery can range from as little as enucleation (removing just the tumor) to as much as a Whipple procedure (pancreaticoduodenectomy). Lymph nodes are often removed to check for tumor spread.

Before any surgery, medicines are often given to control any symptoms caused by the tumor. For example, drugs to block stomach acid (like proton pump inhibitors) are used for gastrinomas. Often, people with insulinomas are treated with diazoxide to keep blood sugar from getting too low. If the tumor was visible on somatostatin receptor scintigraphy³, a somatostatin analog such as octreotide may be used to control any symptoms.

Surgery alone is all that is needed for many pancreatic NETs, but after surgery, close monitoring is important to look for signs that the cancer may have come back or spread.

Treating unresectable tumors

Unresectable tumors can't be removed completely with surgery. Pancreatic NETs are often slow growing, so lab and imaging tests are used to monitor the tumor(s) and look for signs of growth.

People with NETs that have spread outside the pancreas often have symptoms like diarrhea or other hormone-related problems. These can often be helped with medicines like octreotide, lanreotide, diazoxide, and proton pump inhibitors. Some of these might also slow the growth of the tumor.

If further treatment is needed, chemotherapy or targeted drugs (such as sunitinib or everolimus) might be used, but this is usually delayed until a person is having symptoms that can't be controlled with other drugs or has signs of tumor growth on scans. Surgery or ablative techniques might also be used to treat cancer spread to the liver.

For people with poorly differentiated tumors (neuroendocrine carcinomas), chemotherapy is typically the first treatment.

For adults with pancreatic neuroendocrine tumors that are somatostatin (a type of hormone) receptor-positive, a radiopharmaceutical drug called Lutathera (lutetium Lu 177 dotatate) is also an option for treatment.

You may want to consider taking part in a clinical trial. Clinical trials are studies of new drugs, procedures, and other treatments in people. To learn more about clinical trials, seeClinical Trials⁴.

Hyperlinks

- 1. www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/detection-diagnosis-staging/how-diagnosed.html
- 2. www.cancer.org/cancer/types/pancreatic-cancer.html
- 3. <u>www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/detection-diagnosis-staging/how-diagnosed.html</u>
- 4. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>

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