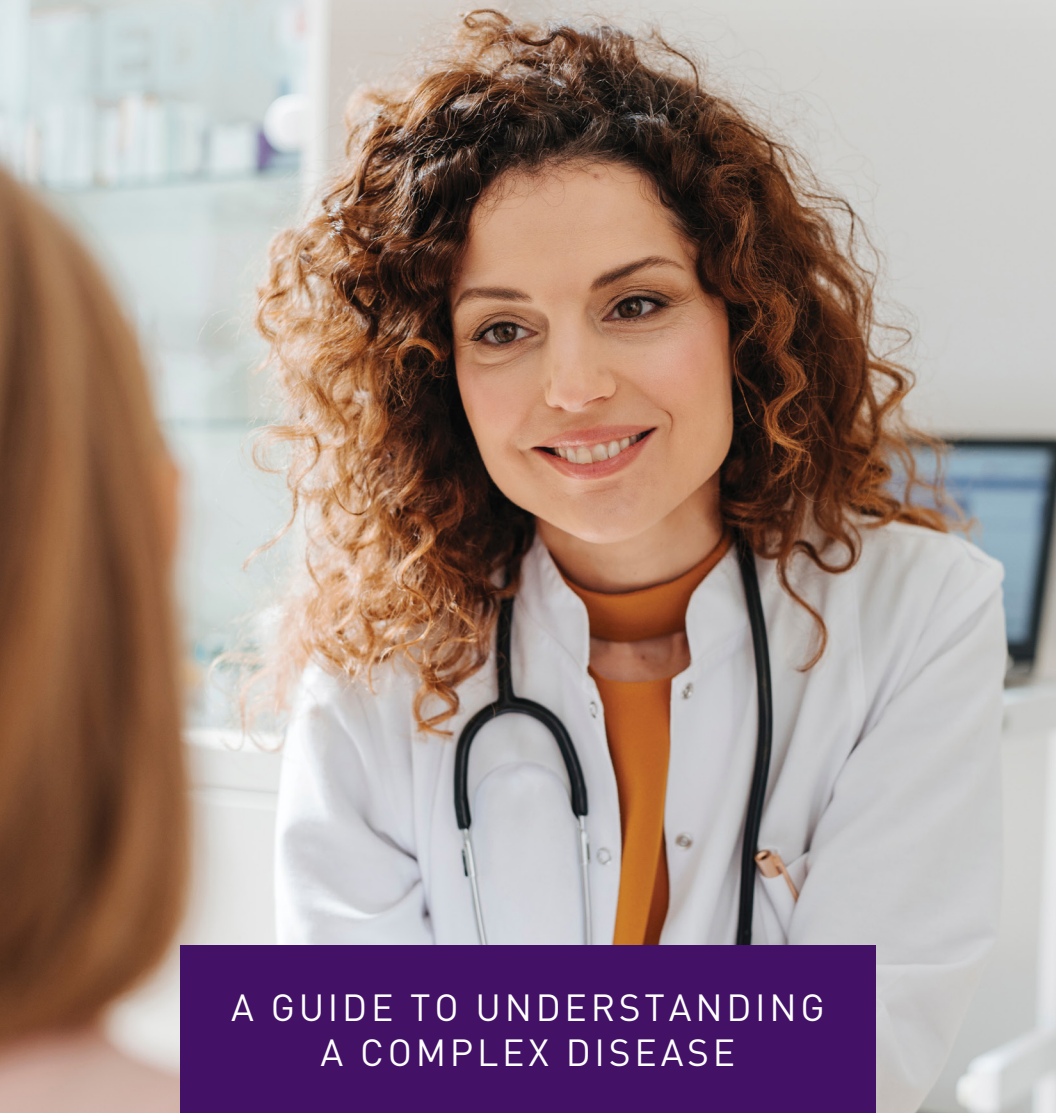
PANCREATIC CANCER ACTION NETWORK®

PANCREATIC NEUROENDOCRINE TUMORS [PNETS]



A GUIDE TO UNDERSTANDING A COMPLEX DISEASE

You are your own best advocate. The Pancreatic Cancer Action Network (PanCAN) strongly recommends that you discuss your treatment goals with your healthcare team and know all of your options at every stage of your disease.

ABOUT THIS BOOKLET

This booklet is a resource for patients and families who want to understand pancreatic neuroendocrine tumors (PNETs), a rare type of pancreatic cancer. A glossary is provided at the end of this booklet for **bold** words in the booklet's text.

The more information and knowledge you have, the more empowered you can be to make decisions. Use this booklet as a reference guide to talk about PNETs with your healthcare team.

Patient Services: We Are Here to Help

PanCAN Patient Services is the place to contact when facing pancreatic cancer. No organization supports pancreatic cancer patients like we do. Through our Patient Services Help Line, we provide more resources and speak with more pancreatic cancer patients and caregivers than any other organization in the world.

Our highly trained and compassionate Case Managers provide free, personal one-to-one support and information about the disease. Case Managers can provide helpful information and resources for all topics referenced in this booklet, including:

- The disease and treatment
- PanCAN's Know Your Tumor® precision medicine service
- Clinical trials
- Diet and nutrition
- Pain and symptom management
- Pancreatic cancer and PNET specialists
- Resources to help patients navigate a new diagnosis, including information on next steps, questions to ask the healthcare team, genetic testing and more
- Support resources, including connecting with others who have PNETs

All services are free of charge.

Contact PanCAN Patient Services toll-free at 877-2-PANCAN or patientservices@pancan.org. Support is available Monday – Friday, 7 a.m. - 5 p.m. Pacific Time. Services available in English and Spanish.

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THE PANCREAS

The **pancreas** is a **gland** located deep in the **abdomen**. It is about six inches long and is shaped like a flat pear. The pancreas is surrounded by important organs, including the stomach, **small intestine, liver, spleen** and **gallbladder**. The wide end of the pancreas is called the head. The middle sections are the neck and body. The thin end of the pancreas is called the tail. Three important blood vessels cross behind the pancreas. These blood vessels are the superior mesenteric artery, **superior mesenteric vein** and **portal vein**. (See Figures 1 and 2 on page 2.)

The pancreas is both an **exocrine gland** and an **endocrine gland**.

Exocrine cells in the pancreas make **enzymes** that help with digestion. When food enters the stomach, the pancreas releases enzymes and other substances, together called **pancreatic juice**, through the main pancreatic duct into the stomach. The **main pancreatic duct** connects with the **common bile duct**, which carries bile from the gallbladder. Together, they connect with the **duodenum** at the **ampulla of Vater**. (See Figure 2 on page 2.) There, bile and pancreatic enzymes help digest fats, carbohydrates and proteins.

Endocrine cells in the pancreas, called **islet cells**, make **hormones**, which control and regulate specific bodily functions. They are usually made in one part of the body and carried through the blood for another part of the body to use. The two main pancreatic hormones are **insulin** and **glucagon**. Insulin lowers blood sugar levels. Glucagon raises blood sugar levels. Together, they maintain proper levels of sugar in the blood. Another hormone produced by endocrine cells is somatostatin, which also regulates hormone levels in the blood.

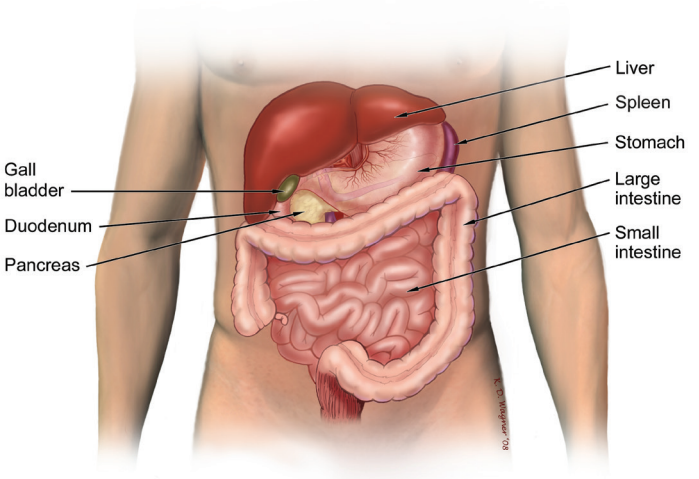


FIGURE 1

The pancreas is located deep in the abdomen and is surrounded by many other organs.

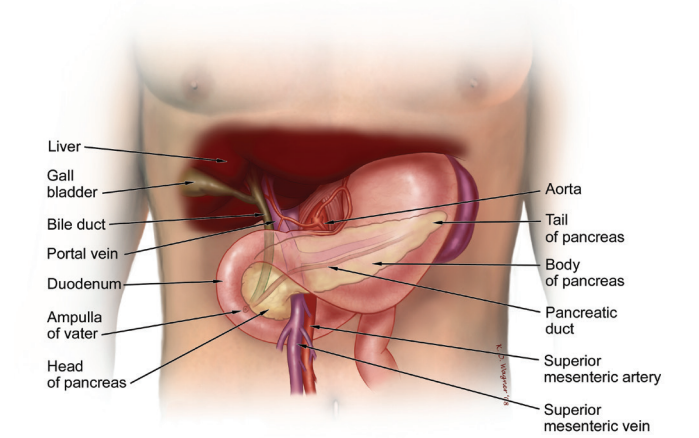


FIGURE 2

To show the entire pancreas in this image, the liver is shifted upward and the intestines are removed.

The Pancreatic Cancer Action Network would like to thank Kathleen Wagner and support from the Hamill Foundation and the Pickelner Fund for Pancreatic Cancer Research at MD Anderson Cancer Center for the illustrations provided on this page.

UNDERSTANDING CANCER

Cells are the body's basic units of life. Each cell carries **genetic** information in the form of **deoxyribonucleic acid (DNA)**, DNA provides instructions for how cells should grow and function.

Cancer starts in one cell in the body. Normally, cells divide to make new cells as the body needs them. When cells grow old, they die, and new cells take their place. Sometimes, a change (called a **mutation**) in the cell's DNA can break this process. A mutation can be passed down from parents (inherited) or can develop over time. A mutation may cause new cells to form when the body does not need them. A mutation may also keep old cells from dying. The extra cells may form a mass of tissue called a tumor. Tumors can be **benign** or **malignant**.

Benign tumors are made of abnormal cells that cannot invade or spread to other parts of the body. A large benign tumor can cause problems if it puts pressure on nearby blood vessels, nerves or organs.

Malignant tumors are cancer. Their cells divide uncontrollably and can invade other tissues and organs. Cancer cells can break away (**metastasize**, meh-TA-sta-size) from the original cancer site (**primary tumor**) and form new tumors in other parts of the body.

PANCREATIC CANCER

Pancreatic cancer starts when abnormal cells in the pancreas grow out of control and form a tumor.

When pancreatic cancer spreads outside the pancreas, it forms **secondary tumors** (metastases, meh-TA-sta-sees) in other tissues or organs. Pancreatic cancer often spreads to the **lymph nodes**, liver, **peritoneum** or lungs. Since the cancer cells started in the pancreas, tumors in other parts of the body are still called pancreatic cancer.

Based on the type of pancreatic cell they start in, pancreatic tumors are classified into two groups: exocrine tumors and neuroendocrine (endocrine) tumors.

PANCREATIC EXOCRINE TUMORS

More than 90% of pancreatic cancers are exocrine tumors. These start in the exocrine cells in the pancreas. The most common exocrine pancreatic cancer is **adenocarcinoma**.

This booklet does not provide comprehensive information on pancreatic exocrine tumors. For more information about exocrine pancreatic cancer, contact PanCAN Patient Services and request the booklet titled *An Overview of Pancreatic Cancer*.

PANCREATIC NEUROENDOCRINE TUMORS (PNETS)

Pancreatic neuroendocrine tumors (PNETs) are also called pancreatic NETs or islet cell tumors, an older term that is used infrequently. They make up less than 10% of all pancreatic tumors. They tend to grow slower than adenocarcinomas. They start in the hormone-producing (endocrine) cells in the pancreas, called islet cells.

There are many types of neuroendocrine tumors. PNETs start in the endocrine cells of the pancreas and those that make hormones are called **functional tumors**. PNETs that do not make hormones are called **nonfunctional tumors**.

Functional PNETs cause the pancreas to make too many hormones, which causes hormone-related **symptoms**. Functional PNETs are usually easier for doctors to find because they can detect the abnormal hormone levels and their related symptoms.

The majority of PNETs are nonfunctional tumors. Nonfunctional tumors do not produce any hormones, so they do not cause any hormone-related symptoms. As a result, these tumors are usually diagnosed once the tumor is more advanced and cause symptoms like pain or **jaundice**.

The following list describes the different types of PNETs classified by the hormones they produce.

Gastrinoma (Zollinger-Ellison Syndrome)

Gastrinomas make gastrin. These tumors typically develop in the head of the pancreas, the stomach or the duodenum. Some patients may develop gastrinomas as a result of an inherited disease called multiple endocrine neoplasia type-1 (MEN1).

Glucagonoma

Glucagonomas make glucagon. They are often in the tail of the pancreas. They are usually large.

Insulinoma

Insulinomas make insulin. They are the most common type of functional pancreatic neuroendocrine tumor. They tend to be small and hard to diagnose.

Somatostatinoma

Somatostatinomas make somatostatin. They are extremely rare and usually very large. They can be anywhere in the pancreas or duodenum.

VIPoma (Verner-Morrison Syndrome or Watery Diarrhea and Hypokalemia Achlorhydria Syndrome)

VIPomas make vasoactive intestinal peptide (VIP). Two out of three VIPomas occur in women.

Nonfunctional Islet Cell Tumor

Nonfunctional PNETs do not make any hormones.

RISK FACTORS

The exact cause of PNETs is unknown. Research suggests certain **risk factors** may increase the chance that someone will get PNETs.

Genetic mutations or syndromes may cause about 10% of PNET cases. These are DNA changes that someone is born with, passed down from a parent. Multiple endocrine neoplasia type 1, von Hippel-Lindau disease, neurofibromatosis type 1 and tuberous sclerosis complex are examples of genetic syndromes that may increase an individual's risk of developing PNETs.

Though more research is needed, diabetes, smoking and alcohol use may also increase someone's risk of getting PNETs.

Having these risk factors does not mean a person will definitely develop a pancreatic NET. Some people with PNETs do not have any risk factors. If you think you may be at risk, talk to your doctor or **genetic counselor** about your concerns.

Multiple Endocrine Neoplasia Type-1 (MEN1) or Wermer Syndrome

MEN1 is a **hereditary** syndrome that causes endocrine tumors in the **parathyroid glands**, pituitary glands and pancreas. Tumors are usually in at least two of these three glands. A large portion of people with MEN1 will develop PNETs. Gastrinomas are the most common PNETs in people with MEN1. The second most common type are insulinomas. The PNETs may be malignant and usually appear in people in their 30s or 40s.

Von Hippel-Lindau (VHL) Disease

VHL disease is a rare cancer syndrome. Some people with VHL do not have a family history of the disease. Patients with VHL may develop kidney tumors, adrenal gland tumors and cysts. Not all tumors that patients with VHL develop are cancerous. People with this syndrome have a slightly higher than normal chance of getting pancreatic cancer, usually nonfunctional PNETs.

Neurofibromatosis Type 1 (NF1)

NF1 is a rare syndrome causing skin coloring changes and nodules on the eyes. Some patients can develop PNETs. Half of all individuals with NF1 do not have a family history.

Tuberous Sclerosis Complex (TSC1 and TSC2)

TSC is rare syndrome causing benign tumors that can lead to skin and nerve conditions. Some people with TSC develop PNETs, which may be nonfunctional or functional.

SYMPTOMS

Pancreatic cancer can cause back **pain**, stomach pain, weight loss, jaundice, appetite loss, nausea, stool changes and **diabetes**. Common symptoms for all pancreatic cancer types are described below. If someone experiences one or more of these symptoms, it does not mean that they have pancreatic cancer. There are other common medical problems or conditions that may also cause similar symptoms. Anyone experiencing these symptoms should speak with a doctor.

Functional PNETs make hormones. The hormones the tumor cells make may cause other symptoms. (See table on page 11 for symptoms specific to each type of functional PNET.) Nonfunctional PNETs do not cause the pancreas to make hormones. This means they do not have hormone-related symptoms. They are generally found when a large tumor causes pain or jaundice.

ASCITES

Pancreatic cancer may cause a symptom called ascites. Ascites is extra fluid built up in the abdomen. It causes the belly to swell and distend. Pancreatic cancer patients may have ascites at any time, but it is especially common in patients whose cancer has spread. When cancer spreads in the abdomen, it can irritate the abdominal lining (peritoneum) that causes fluid buildup. This fluid buildup can cause discomfort, difficulty breathing, nausea and decreased appetite. Water pills, called **diuretics**, may slow the fluid buildup. Ascites can also be relieved by draining the fluid through a procedure called **paracentesis**.

BLOOD CLOTS

Deep vein thrombosis (DVT) is a serious condition when blood clots form in the veins, usually in the legs. Cancer causes changes in the blood that can make clots more likely. Blood clots may go unnoticed and cause no symptoms. However, they often cause swelling, pain and tenderness in the affected area. Swelling in only one leg is often a sign of DVT. A piece of the clot may break loose and travel to the lungs, damaging the lung tissue. This is called a pulmonary embolism and is a serious condition. DVT is commonly treated with anticoagulant drugs which thin the blood, preventing existing clots from getting larger and new clots from forming.

DIABETES

Diabetes is a condition in which the body does not make or properly use a pancreatic hormone called insulin. Insulin helps the body use glucose (sugar) efficiently. Normally, insulin allows glucose to enter cells used for energy. With diabetes, either the body does not make enough insulin or the amount that is made is not fully effective. Research suggests that a sudden onset of type 2 diabetes in people aged 50 or older may be an early symptom of pancreatic cancer, especially in those who have a low **body mass index (BMI)**, keep losing weight or do not have a family history of diabetes. A sudden change in blood sugar levels in diabetics who previously had well-controlled diabetes may also be a sign of pancreatic cancer.

DIGESTIVE DIFFICULTIES

Pancreatic cancer can cause poor appetite, indigestion, nausea and vomiting. These issues may occur if the tumor invades or presses against the duodenum, blocking food from passing through the intestine. Digestive difficulties may also happen

if a pancreatic duct is blocked and in rare instances, some patients may experience pancreatic enzyme insufficiency. Dietary changes, pancreatic enzyme products and other treatments can help lessen these symptoms.

JAUNDICE

People with pancreatic cancer commonly have jaundice. Jaundice is a yellowing of the skin and eyes caused by too much **bilirubin** (a component of bile) in the blood. A tumor in the head of the pancreas can cause the bile duct to narrow and block bile flow. This blockage causes a buildup of bilirubin. People with jaundice may also have itchy skin, abnormally dark urine and light or clay-colored stools. If surgery to remove the tumor is possible, this can provide relief. In some cases, patients can get a biliary bypass surgery so the bile can flow around the tumor. Otherwise, patients usually get a **stent** to keep the bile duct open.

PAIN

The pancreatic tumor invading or pushing against nearby organs or nerves can cause pain in the upper stomach area or mid-back. The tumor blocking the digestive tract can also cause pain. Pain can be treated with medicines and procedures like a **celiac plexus block**. Many pain medicines cause constipation, which can worsen pain. A doctor can prescribe medicines to avoid constipation.

STOOL CHANGES

Many pancreatic cancer patients experience **diarrhea**, constipation, or both. Diarrhea is loose, watery, oily or foul-smelling stools. If patients do not have enough pancreatic enzymes in the intestines, it can cause food to move too quickly through the digestive tract. This leads to malabsorption and results in diarrhea.

Constipation is especially common in patients taking pain medicine. These medicines slow the passage of food through the intestines. If the digestive system works too slowly, it can cause stools to become dry, hard and difficult to pass. Diet changes and other medicine may help with stool changes.

UNEXPLAINED WEIGHT LOSS

Pancreatic cancer and its treatment can cause weight loss. Cancer-induced weight loss, called **cancer cachexia**, affects the way the body uses calories and protein. It can cause the body to burn more calories than usual and break down muscle. A person may also notice a change in appetite or desire for certain foods.

FUNCTIONAL PNET SYMPTOMS

Type of Functional PNET	Common Symptoms
Insulinoma	**Low blood sugar, which can cause heart palpitations, shakiness, sweating, confusion, seizures**
Gastrinoma (Zollinger-Ellison Syndrome)	**Acid reflux, burning belly pain, diarrhea, fat in stool, weight loss**
Glucagonoma	**High blood sugar, severe skin swelling or irritation, mouth sores, anemia, weight loss, skin rash, blood clots**
VIPoma (Verner-Morrison Syndrome or Watery Diarrhea and Hypokalemia Achlorhydria Syndrome)	**Severe watery diarrhea, which can lead to low blood potassium levels and cause muscle weakness, fatigue, nausea**
Somatostatinoma	**Diabetes, gallstones, weight loss, diarrhea, fat in stool, nausea, vomiting**

DIAGNOSIS AND STAGING

Diagnosing pancreatic cancer can be difficult for several reasons. First, the pancreas is located deep in the abdomen, surrounded by other organs that can make seeing or feeling a tumor difficult. Additionally, the symptoms of pancreatic cancer can be vague, often develop gradually, or may be mistaken for other medical problems. While there is no standard diagnostic test for pancreatic cancer, doctors can use symptom information, imaging tests, blood tests, urine tests and a **biopsy** (sample of tumor tissue) to make an accurate diagnosis. This information also helps them figure out the type of pancreatic cancer and how much it has spread.

It is important to have an accurate diagnosis since the treatments for pancreatic neuroendocrine tumors are different than those for adenocarcinoma (the most common type of pancreatic cancer).

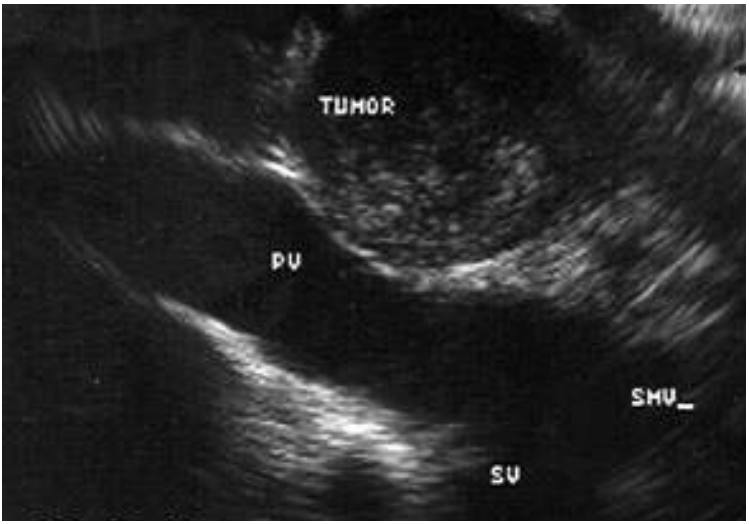
IMAGING TESTS

It is very difficult to distinguish a pancreatic neuroendocrine tumor from an adenocarcinoma tumor in imaging tests. A doctor will make a diagnosis based on the patient's symptoms, hormone levels in the blood or urine, results of imaging tests and a biopsy.

There is not one standard imaging test for diagnosing PNETs. Doctors may use one or more types of imaging tests to figure out the size and location of the cancer. These tests can also help determine whether the cancer has spread. Keep in mind that if a diagnostic imaging test is positive, this does not always mean that a person has pancreatic cancer. The opposite is also true — a negative diagnostic imaging test does not always mean that a person does not have pancreatic cancer. The following are imaging tests that may be used.

Endoscopic Ultrasound (EUS)

During an EUS, the doctor passes a thin, lighted tube called an endoscope with a small ultrasound probe through the patient's mouth into the stomach and duodenum. The probe takes detailed pictures of the pancreas, bile duct and digestive tract. An EUS allows a doctor to see the size and location of a tumor in the pancreas. They can also see whether the tumor has spread to nearby lymph nodes, blood vessels or other places. Patients can also get a type of biopsy called a fine-needle aspiration (FNA) during an EUS (see page 23).



Endoscopic ultrasound (EUS) can be used to show tumor location and size.

Reasons for Use and Other Considerations

EUS is an outpatient procedure usually done in a hospital or outpatient surgery center. Patients are prescribed a sedative to help them relax and anesthesia to block pain. EUS is one of the most common imaging procedures used to diagnose pancreatic cancer, as it is often the best way to get tumor samples.

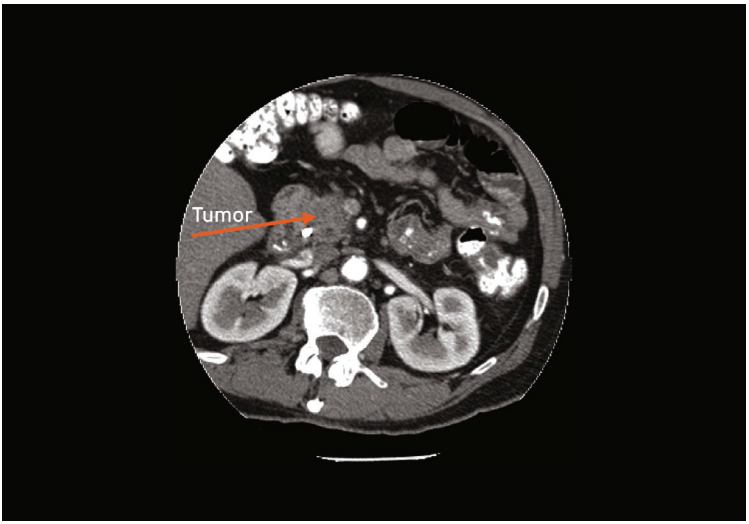
If, based on symptoms or blood tests, the doctor suspects the patient has small pancreatic masses but does not see them with a CT (see page 15) or MRI scan (see page 17), EUS may show them. Studies show that EUS is equal to or better than CT scans in showing early pancreatic cancer. As a result, researchers are studying using EUS to screen people at higher risk for developing pancreatic cancer.

Complications from EUS are very rare. They include infection of a pancreatic cyst, pancreatitis, gastrointestinal bleeding and reactions to anesthesia.

Computed Axial Tomography (CAT or CT) Scan

A CT scan takes detailed pictures of the body. During a CT scan, the patient lies still on a table. To get a better picture, sometimes the person operating the CT scanner might ask the patient to hold their breath for short periods of time. A donut-shaped scanner moves around the body to take many X-rays. A computer joins all the pictures together to create a 3D image of the body.

CT images show bones, blood vessels, muscles and organs. A CT scan used with an oral or **intravenous (IV)** contrast substance (dye) may show small pancreatic tumors and whether the cancer has spread. Patients may hear their doctor refer to this as a CT or CAT scan with contrast. Angiography, a CT scan that looks at the blood vessels of the pancreas, can show where the tumor is in relationship to the blood vessels. This is important for the doctor to know to determine if the cancer is operable.



Marked area on CT Scan shows a pancreatic tumor.

Radiologists have pancreatic protocols, which are specific ways to get clear, detailed images of the pancreas, liver and key blood vessels through a CT scan. This is the preferred type of CT scan for diagnosing pancreatic cancer. A high quality CT scan may be enough if a pancreatic protocol CT scan is not possible.

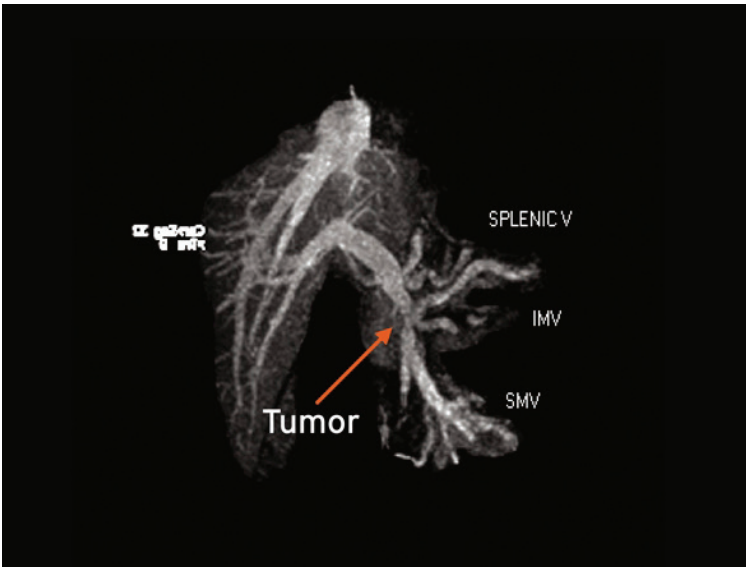
Reasons for Use and Other Considerations

Doctors usually order CT scans when they suspect someone has pancreatic cancer. The images often help the doctor understand if the tumor can be surgically removed. CT scans use X-rays, a form of radiation. When CT is used for screening and surveillance, repeated radiation exposure may be a concern. Discuss the risks and benefits with the healthcare team. Additionally, if the patient is allergic to contrast substances, they must get different imaging tests.

Magnetic Resonance Imaging (MRI)

MRI uses radio waves and magnets to take pictures of organs and structures inside the body by measuring their energy. Like a CT scan, an MRI takes many pictures while the patient lies on a table and then a computer joins the pictures to create a 3D image of the body.

A pancreas protocol MRI can help with pancreatic cancer staging, especially when tumors do not appear on a CT scan or when patients are allergic to contrast substances used in CT scans.



Marked area on MRI shows pancreatic tumor.

Reasons for Use and Other Considerations

While most MRIs do not require contrast, if the MRI requires the use of contrast, it is important to note that some patients may be allergic or sensitive to the contrast used. The contrast substance for an MRI is usually different from what is used with a CT scan. Therefore, patients who are allergic to the CT scan contrast substance can get an MRI. Also, MRI scans do not involve exposure to radiation.

MRI scans take longer than CT scans. During a traditional MRI, a patient must lie still in a long tube. Claustrophobic patients may need to take medicine to calm their anxiety before entering this type of MRI scanner. MRI scans are loud, so patients will often wear ear plugs to protect their ears. A different type of MRI scanner called an "open MRI" has open sides. This may help patients who are afraid of being in a closed space.

If a patient needs imaging of the bile and pancreatic ducts, they can get an MRCP (see page 19) when they get an MRI.

Magnetic Resonance Cholangiopancreatography (MRCP)

MRCP is a special type of MRI. It uses computer software to image pancreatic and bile ducts, where tumors often form. It does not need a contrast substance. MRCP is an excellent tool for seeing pancreatic cysts and duct blockages. An MRCP can happen at the same time as an MRI.

Reasons for Use and Other Considerations

MRCP gives a similar picture to ERCP (see page 21), but without the same risks. If a stent is not needed, MRCP may be used instead of ERCP for diagnosis.

MRCP may also be used to diagnose other conditions like bile duct stones, tumors in the small intestine or a pancreatic tumor type called intraductal papillary mucinous neoplasm.

NUCLEAR IMAGING

Positron Emission Tomography (PET) Scan

PET scans make images based on the level of chemical reactions happening in cells. The most common PET imaging study is FDG-PET. The patient gets a small amount of fluorodeoxyglucose (FDG) injected into their body. Then they rest so the FDG can move around the body. The PET scanner tracks the signals the FDG gives off. A computer turns these signals into whole-body images. Cancer cells use more FDG than most normal cells, so they are brighter on computer images.

Reasons for Use and Other Considerations

PET scans may help doctors tell the difference between cancerous and non-cancerous pancreatic tumors. They may also help detect pancreatic cancer spreading to other parts of the body. PET may be used when other scans show changes like abnormal liver growths or enlarged lymph nodes.

PET is often used with CT scans to get a more complete image. New scanners can do a combined PET-CT scan. Researchers

are still studying PET scans in pancreatic cancer. PET scans are not a substitute for high quality, contrast CT scans, but they may be used along with CT for those at high risk of getting pancreatic cancer.

Gallium-68 DOTATOC PET/CT Scan

Many PNETs have a high number of somatostatin receptors (SSTRs). If the doctor suspects a PNET, they might use tests to look for SSTRs. The gallium-68 DOTATOC PET/CT scan is one of these tests.

Patients will receive a somatostatin analog (SSA) attached to a small, safe amount of a radioactive compound (like gallium-68). This is called radiolabeling. An SSA will bind to any SSTRs on the tumor. The radioactive compound will act like a flag, causing it to show up on the scans.

The gallium-68 DOTATOC PET/CT scan uses an SSA called DOTATOC, which is radiolabeled with gallium-68. Patients get the substance injected into their vein. Then, a PET or CT scan takes a picture of the body, showing where the DOTATOC has attached to any tumors.

Reasons for Use and Other Considerations

The gallium-68 DOTATOC PET/CT scan can be very effective at finding small tumors and metastases. It can also help the healthcare team figure out if a pancreatic tumor is a PNET or exocrine pancreatic cancer. Doctors might order this test if blood or urine tests show high levels of pancreatic hormones, since that could be a sign of PNETs. It may be used along with CT or MRI scans to find exactly where the tumors are.

Octreoscan

An Octreoscan, also called an octreotide scan, is like the gallium-68 DOTATOC PET/CT scan. It is also a test to look for SSTRs. An Octreoscan uses a somatostatin analog (SSA) called octreotide, which has a radioactive substance called indium-111 attached to it. Together, they bind to SSTRs to help show tumors on a scan. Patients get the substance injected into their vein. Then, a PET or CT scan takes a picture of the body, showing where the octreotide has attached to any tumors.

Reasons for Use and Other Considerations

The Octreoscan can help the healthcare team figure out if a pancreatic tumor is a PNET or exocrine pancreatic cancer. Doctors might order this test if blood or urine tests show high levels of pancreatic hormones, since that could be a sign of PNETs. It may be used along with CT or MRI scans to find exactly where the tumors are.

Endoscopic Retrograde Cholangiopancreatography (ERCP)

During an ERCP, the doctor guides a thin, lighted tube called an endoscope through the patient's mouth into the stomach and the duodenum. They inject a dye through a narrower tube, called a catheter, inside the endoscope. X-ray pictures show whether a tumor or other condition has narrowed or blocked the pancreatic ducts.

ERCP is usually used to look at or treat jaundice and blocked pancreatic or bile ducts. During the ERCP, the doctor can place a stent into the blocked duct to keep it open and allow bile to flow. ERCP can also be used to get biopsies (see page 22).

Reasons for Use and Other Considerations

ERCP is an outpatient procedure usually done in a hospital or **ambulatory surgery center**. Patients are prescribed a sedative to help them relax and anesthesia to block pain.

Complications from ERCP are uncommon. About 5–7% of patients get pancreatitis (inflammation of the pancreas). Often the pancreatitis is mild, but it can be serious. Other rare complications of ERCP are gastrointestinal bleeding, tearing from the endoscope, allergic reactions to anesthesia and infection. Sometimes patients are admitted to the hospital for one night of observation after an ERCP.

Laparoscopy

Diagnostic laparoscopy is a minimally invasive surgery. The surgeon directly views the abdominal organs to see if a pancreatic tumor has spread to other places. The surgeon inserts a camera through a small cut in the abdomen to look at the organs. Sometimes, the surgeon may use other small tools to help move organs or structures so they can see the area better. The patient receives general anesthesia, so they are completely asleep.

Reasons for Use and Other Considerations

Laparoscopy may be used if it is unclear whether the pancreatic tumor has spread. If the tumor has not spread, the surgeon may then remove the tumor by making a larger cut in the abdomen. The laparoscopic cut is small. Therefore, recovery time from laparoscopy is generally short. Complications are rare but include allergic reactions to anesthesia and infection.

BIOPSY

A biopsy is the only way to know for sure that the tumor is a PNET. During a biopsy, the doctor removes tissue samples from the tumor. They can get these samples through surgery or procedures like EUS or ERCP (see page 21). A **pathologist**, a doctor who identifies diseases by studying cells and tissues, will look at the samples. They will see if there are cancer cells, what type of cancer cells they are and how much the cancer cells look like normal cells (**differentiation**). This information can give a correct diagnosis and guide treatment decisions.

PNETs can be hard to diagnose. Therefore, it is very important that a pathologist experienced in pancreatic or gastrointestinal tumors looks at the samples.

Fine-needle Aspiration (FNA)

FNA is the most common way to biopsy a pancreatic tumor. It uses a thin needle to get the tumor sample. There are two ways of doing an FNA. In a percutaneous FNA, the needle is put through the skin of the abdomen into the pancreas. This cannot be used for all tumors.

An EUS-guided FNA is done during an endoscopic ultrasound (see page 13). The doctor guides a thin, lighted tube called an endoscope down the patient's throat. Then, they pass a needle through the tube to get to the tumor. The doctor can get both imaging and a biopsy at the same time. They can get many samples easily from any part of the pancreas. Done by a specialized and experienced doctor, this is usually the most accurate way to get a pancreatic biopsy.

Biopsies During ERCP

A brush biopsy or forceps biopsy can be done during an ERCP (see page 21). In a brush biopsy, the doctor passes a small brush through the endoscope to rub off cells from the bile or pancreatic ducts. An ERCP brush biopsy is usually less effective in diagnosing pancreatic cancer than other biopsy methods. In a forceps biopsy, a doctor passes forceps (tongs) through the endoscope to grab a small piece of the tumor.

Core Needle Biopsy

A core needle biopsy removes a small cylinder of tissue (core), getting a larger sample than an FNA. It is usually done percutaneously, meaning the needle is inserted through the skin of the abdomen. In rare cases, it can be done during an EUS. Patients may need a core needle biopsy to get enough tissue for tumor biomarker testing (see page 24).

After the Biopsy

Treatment depends on the specific type of pancreatic cancer. A confirmed diagnosis is recommended before starting chemotherapy or radiation. If the tumor is surgically **resectable** and other tests and symptoms suggest pancreatic cancer, the surgeon may operate before having a confirmed diagnosis.

After a confirmed pancreatic cancer diagnosis, the doctor may order more or different tests to help decide what treatment would be best. Every tumor is different, and a tumor may have changes, called mutations. These mutations may lead to more treatment options (see "Precision Medicine" section on page 44). All patients diagnosed with pancreatic cancer should get genetic (germline) testing for inherited mutations and tumor biomarker testing. Information about inherited mutations may also help family members understand their risk (see page 6).

GENETIC TESTING AND COUNSELING

All patients diagnosed with pancreatic cancer should get genetic (germline) testing. Genetic testing looks for specific mutations (changes) in genes that the patient may have inherited from their parents. Genetic testing can help doctors pick the best treatment possible by learning more about the tumor's biology. The results can also help family members know their risk. Patients can get tested at diagnosis or later (see page 44).

PanCAN recommends all pancreatic cancer patients get genetic (germline) testing and genetic counseling. A genetic counselor is a healthcare professional who evaluates a person's risk of getting hereditary (inherited) diseases over time. They can help figure out which genetic tests may make sense. Patients should tell their doctor about family history of cancer – including melanoma and cancers of the pancreas, colon, rectum, breast and ovaries – and other digestive diseases, including pancreatitis. Even patients without a family history or suspicion of an inherited mutation should get genetic testing.

If a mutation is found, at-risk relatives should be offered genetic counseling. If they also have the mutation, they may be able to enroll in surveillance programs. Identifying germline mutations can also help doctors choose the best treatment possible for each patient.

BLOOD TESTS

There is not one specific blood test that can find or diagnose a PNET. However, blood tests can help with diagnosis. They can show high hormone levels, including **pancreatic polypeptide (PP)**. They can also show a molecule called **chromogranin A (cgA)**. More than 60% of PNET patients have a high cgA level. A high cgA level may suggest a PNET. It will not show what type of PNET is there. Someone with a normal cgA level may still have a tumor. There are also commercially available multi-cancer early detection tests that may be able to detect the presence of cancer in the body, including PNET or pancreatic exocrine tumors. Blood tests alone will not tell for certain whether someone has a PNET, but combined with imaging tests, they can give doctors more information to make a diagnosis.

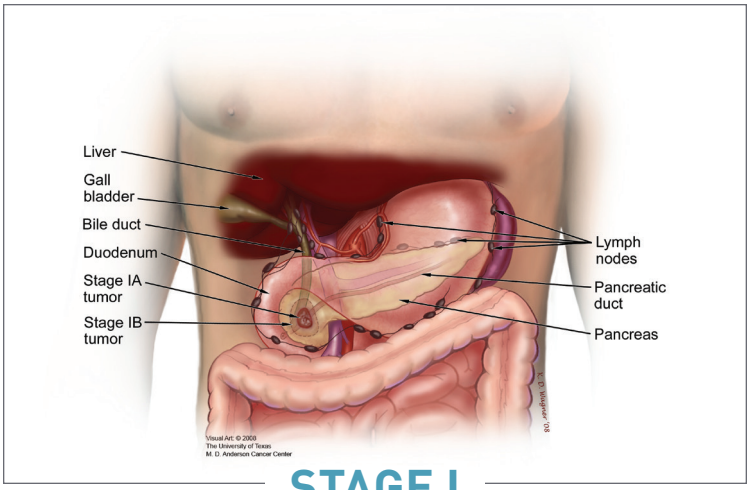
STAGING

Staging is the process the doctor uses to describe the cancer's size and how much it has spread in the body. After a pancreatic cancer diagnosis, patients may need more imaging tests and surgery to know the cancer stage. Knowing the correct stage helps the doctor determine the outlook and best treatment plan.

There are three ways to describe the stages of pancreatic cancer: stage number, extent and surgical resection category. The stage number is written in roman numerals (I=1, II=2, III=3, IV=4). It describes the size and location of the cancer. The higher the number, the more the cancer has grown or spread. Extent describes how much the cancer has spread. Localized

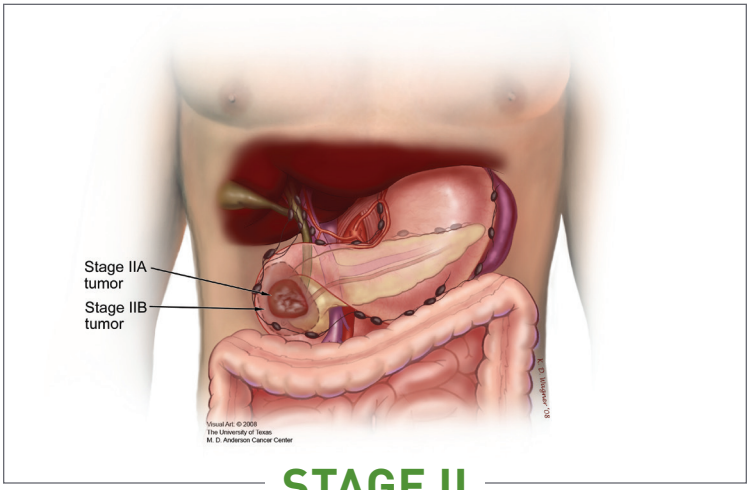
means it is in one area, locally advanced means it is starting to spread and metastatic means it has spread to faraway organs. The surgical resection category describes whether the tumor can be surgically removed. The doctor may use one or more of these methods to describe the stage. This chart details each stage. Also, see Figures 3–6 on pages 27-28.

	Description	*Extent of the Tumor*
STAGE I	**Tumor is only in the pancreas and measures less than 2 centimeters (cm). The tumor does not involve any lymph nodes or other organs.**	**Localized**
STAGE II	**Tumor measures 2-4 cm and is limited to the pancreas or directly extends beyond the pancreas and may be invading the duodenum or common bile duct.**	**Localized**
STAGE III	**Tumor involves major local arteries and may involve adjacent organs. Cancer may or may not be in nearby lymph nodes.**	**Locally Advanced**
STAGE IV	**Disease has metastasized (spread) to another part of the body, like the liver, abdominal wall, lungs, or faraway lymph nodes. Primary tumor may be any size.**	**Metastatic**



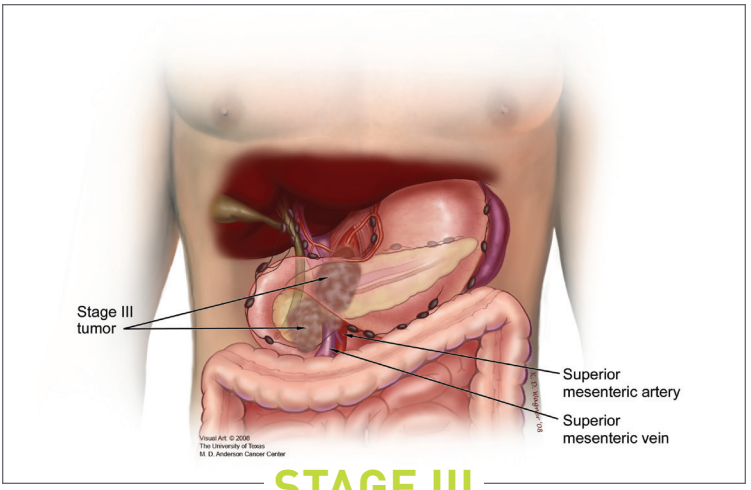
STAGE I

Pancreatic Cancer
Figure 3



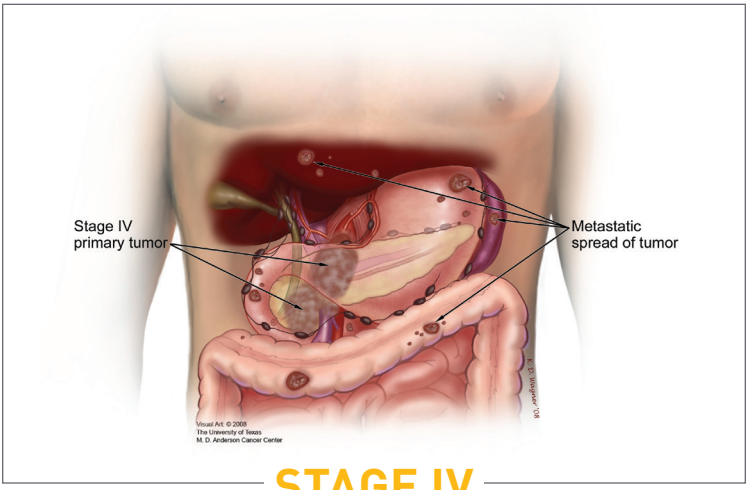
STAGE II

Pancreatic Cancer
Figure 4



STAGE III

Pancreatic Cancer
Figure 5



STAGE IV

Pancreatic Cancer
Figure 6

The Pancreatic Cancer Action Network would like to thank Kathleen Wagner and support from the Hamill Foundation and the Pickelner Fund for Pancreatic Cancer Research at MD Anderson Cancer Center for the illustrations provided on these pages.

PNETs are also described in terms of their grade and differentiation. This is usually decided after viewing a sample of the tumor cells under a microscope.

Tumor grade is a measure of how fast the cells grow and spread. PNETs can be grade 1, 2, 3 or 4 depending on certain measurements and differentiation. Differentiation refers to how similar the tumor cells look to normal, healthy cells. Tumor cells that do not look similar to normal, healthy cells are called "poorly differentiated." These cells tend to be more aggressive and faster growing. Tumor cells that have some similarities to healthy cells are called "moderately differentiated." Tumor cells that look very similar to healthy cells are called "well differentiated." These cells tend to be slower growing and less aggressive. It is important to note that even if a tumor is classified as well differentiated, it may still have a high grade.

Well differentiated	**Well-differentiated cells look more like healthy cells. These tend to grow and spread slowly.**
Moderately differentiated	**These cells have some similarities with healthy cells, and some with poorly differentiated cells. These tend to grow and spread slowly.**
Poorly differentiated	**Poorly differentiated cells look less like healthy cells. These tend to be more aggressive and faster growing.**
Undifferentiated	**These cells do not have specialized structures or functions. These tend to be more aggressive and faster growing.**

Grade 1	**These cells divide and grow slowly. Grade 1 tumors are well differentiated.**
Grade 2	**These cells divide and grow at an intermediate rate and are often moderately differentiated.**
Grade 3	**These cells divide and grow at a fast rate and are often poorly differentiated.**
Grade 4	**These cells divide and grow at a fast rate. These cells are undifferentiated.**

SURGICAL RESECTION CATEGORY

In general, tumors are split into three categories that help doctors decide whether surgery would be useful and safe.

Resectable

Tumors that can be surgically removed. The tumor is only in the pancreas or extends just beyond it but does not involve any major local arteries or veins.

Borderline Resectable

Tumors that may or may not be surgically removed at diagnosis. The tumor may or may not involve major nearby arteries (**celiac axis** and superior mesenteric artery) or veins. The cancer has not metastasized (spread) to other organs. Patients diagnosed with borderline resectable pancreatic cancer may receive neoadjuvant therapy, which is chemotherapy, radiation or both treatments before surgery. If the tumor affects blood vessels, **neoadjuvant therapy** may improve the chances that surgery can remove all of the cancer.

Different institutions and surgeons define the term "borderline resectable" differently. It is critical to get an opinion from a specialized pancreatic surgeon with experience in advanced techniques, like vein resection, at an institution that performs a high volume of pancreatic surgeries.

Unresectable

Tumors that cannot be surgically removed. The tumor has either metastasized (spread) to other organs or cannot be completely removed with surgery.

TREATMENT

CHOOSING A DOCTOR, HOSPITAL AND TREATMENT PLAN

PNETs are rare. Seeing pancreatic cancer specialists — doctors who diagnose and treat a high volume of pancreatic cancer patients — improves outcomes. This is especially true for patients considering surgery. General oncologists and surgeons may not often see patients with this type of cancer. Pancreatic surgery is also very complicated. Therefore, it is important to find a surgeon at a hospital that performs many pancreatic surgeries. PanCAN has a list of PNET specialists and high-volume surgeons.

Before a visit with the doctor, patients should gather their medical paperwork, including test results. Having this information may help the patient avoid redoing tests. Each hospital will usually need to review the biopsy slides and imaging studies. It helps to bring original slides and films or digital copies of the films.

Patients have the right to get a second opinion. PanCAN strongly recommends seeking a second opinion as needed or at any point in the diagnosis. Getting a second opinion is common. It does not mean the first doctor is wrong. It just means the patient wants to confirm the diagnosis and treatment options before deciding on next steps. Speaking to other doctors before choosing a specialist can give patients valuable information.

You should feel comfortable and supported by your healthcare team. PanCAN strongly recommends seeking a healthcare team that suits all of your physical, mental, social and emotional needs.

Whenever possible, PanCAN recommends consulting with a multidisciplinary team of specialists. An ideal team would include expertise in radiology, gastroenterology, medical oncology, radiation oncology, surgery, pathology, supportive (palliative) care and nutrition.

TREATMENT OPTIONS FOR PNETS

After diagnosis, the patient will need to consider treatment options. Pancreatic cancer treatment depends on the disease stage, the patient's general health, and whether the tumor is benign or malignant.

Low grade, well-differentiated PNETs grow slowly and are less aggressive than other pancreatic cancer types. There are also different treatment options for these tumors. High grade, poorly differentiated tumors are more aggressive and faster growing. However, they tend to respond well to chemotherapy treatments.

There is not a standard of care, or standard treatment, for PNETs. Commonly used treatments for PNETs include surgery, chemotherapy, radiation therapy, targeted therapy, liver-directed therapy, hormone therapy and clinical trials. They may be used alone or together. Patients may get standard (approved) treatments or may take part in clinical trials (see page 42). PanCAN strongly recommends clinical trials at diagnosis and during every treatment decision. Every treatment available today was approved through a clinical trial.

SURGERY

For patients with localized PNETs, surgery is the best option for long-term survival of pancreatic cancer. Data show high-volume surgeons at high-volume hospitals have higher success rates and fewer complications. High-volume surgeons may also be better able to understand if a patient can have surgery. PanCAN strongly recommends patients see a surgeon who performs a high volume of pancreatic surgeries (more than 15 per year) – both to understand if surgery is an option and to perform the surgery. In general, chemotherapy or other treatment is not recommended after surgery for localized PNETs.

Surgical resection for non-functioning PNETs is generally recommended. If the tumor is very small or located in a part of the pancreas that is less likely to cause symptoms, a doctor might recommend close observation rather than surgery. Surgical resection for functional PNETs depends on the type of tumor. Some functional PNETs like gastrinomas are more likely to become malignant, so doctors might recommend surgery. If the tumor is small enough to be removed safely, a commonly used technique for PNETs is called enucleation. This is a type of **laparoscopic minimally invasive surgery** that uses small instruments to remove only the tumor itself, rather than surrounding tissue.

Even if the patient cannot have their whole tumor removed, at times they can have a part of it removed. Removing only part of the tumor is called debulking. Some patients who have had this surgery may later find that the tumor has reappeared in the remaining part of their pancreas. In these cases, another surgery to remove the tumor is sometimes possible.

CHEMOTHERAPY

Chemotherapy uses drugs to destroy or shrink cancer cells by stopping them from growing and dividing. It is systemic treatment. This means that the drugs travel through the bloodstream to damage cancer cells throughout the body. Chemotherapy can be given alone or with other treatment types, like surgery, targeted therapy or radiation.

Several chemotherapy drugs are often used to treat PNETs. They include **streptozocin, fluorouracil (5-FU), doxorubicin, DTIC-Dome® (dacarbazine), Platinol AQ® (cisplatin), Temodar® (temozolomide), etoposide (VP-16) and Xeloda® (capecitabine)**. These drugs can be used with each other. For example, cisplatin, a common chemotherapy drug, is often used in combination with etoposide (VP-16) in the treatment of poorly differentiated PNETs.

Chemotherapy drugs can be injected into a vein (intravenously) or taken by mouth (orally). Usually, chemotherapy is an outpatient treatment at a hospital, clinic or doctor's office. The time needed for each treatment session depends on the type of chemotherapy.

A doctor may also prescribe chemotherapy drugs off label. **Off-label** treatments are approved by the United States **Food and Drug Administration (FDA)** to treat another cancer, not pancreatic cancer. But since these treatments have shown some promise in pancreatic cancer and are already FDA-approved for another cancer, a doctor may prescribe a chemotherapy drug off label when it makes sense for the patient.

Chemotherapy attacks and harms all quickly dividing cells, including healthy cells. So, it can cause side effects. Healthy cells that divide quickly are more likely to be damaged. These include bone marrow, blood cells, hair follicles and cells in the reproductive and digestive tracts. Common side effects are low blood cell counts, loss of hair, nausea, vomiting, diarrhea, fatigue, appetite loss and neuropathy (tingling or numbness in the hands and feet). Patients can get medicine and other supportive care for many of the common side effects (see page 47).

RADIATION THERAPY

Radiation therapy directs high-energy X-rays at the tumor to shrink it or slow its growth. Radiation therapy also helps lessen pain and other symptoms the tumor causes. Patients may get radiation therapy alone or with chemotherapy.

The goal of radiation is to treat the tumor or tumor bed (area around the tumor) with a high enough dose to keep the cancer from growing or coming back, while not harming the healthy organs or tissue nearby. Radiation may shrink the tumor. Most often, radiation destroys the cancer cells, but the tumor size does not change. Because radiation therapy is directed to a specific area, it is called a localized treatment.

There are three main types of radiation therapy considered for PNETs: **external beam radiation therapy, radioembolization (see liver-directed therapy section below) and peptide receptor radionuclide therapy (PRRT)**. Patients whose PNETs have somatostatin receptors may get PRRT (see page 38).

For patients with metastatic PNETs, radiation is sometimes used to spot treat specific metastatic sites, like those in the bones.

Patients should discuss the radiation treatment options with their radiation oncologists. Ideally, these doctors will be part of the patient's multidisciplinary team.

Radiation therapy treatment sessions do not hurt. Patients may have some discomfort in their stomach area toward the end of the treatment series. Radiation therapy effects can build up over time. Different types of radiation therapy have different effects. The most common side effects of radiation therapy for pancreatic cancer are appetite loss, skin redness and irritation, nausea, vomiting, diarrhea and fatigue. Patients should talk to their radiation oncologist if they have side effects after treatment. A healthcare professional can prescribe medicine or supportive care to treat many side effects.

Peptide Reception Radionuclide Therapy (PRRT)

PRRT is a type of internal radiation therapy used to treat PNETs that have somatostatin receptors (SSTRs) on their surface. In PRRT, a radioactive substance is attached to a synthetic form of somatostatin. Patients get an IV of the radioactive substance. The substance then attaches to the somatostatin receptors on the tumor and delivers radiation to the tumor from inside the patient's body. **LUTATHERA®** (lutetium Lu 177 dotatate) is a type of PRRT approved for the treatment of PNETs.

TARGETED THERAPY

Targeted therapy uses drugs to attack unique parts of cancer cells. It does little harm to healthy cells. Targeted therapies often work by binding to a particular molecule in the cancer cell. This blocks the process that changes normal cells into cancer, stopping the tumor's abnormal growth.

Sutent® (sunitinib) is an FDA-approved targeted therapy for advanced PNETs. It targets receptors that are on some PNETs and stops the blood vessels in the tumor from growing or developing. Common side effects from Sutent® are fatigue, diarrhea, nausea, vomiting, heartburn, taste changes, high blood pressure and low blood cell counts.

Afinitor® (everolimus) is an FDA-approved targeted therapy for advanced PNETs. It controls cell growth and the production of new proteins, cells and blood vessels. Common side effects from Afinitor® are mouth sores, diarrhea, fatigue, rash and infections.

Researchers are studying other targeted therapies for pancreatic cancer in the laboratory and in clinical trials.

LIVER-DIRECTED THERAPY

For neuroendocrine tumors that have spread only to the liver, liver-directed therapies may be an option. These include surgery, hepatic artery embolization, chemoembolization, radiofrequency ablation and radioembolization.

Liver Surgery

Surgery may be possible if the tumor has spread to the liver. Research shows that patients who have liver metastases removed through surgery live longer.

Hepatic Artery Embolization (HAE)

HAE is a minimally invasive procedure that decreases blood supply to a liver tumor. A thin tube called a catheter is put into an artery in the inner thigh. The catheter is threaded up into the hepatic artery which supplies blood to the liver and the tumor. Small beads are injected into the artery to block blood and nutrient flow to the tumor. The goal is to lessen pain, stop hormone overproduction and possibly shrink the tumor. The procedure can cause nausea, vomiting, abdominal pain or discomfort, hiccups, low grade fever, weakness, liver abscess or infection, stomach or bowel bleeding or bowel action slowing down or stopping.

Chemoembolization

Chemoembolization uses the same process as the hepatic artery embolization. Chemotherapy drugs are injected through the catheter into the blood vessel leading to the cancer. Then, small beads are injected into this vessel to block the blood flow. This traps the chemotherapy drugs inside the tumor so it does not spread to other parts of the body. Side effects are similar to those that may occur with hepatic artery embolization.

Radiofrequency Ablation (RFA)

RFA heats and destroys cancer cells. The doctor uses imaging like ultrasound, CT, or MRI to help guide an electrode into the tumor. Radio waves then pass through the electrode to heat and destroy the tumor. This procedure can be done surgically, percutaneously (through the skin) or laparoscopically (minimally invasive surgery). Side effects of this procedure can include infection, pain, fever and bleeding.

Radioembolization (Y-90 microspheres)

Sometimes RFA, HAE and chemoembolization are not possible. In this case, experimental Y-90 microspheres may be used. Y-90 microspheres are tiny beads filled with a radioactive element called yttrium-90. They are injected into the hepatic artery and travel to the liver metastases to deliver radiation directly to the tumors. Most of the radiation is delivered to the tumor within two weeks. It usually does not affect cells outside of the liver. This procedure can cause infection, allergic reaction to the contrast substance and bruising or bleeding at the injection site. If the microspheres get stuck in the wrong place, the patient may develop an ulcer in the stomach or duodenum (first part of the small intestine).

HORMONE THERAPY

When PNETs make too many hormones, they can cause symptoms like diarrhea, blood sugar problems and high calcium levels in the blood (hypercalcemia). Hormone therapies can help lessen these symptoms. They may also help stop the tumor from growing.

Sandostatin® (octreotide) is a hormone therapy often used to treat these symptoms. It is given either intravenously (through the veins) or subcutaneously (an injection under the skin). Sandostatin® is similar to the hormone somatostatin that the pancreatic islet cells make. Like somatostatin, Sandostatin® keeps large amounts of hormones from entering the blood. Some research suggests that Sandostatin® may also slow tumor growth.

Somatuline® Depot (Lanreotide) is another hormone therapy that is FDA-approved for certain types of inoperable PNETs. It is given as a subcutaneous (under the skin) injection. Somatuline® Depot is also like somatostatin. It binds to somatostatin receptors in the tumor to slow tumor growth.

CLINICAL TRIALS

Clinical trials are research studies. They investigate potential treatments, diagnostic tools, early detection methods and ways to prevent diseases like pancreatic cancer. Many pancreatic cancer clinical trials are looking at new investigational treatments and how patients respond to them. New treatments must show positive results in laboratory or animal studies before they can be tested in humans.

Clinical trials may test new treatments, treatments already available for other diseases or both. All cancers are different; therefore, a drug that is already FDA-approved to treat one type of cancer may not be approved to treat pancreatic cancer. For any pancreatic cancer therapy to be approved, it must go through clinical trials with pancreatic cancer patients. The FDA closely watches clinical trials to protect the participants and the public. Clinical trials are the safest and quickest way to know whether new treatments work for patients.

A new treatment must pass through three clinical trial phases before it is eligible for FDA approval. The treatment must prove safe and effective at each phase for it to move onto the next phase of clinical trial testing.

Phase I

Phase I is the first step in testing a new investigational treatment or treatment combination in humans. At this point, the experimental treatment has shown effectiveness in the laboratory. A small group of people (usually 20 – 40) receive the new investigational treatment. The goal of phase I studies is to learn if the drug is safe, how much of it patients should receive and how the body processes it. Participants are closely monitored for side effects. Doses are changed as needed. Often, patients who have already had multiple treatments are more likely to be able to join phase I trials than later-phase trials. This is typically because they have more flexible eligibility criteria. Phase I trials may be open to patients with any type of solid tumor – like breast, lung, and prostate tumors – and not just those with pancreatic tumors. Patients often choose to take part in phase I clinical trials when they are not eligible for later-phase trials or when they are not responding to current treatments.

Phase II

Phase II clinical trials involve a larger group of people (usually 25 – 100). Participants usually have a specific disease, like pancreatic cancer. The goal of a phase II clinical trial is to see the investigational treatment's effect against pancreatic cancer while testing its safety even more.

Some phase II trials are randomized. This means that patients are assigned by chance to different treatment groups. These treatment groups could be the standard of care treatment and the experimental treatment. Or they could be two experimental treatments.

Phase III

Phase III studies test how the new treatment compares with the approved standard of care treatment. These trials may involve 100 – 1,000 or more people. They figure out if the new investigational treatment is more effective than the

standard of care in the study participants. Phase III trials are randomized. This means that patients are assigned by chance to different treatment groups — the new treatment group or the control group. The control group is usually the standard of care treatment. Patients in the control group will typically not receive a placebo, or sugar pill, as it would be unethical to not provide treatment. To prevent bias, neither the doctor nor the patient gets to choose the treatment group. In some phase III trials, neither the patient nor the doctor knows which treatment the patient is receiving. If the new treatment is effective and meets safety requirements through all three phases, the trial sponsor may apply to the FDA for approval of the new treatment.

Phase IV

Phase IV trials happen after a therapy is approved by the FDA. As more people get the treatment, researchers look at long-term safety, cost effectiveness and side effects.

PRECISION MEDICINE

Precision medicine is an emerging field in cancer treatment. It is treatment based on the patient's biology. **Biomarker testing of tumor tissue** shows your tumor's biology, such as genes and proteins in the tumor. **Genetic testing for inherited mutations** shows mutations (changes) you were born with. This information can help the doctor identify precision treatments for each patient, instead of treating all pancreatic cancer patients with the same drugs.

Researchers are studying drugs in clinical trials that may target specific mutations. If a treatment is based on stopping tumor growth by targeting a specific mutation, the patient must have that mutation. The only way for patients to know if they have a mutation that can be targeted in this way is to receive tumor biomarker testing and genetic testing for inherited mutations. Tumor biomarker testing uses a biopsy of the patient's tumor. Genetic testing uses a blood or saliva sample.

Every pancreatic cancer patient is different. PanCAN strongly recommends all pancreatic cancer patients get genetic testing for inherited mutations as soon as possible after diagnosis and biomarker testing of their tumor tissue to help determine the best treatment options. Patients should talk to their healthcare team about both tests.

PanCAN's Know Your Tumor®

Know Your Tumor is PanCAN's precision medicine service. It gives eligible pancreatic cancer patients and their doctors information about the patient's biology and related treatment options. Many patients who have used Know Your Tumor have found it an important part of their treatment decision-making process.

SIDE EFFECTS

Side effects of treatment will depend on the patient and their treatment type, dosage and length. Some patients may not have any side effects. The doctor and patient often must balance possible side effects with the benefits of treatment. The healthcare team can help patients manage side effects, but they can only help if they know what the patient is experiencing. Tell them about any side effects or pain.

The next pages list common treatment side effects and tips for managing them. This does not include all possible side effects. Please talk to your doctor before using these tips.

SUGGESTIONS FOR MANAGING SIDE EFFECTS

Loss of Appetite

Schedule six to eight small meals and snacks per day. The doctor can prescribe medicine to help the patient's appetite.

Constipation

Drink plenty of non-caffeinated fluids. Eat foods high in fiber. Avoid fatty and fried foods. Moderate exercise can help.

Diarrhea or Abdominal Cramping

A doctor can prescribe medicines or tell the patient which over-the-counter medicines might be right for them. A dietitian can guide dietary changes.

Fatigue

A doctor can prescribe medicines that may boost red blood cells and help prevent fatigue. A dietitian can guide beneficial dietary changes that may help manage exhaustion. It is important for patients to stay active. Short walks can boost energy and short rests throughout the day may also help.

Hair Loss

Avoid frequent hair washing. Use a gentle shampoo. Gently pat hair dry. Use a wide-tooth comb instead of a brush. Avoid using hair clips, rubber bands, hair products and hair dryers. Wear head coverings outside.

Hand/Foot Syndrome

This condition causes redness, tenderness, dryness and peeling of the palms and soles. Numbness or tingling may also develop. To avoid harming the hands and feet, wear cotton socks or gloves. Avoid tight-fitting shoes. Soak hands in cool water for 10 minutes and then apply a mild moisturizer or petroleum jelly. Cooling the skin with ice packs may also help relieve pain and tenderness. Ask the doctor if an oral vitamin B6 supplement is appropriate.

Low White Blood Cell Count

A doctor can prescribe medicines or change chemotherapy dosage.

Low Red Blood Cell Count

The patient may need a blood transfusion. A doctor may prescribe medicine or change chemotherapy dosage.

Low Blood Platelet Count

The patient may need a blood transfusion. A doctor may prescribe medicine or change chemotherapy dosage.

Mouth Sores

Eat soft, moist, bland foods. Avoid spicy and acidic foods. Caffeine and alcohol may irritate the mouth. Drinking through a straw may help. High protein foods will help mouth sores recover faster. Rinse mouth with cool water or a mild mix of baking soda and water. Use a soft-bristle toothbrush.

Nail Changes

Avoid biting nails, pushing back cuticles, and using fake nails or wraps. Talk to a doctor before having a manicure or pedicure. Wear gloves during household chores. Moisturize hands and feet often. If the nail area becomes red or swollen, treat with antibacterial soap, antibacterial ointment or antifungal ointment to prevent infection.

Nausea and Vomiting

A doctor can prescribe medicines or tell the patient which over-the-counter medicines might be right for them. A dietitian can guide diet changes. Do not eat a lot of fried, spicy, or rich foods. Drink cool or room temperature liquids between meals to stay hydrated and avoid feeling too full. A motion sickness wristband may help control nausea. Wear loose clothing. Get fresh air.

Neuropathy

This condition causes tingling or numbness in the hands, feet, and sometimes other body parts. To protect hands and feet,

wear cotton socks or gloves. Avoid tight-fitting shoes. Avoid hot or cold temperatures. Ask the doctor about pain medicines, antidepressants, antiseizure medicines or other treatments.

Skin Rash, Redness or Irritation

Some medications can cause skin changes including rash. Changes in treatment dosage and in personal care may help soothe the skin. Examples include washing the affected area with warm water and mild soap, using lotions without alcohol, perfumes or other irritants, avoiding direct sunlight and using sunscreen with an SPF of 15 or higher. Talk to a doctor before using over-the-counter treatments.

Taste Changes (food may taste bland or metallic)

Avoid foods that cause bad tastes. Changes in treatment dosage may help. Eat small meals often. Eating tart foods may help if you have metallic or bitter taste. Cold food might taste better than hot food.

FINANCIAL ASSISTANCE

Treatment for pancreatic cancer can become expensive, especially for patients with limited access to resources or health insurance coverage. It is important that patients reach out to their healthcare team if they have concerns about paying for care. Social workers, nurse case managers, counselors and other professionals in most clinics have access to community, state and federal resources that may be able to help. These professionals can also connect patients with transportation resources, local support groups and caregiver assistance.

CULTURALLY SENSITIVE CARE

Culturally sensitive care is important when being treated for pancreatic cancer. Patients of different ages, races, cultures, religions, orientations and lived experiences might have different goals. Some patients may value pain management, while others might value curative treatment over comfort. Patients should be open with their healthcare team about these priorities so that caregivers can provide respectful, dignified care that meets any physical, social, emotional and spiritual needs.

GLOSSARY

Abdomen: The belly area. The part of the body between the ribs and the hips. It holds the stomach, liver, gallbladder, spleen, intestines, pancreas, kidneys and bladder.

Adenocarcinoma: The most common type of pancreatic cancer. It grows from the cells lining the pancreatic duct that make enzymes for digestion.

Adjuvant therapy: A treatment given after surgery. It may be chemotherapy, radiation therapy, hormone therapy, targeted therapy or immunotherapy.

Ambulatory surgery center: A facility that does minimally invasive, outpatient surgeries. Patients must stay at the center for two to four hours after most ambulatory surgeries.

Ampulla of Vater: The place where the liver and pancreas ducts join when they enter the small intestine.

Anesthesia: The loss of feeling or awareness caused by drugs. Local anesthesia causes feeling loss in one part of the body. General anesthesia puts the person to sleep.

Antigen: A substance that causes the immune system to respond.

Ascites: Abnormal buildup of fluid in the belly. It is usually related to cancer.

Benign: A term used to describe a growth that is not cancerous. Benign tumors do not spread to nearby tissues or other parts of the body.

Bile: A fluid the liver makes. The gallbladder stores it. Bile is released into the small intestine, where it helps digest fat.

Bilirubin: A substance the liver makes when the body breaks down hemoglobin. Hemoglobin carries oxygen in red blood cells. Bilirubin is yellowish-green and is eliminated in "bile," a fluid made by the liver and stored by the gallbladder. When bile ducts become blocked, jaundice can occur.

Biopsy: A procedure to remove tissue from the body so it can be looked at to see whether there is cancer.

Blood clot: A clump of blood that forms in a vein. When it forms in a deep vein, it is called deep vein thrombosis (DVT). See "deep vein thrombosis."

Body mass index (BMI): A number that measures a person's body fat based on their height and weight. For adults, BMI is grouped into weight status categories: underweight, normal weight, overweight and obese.

Cancer: A group of cells in the body that grows and divides uncontrollably and can invade and damage tissues and organs. Cancer cells sometimes spread from the first cancer site and form new tumors in other parts of the body.

Cancer cachexia (pronounced kə-kĕk'sē-ə): Weight loss due to the body's improper use of calories and proteins. Cancer cachexia causes fatigue and weakness. It may weaken the body's response to treatment.

Catheter: A tube that allows fluid to pass into or out of a body cavity or blood vessel.

Celiac axis: A short, thick artery. It comes from the largest artery in the body, the aorta. The celiac axis starts just below the diaphragm and divides into the gastric, hepatic and splenic arteries.

Celiac plexus block: A procedure to destroy the nerves in the celiac plexus of the stomach area. A substance like alcohol is injected into the celiac plexus. It helps the patient no longer feel pain.

Clinical trial: A research study that investigates new treatments or new combinations of treatments. Pancreatic cancer clinical trials are the only way for researchers to know if treatments developed in the laboratory will help people with pancreatic cancer. They also give patients the chance to get a promising new treatment.

Common bile duct: The duct that carries bile from the gallbladder and liver into the upper part of the small intestine.

Constipation: Having hard, dry bowel movements. It can cause discomfort passing stools or not passing stools often.

Cyst: An enclosed, fluid-filled sac in the body.

Deep vein thrombosis (DVT): A blood clot in a deep vein. It is usually in the legs or feet. DVT can cause serious problems if the clot breaks loose and travels to the lungs. Symptoms of DVT include swelling, pain when walking or flexing the foot and sometimes redness in one leg.

Deoxyribonucleic acid (DNA): The molecules inside cells that carry genetic information and pass it from one generation to the next.

Diabetes: A disease that causes the body to not make or use the hormone insulin. In type 1 diabetes, the pancreas does not make insulin. In type 2 diabetes, the pancreas does not make enough insulin, or the body does not use it properly. It is manageable but not curable.

Diarrhea: Loose bowel movements that happen a lot.

Dietitian: A healthcare professional trained in food, nutrition, biochemistry and physiology. A dietitian can help each pancreatic cancer patient understand the right diet for them.

Diuretic: A substance that increases urination.

Doxorubicin: A chemotherapy drug used to treat PNETs.

DTIC-Dome® (dacarbazine): A chemotherapy drug used to treat PNETs.

Duodenum: The first portion of the small intestine. It is just below the stomach.

Endocrine gland: An organ that puts hormones into the bloodstream for other body parts to use. The endocrine gland of the pancreas makes insulin and glucagon. These hormones work together to control blood sugar levels.

Enzyme: A protein that causes a chemical reaction in the body. Pancreatic enzymes help the body digest food.

Etoposide (VP-16): A chemotherapy drug used to treat PNETs.

Exocrine gland: An organ that sends chemicals through ducts into the body. The exocrine gland of the pancreas makes three types of enzymes that help digest food. Lipase helps break down fats, amylase helps break down carbohydrates and protease helps break down proteins.

External beam radiation therapy: Radiation therapy delivered by a machine outside of the body. The machine directs radiation through the skin to the tumor or the area where the tumor was surgically removed.

Familial: A trait that is common in a family who is genetically related. This trait may be caused by genetic factors, environmental factors, or both.

5-FU (fluorouracil): A chemotherapy drug used to treat pancreatic cancer. It is often used to treat PNETs and in clinical trials in combination with other drugs or radiation.

Food and Drug Administration (FDA): A United States government agency. It promotes and protects public health by ensuring medical treatments and devices are safe and effective.

Gallbladder: A small organ below the liver. It stores bile, made by the liver.

Gastrin: The major hormone that controls acid released in the stomach.

Gastrointestinal: A word that applies to the organs and structures that process and prepare food to be used for energy.

Gemzar® (gemcitabine): An FDA-approved chemotherapy drug for pancreatic cancer that cannot be surgically removed.

Genetic: A word that applies to a trait that is transferred from parent to child through genes.

Genetic counselor: A health professional with a graduate degree in medical genetics and counseling. Genetic counselors work with families who may be at risk for inherited conditions. They help families understand their risk for diseases based on genes.

Gland: An organ that makes and releases substances. The pancreas is a gland.

Glucagon: A hormone the pancreatic islet cells make. Glucagon increases the level of glucose (sugar) in the blood.

Hereditary: A trait inherited through genes passed from parent to child.

Hormone: A chemical made by a gland. It travels through the blood and influences how cells or organs in a different part of the body act.

Immunotherapy: A type of treatment that helps the body's immune system fight cancer. It may also control side effects from other cancer treatments.

Insulin: A hormone the pancreatic islet cells make. Insulin lowers the level of glucose (sugar) in the blood.

Internal radiation therapy (brachytherapy): Radiation therapy that works by implanting radioactive material in or near the cancer.

Intravenous (IV): Injection of a liquid directly into a vein.

Islet cell: A pancreatic cell that makes hormones and releases them into the bloodstream.

Jaundice: A yellowing of the skin or eyes. It's caused by too-high levels of bilirubin in the blood. In most pancreatic cancer patients that get jaundice, it happens when the bile duct is blocked.

Liver: A large, glandular organ in the upper abdomen. It cleans the blood and releases bile to help digest food.

Lymph nodes: Small organs that filter harmful substances in the body. They have immune cells that fight infections and diseases. Lymph nodes are part of the lymph system. The lymph system is made up of the tissues and organs that make, store and carry white blood cells that fight infections and diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and lymphatic vessels.

Malignant: A word to describe a tumor that is cancer.

Metastasis (Metastasize): The spread of cancer from one part of the body to another.

Mutation: A change in the DNA of a cell. Certain mutations can lead to cancer. Mutations can be inherited or can happen over time.

Neoadjuvant therapy: A treatment given before surgery. Neoadjuvant therapy may be chemotherapy, radiation therapy, hormone therapy, targeted therapy, immunotherapy or a combination of these.

Neoplasm: A new, abnormal mass of cells. A group of these cells is called a tumor. A tumor can be benign (non-cancerous) or malignant (cancerous).

Off-label: Treatments that are approved by the FDA to treat another cancer but are not approved for pancreatic cancer. Because they have shown some promise for pancreatic cancer in clinical trials and already have FDA approval for another cancer, the doctor can prescribe an off-label treatment when it makes sense for the patient.

Pancreas: A long gland behind the stomach. It makes enzymes that help with digestion and releases hormones that control blood sugar levels.

Pancreatic duct: The main exocrine duct of the pancreas. Pancreatic enzymes from smaller ducts empty into the pancreatic duct.

Pancreatic enzymes: Proteins the pancreas makes that help digest food. The three types are amylase, lipase and protease. Together these enzymes are "pancreatic juice."

Pancreatic neuroendocrine tumors (pancreatic NETs or PNETs): Rare pancreatic tumors. They start in the endocrine (hormone-producing) cells in the pancreas called islet cells.

Pancreatitis: Inflammation of the pancreas. Pain is the main symptom.

Paracentesis: A surgery to remove fluid from the stomach area.

Parathyroid glands: A group of small endocrine glands in the neck, behind the thyroid gland. They help control calcium levels in the blood.

Pathologist: A doctor who identifies diseases by studying cells and tissues under a microscope. They are important in getting a correct diagnosis.

Peritoneum: A thin membrane lining the cavity of the abdomen.

Phase: A step in the clinical trials process. There are four phases of clinical trials.

Platinol AQ® (cisplatin): A chemotherapy drug used to treat PNETs.

Portal vein: A large vein that carries blood from the spleen, stomach, pancreas and intestines to the liver.

Primary tumor: The original tumor. In pancreatic cancer, the primary tumor is in the pancreas.

Radiologist: A doctor who diagnoses and treats diseases using medical imaging.

Resectable: Able to be removed by surgery.

Risk factor: Something associated with a higher chance of getting a disease. It is not necessarily a cause of the disease.

Secondary tumor: A cancerous tumor that has spread from where it started (the primary tumor) to another place in the body. Secondary tumors are still pancreatic cancer even though they are not in the pancreas.

Small intestine: The tube-shaped portion of the digestive (gastrointestinal) system. It is between the stomach and the large intestine. The bloodstream absorbs most nutrients through the small intestine.

Spleen: An organ that filters the blood. It is in the upper left side of the abdomen, near the tail of the pancreas.

Stage: A measure of how far the cancer has grown. It uses the size of the tumor and where it has spread. Stages range from I to IV. Stage I is the earliest form of cancer.

Stent: A small metal or plastic tube. It is inserted into the center of a vein, artery or duct to open a blocked passageway.

Superior mesenteric artery: A major artery that comes from the largest artery in the body, the aorta. The superior mesenteric artery is behind the neck of the pancreas. It supplies blood to the small intestines, colon and part of the pancreas.

Streptozocin: A chemotherapy drug used to treat PNETs.

Superior mesenteric vein: A major vein behind the neck of the pancreas.

Symptom: A sign that a person has a condition or disease. Some examples of symptoms for pancreatic cancer include jaundice, weight loss, fatigue, nausea, vomiting and pain.

Targeted therapy: A type of treatment that attacks unique aspects of cancer cells. It does little harm to healthy cells.

Temodar® (temozolomide): A chemotherapy drug used to treat PNETs. It is often paired with Xeloda® for PNETs.

Xeloda® (capecitabine): A chemotherapy drug used to treat PNETs. It is often paired with Temodar® for PNETs.

The Pancreatic Cancer Action Network (PanCAN)
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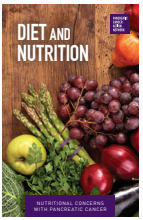
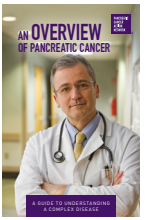
Other booklets in the Pancreatic Cancer Action Network's educational library





Want to know more about any of the services we offer? Contact PanCAN Patient Services, Monday through Friday, 7 a.m. to 5 p.m. Pacific Time.

Call toll-free **877-2-PANCAN**
Email **patientservices@pancan.org**

Because of the philanthropy of generous friends, we are able to provide all of our resources and services to you, ***free of charge.***

PanCAN's mission is to take bold action to improve the lives of everyone impacted by pancreatic cancer by advancing scientific research, building community, sharing knowledge, and advocating for patients. We do this through:

SCIENTIFIC RESEARCH

Funding the most promising research and innovative initiatives, including our Precision Promise℠ clinical trial and our Early Detection Initiative.

GOVERNMENT ADVOCACY

Driving legislative support for increased federal research funding.

PATIENT SERVICES

Providing information about the disease, treatment options and support to patients and families.

COMMUNITY ENGAGEMENT

Mobilizing a national network of volunteers who raise awareness and funds through large-scale community events like PurpleStride®, the ultimate event to end pancreatic cancer, and individual DIY fundraising.

ACTION FOR PATIENTS BEGINS HERE

The mission of the Pancreatic Cancer Action Network (PanCAN) is to take bold action to improve the lives of everyone impacted by pancreatic cancer by advancing scientific research, building community, sharing knowledge and advocating for patients.

Our vision is to create a world in which all patients with pancreatic cancer will thrive.

Through our Patient Services program, we provide extensive individualized support and hope. PanCAN Patient Services connects patients, their caregivers and family members to reliable information and resources. Our highly educated and expertly trained staff's passion is equaled only by their depth of knowledge about pancreatic cancer.

To learn more about our free, personalized resources and services, visit pancan.org or call 877–2–PANCAN.

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