cancer.org | 1.800.227.2345

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 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.

• 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 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.

will need to be done. Intraoperative ultrasound is used during the surgery to better understand structures near the pancreas tumor.

Potentially curative surgery

Pancreatic NETs that have not spread outside the pancreas should be completely removed, if possible, because these tumors are more likely to be cured with surgery. Sometimes, however, 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 to help prevent or relieve symptoms. a71hSee "Pleri0 gs (understncreas t1 01sthe.) T, th thse tumors a phs gr 0 0 th2 53

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 havingthis 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.

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:

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) while you are sedated. Often this is part of an endoscopic retrograde cholangiopancreatography (ERCP). The doctor passes the endoscope down the throat and all the way into the small intestine. The doctor can then insert the stent into the bile duct through the endoscope. The stent can also be put in place through the skin during a percutaneous transhepatic cholangiography (PTC). (This is described in Tests for Pancreatic Neuroendocrine Tumor⁴.)

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.

More information about Surgery

Wilkins; 2015.

Last Revised: August 22, 2024

Ablation or Embolization Treatments for Pancreatic Neuroendocrine Tumor

Ablation or embolization can sometimes be used to help treat a pancreatic neuroendocrine tumor (NET) that has spread to other organs, especially the liver.

- When are ablation and embolization used?
- Ablative treatments (ablation)
- Embolization

When are ablation and embolization used?

Ablation and embolization treatments are different ways of destroying tumors, rather than removing them with surgery. When pancreatic NETs have spread to other sites (for example, the liver), these treatments can often reduce tumor size and improve symptoms. Ablation and embolization can also help treat pancreatic NET that has not spread to other organs, and is not able to be surgically removed. These treatments are very unlikely to cure cancers on their own. They are more likely to be used to help prevent or relieve symptoms, and are often used along with other types of treatment.

Ablative treatments (ablation)

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 thigh and threading it up into the hepatic artery feeding the tumor. Blood flow is blocked (or reduced) by injecting materials to 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 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.

Oncology: Neuroendocrine and Adrenal Tumors. V.2.2024. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf on August 4, 2024.

Schneider DF, Mazeh H, Lubner SJ, Jaume JC, Chen H. Chapter 71: Cancer of the endocrine system. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Last Revised: August 22, 2024

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
- More information about radiation therapy

External beam radiation therapy

External beam radiation therapy¹ uses a machine to deliver a beam of radiation to a 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
- Fatigue
- · Loss of appetite
- ...Weight-loss

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 <u>Managing Cancer-related Side Effects</u>⁵.

Hyperlinks

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

References

- 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

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

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

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 2. www.cancer.org/cancer/managing-cancer/side-effects.html

References

National Cancer Institute. Physician Data Query (PDQ). Pancreatic Neuroendocrine Tumors (Islet Cell Tumors) Treatment – Patient Version. 10/7/22. Accessed at https://www.cancer.gov/types/pancreatic/patient/pnet-treatment-pdq on August 4, 2024.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. V.2.2024. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf on August 4, 2024.

Mpilla GB, Philip PA, El-Rayes B, Azmi AS. Pancreatic neuroendocrine tumors: Therapeutic challenges and research limitations. World J Gastroenterol. 2020 Jul 28;26(28):4036-4054. doi: 10.3748/wjg.v26.i28.4036. PMID: 32821069; PMCID: PMC7403797.

Schneider DF, Mazeh H, Lubner SJ, Jaume JC, Chen H. Chapter 71: Cancer of the endocrine system. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Last Revised: August 22, 2024

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 kn2 Tfth. It has

Belzutifan can be used in people with <u>von Hippel-Lindau (VHL)</u>¹ disease who have an advanced pancreatic NET.

Common side effects of this drug include low red blood cell counts (anemia), feeling tired and/or dizzy, nausea, headache, increased blood sugar levels, and changes in lab tests showing the drug might be affecting the kidneys. Less common but more serious side effects can include very low red blood cell counts (severe anemia), which might require blood transfusions, and low oxygen levels in the body, for which you might need oxygen therapy or even be admitted to the hospital.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Cancer</u> Therapy².

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

Hyperlinks

- www.cancer.org/cancer/types/kidney-cancer/causes-risks-prevention/riskfactors.html
- 2. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 3. www.cancer.org/cancer/managing-cancer/side-effects.html

References

Jonasch E, Donskov F, Iliopoulos O, et al. Belzutifan for renal cell carcinoma in von Hippel-Lindau disease. *NEJM* 2021;385:2036-2046.

Ma ZY, Gong YF, Zhuang HK, Zhou ZX, Huang SZ, Zou YP, Huang BW, Sun ZH, Zhang CZ, Tang YQ, Hou BH. Pancreatic neuroendocrine tumors: A review of serum biomarkers, staging, and management. *World J Gastroenterol.* 2020 May 21;26(19):2305-2322. doi: 10.3748/wjg.v26.i19.2305. PMID: 32476795; PMCID: PMC7243647.

PMC7403797.

National Cancer Institute. Physician Data Query (PDQ). Pancreatic Neuroendocrine Tumors (Islet Cell Tumors) Treatment – Patient Version. 10/7/22. Accessed at https://www.cancer.gov/types/pancreatic/patient/pnet-treatment-pdq on August 4, 2024. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. V.2.2024. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf on August 4, 2024.

Pelle E, Al-Toubah T, Morse B, Strosberg J. Belzutifan in a Patient With VHL-Associated Metastatic Pancreatic Neuroendocrine Tumor. *J Natl Compr Canc Netw.* 2022 Dec;20(12):1285-1287. doi: 10.6004/jnccn.2022.7047. PMID: 36509068.

neuroendocrine tumors. NEJM. 2011;364:501513.

Schneider DF, Mazeh H, Lubner SJ, Jaume JC, Chen H. Chapter 71: Cancer of the endocrine system. In: Niederhuber JE, Armitage JOT.8orshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Yao JC, Evans DB. Chapter 85: Pancreatic neuroendocrine tumors. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

Yao JC, Shah MH, Ito T, et al. Everolimus for advanced pancreatic neuroendocrine tumors. *NEJ M.* 2011;364:514523.

Last Revised: August 22, 2024

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

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.

Pembrolizumab (Keytruda)

Pembrolizumab is a type of immunotherapy drug known as an immune checkpoint inhibitor. It works on PD-1, a protein on immune cells called T cells that normally helps keep them from attacking other cells in the body (including cancer cells). By blocking PD-1, pembrolizumab boosts the immune response against cancer cells. This can shrink some tumors or slow their growth.

This drug might be an option to treat some advanced cancers, typically after other treatments have been tried or when no other good treatment options are available, if the cancer cells have any of the following:

- A high level of microsatellite instability (MSI-H) or a defect in a mismatch repair gene (dMMR)
- A high tumor mutational burden (TMB-H), meaning the cancer cells have many gene mutations

This drug is an intravenous (IV) infusion, typically given every 3 or 6 weeks.

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 (b g stvo3ain, 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 t g

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. .

Proton pump inhibitors

Gastrinomas make too much gastrin, which increases stomach acid levels, and can lead to stomach ulcers. Proton pump inhibitors, for example omeprazole (Prilosec), esomeprazole (Nexium), or lansoprazole (Prevacid), block stomach acid production and may be given to decrease the chance of ulcers forming.

Diazoxide

Insulinomas make too much insulin which causes very low blood glucose (sugar) levels. Diazoxide, a drug that keeps insulin from being released into the bloodstream, or 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-system.html</u>

References

Anatomy Gallery: Respiratory System²

Explore our 3D interactive tour of the respiratory system.

Frankton S, Bloom SR. Gastrointestinal endocrine tumours. Glucagonomas. *Baillieres Clin Gastroenterol.* 1996 Dec;10(4):697-705. doi: 10.1016/s0950-3528(96)90019-6. PMID: 9113318.

National Cancer Institute. Physician Data Query (PDQ). Pancreatic Neuroendocrine Tumors (Islet Cell Tumors) Treatment – Patient Version. 10/7/22. Accessed at https://www.cancer.gov/types/pancreatic/patient/pnet-treatment-pdq on August 4, 2024.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. V.2.2024. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf on August 4, 2024.

Nikou GC, Toubanakis C, Nikolaou P, Giannatou E, Safioleas M, Mallas E, Polyzos A. VIPomas: an update in diagnosis and management in a series of 11 patients. *Hepatogastroenterology*. 2005 Jul-Aug;52(64):1259-65. PMID: 16001675.

Romeo S, Milione M, Gatti A, Fallarino M, Corleto V, Morano S, Baroni MG. Complete clinical remission and disappearance of liver metastases after treatment with somatostatin analogue in a 40-year-old woman with a malignant insulinoma positive for somatostatin receptors type 2. *Horm Res.* 2006;65(3):120-5. doi: 10.1159/000091408. Epub 2006 Feb 9. PMID: 16479142.

Stehouwer CD, Lems WF, Fischer HR, Hackeng WH, Naafs MA. Aggravation of hypoglycemia in insulinoma patients by the long-acting somatostatin analogue octreotide (Sandostatin). *Acta Endocrinol (Copenh)*. 1989 Jul;121(1):34-40. doi: 10.1530/acta.0.1210034. PMID: 2545062.

U.S. Food and Drug Administration: FDA grants accelerated approval to pembrolizumab for first tissue/site agnostic indication. Available at www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm560040.htm³. Accessed August 8, 2024.

Last Revised: August 22, 2024

Treating Pancreatic Neuroendocrine Tumor, Based on Extent of the Tumor

Treatment of pancreatic neuroendocrine tumors (NETs) depends largely on whether they can be resected (removed) completely or not. 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.

- Treating resectable tumors
- 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

PMC6601637.

Yao JC, Evans DB. Chapter 85: Pancreatic neuroendocrine tumors. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

Last Revised: August 22, 2024

Written by

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

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

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

cancer.org | 1.800.227.2345