NCCN GUIDELINES FOR PATIENTS®

2025

Neuroendocrine Tumors

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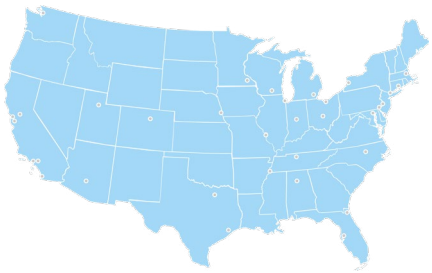
About the NCCN Guidelines for Patients®

National Comprehensive Cancer Network®



Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Neuroendocrine and Adrenal Tumors Version 2.2025 – May 28, 2025.

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NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

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About neuroendocrine tumors

A neuroendocrine neoplasm (NEN) is the general term for all types of neuroendocrine tumors (NETs) and cancers. NENs start in your neuroendocrine cells. These cells can produce and release hormones into the bloodstream. This chapter gives the basics of the types of NENs and how they're diagnosed and treated.

What's a NET?

Neuroendocrine neoplasm (NEN) is the general term for all types of neuroendocrine tumors (NETs) and cancers. NENs include NETs and neuroendocrine carcinomas (NECs). Most NENs are cancer. Since NETs are more common, you'll find the term NET used most often throughout this book.

A NET develops from neuroendocrine cells. Neuroendocrine cells act as a bridge between the nervous and endocrine systems, receiving signals from nerve cells and responding by producing and releasing hormones. They play a vital role in regulating various bodily functions, including digestion, blood pressure, and heart rate.

NETs can develop anywhere in the body, but are most commonly found in the lungs, pancreas, rectum, appendix, and small intestine. A NET may grow slowly or quickly and spread to other parts of the body. NETs are usually slow growing and NECs are usually fast growing.

Types of neuroendocrine tumors

NETs often release extra hormones, which may or may not cause symptoms.

- **Functioning NETs** produce extra hormones causing symptoms. Symptoms vary depending on the location of the tumor and type of hormone released.
- **Nonfunctioning NETs** don't cause symptoms. Many people with NETs do not have symptoms. Nonfunctioning NETs are more common than functioning NETs.

NETs are also grouped based on where the tumor starts in your body. The most common types include:

- **Gastrointestinal neuroendocrine tumors (GI NETs)** start in your gastrointestinal (GI) tract, which includes your stomach, intestines, rectum, and appendix.
- **Lung (pulmonary) NETs** start in your lungs or bronchi. Bronchi are tubes that carry air from your windpipe (trachea) to your lungs.
- **Pancreatic neuroendocrine tumors (PanNETs or pNETs)** start in the hormone-producing cells of the pancreas. This cancer is different from what we think of as pancreatic cancer (adenocarcinoma of the pancreas). PanNETs used to be called carcinoid tumors.

NETs can be called by different names depending on where they are in the body or what type of cell they look like. You can also

have more than one NET and more than one type of NET.

What's the neuroendocrine system?

The neuroendocrine system manages the communication between the body's nervous system and endocrine system. The nervous system is responsible for transmitting signals between different parts of the body and the brain. The endocrine system is a complex network of glands and organs. It's often referred to as the body's messenger system because it uses hormones to regulate your metabolism, energy level, growth and development, and mood.

The hypothalamus and the pituitary gland are considered the control centers for much of the neuroendocrine system. Their role is to direct hormones to specific locations throughout the body.

Endocrine system

The endocrine system is made up of the following glands and organs.

- **Hypothalamus** secretes hormones to control water balance, sleep, temperature, appetite, and blood pressure.
- **Pineal gland** produces melatonin. Melatonin is a hormone that helps the body know when it's time to sleep.
- **Pituitary gland** controls the activity of multiple hormone-secreting glands.
- **Thyroid** maintains your metabolism.
- **Parathyroid** helps regulate the amount of calcium in the body.
- **Thymus** makes white blood cells that fight infections.
- **Adrenal glands** help to regulate blood pressure, metabolism, and aspects of sexual development and function.
- **Pancreas** helps with hormone production and digestion.
- **Ovaries** produce hormones (estrogen and progesterone) and contain the egg cells necessary for reproduction.
- **Testes** produce testosterone and sperm. Sperm is also necessary for reproduction.

How are NETs diagnosed and treated?

Diagnosis and treatment of NETs depend on the following:

- Type of tumor and where it's found in the body
- How the tumor cells look under a microscope
- If the tumor produces excess hormones and, if so, what type of hormone
- If the tumor is causing hormone-related symptoms
- How quickly the tumor grows
- If the tumor has spread to other parts of the body

Treatment is often a combination of therapies, which may include surgery, radiation therapy, and drug (systemic) therapy.

This guide will discuss in greater detail how NETs are diagnosed, staged, and treated. It'll provide an overview of the types of tests and treatments and what to expect during testing and treatment.

How this guide can help you

Making decisions about cancer care is stressful. There's a lot to learn, and you don't know what the future holds.

Use this guide to get the information and support you need.

Patients, doctors, and other health care professionals trust the NCCN Guidelines for Patients. This guide uses clear, everyday language to explain current cancer care recommendations made by respected experts in the field. Their recommendations are based on the latest research and practices at leading cancer centers.

Your health is unique to you, so your cancer care should be, too. As you read this guide, you'll learn which treatments are likely to provide the best results for you. And you'll be better prepared to talk with your care team.

How can I get the best care?

Advocate for yourself. You have an important role to play in your care. Many people feel more satisfied when they actively take part in planning their cancer care.

The NCCN Guidelines for Patients will help you play a larger role in your care. Discuss the recommendations in this guide with your care team. Ask questions about your options and share your goals and concerns.

Don't know what to ask? You're not alone. That's why we include suggested questions to ask at the end of chapters.

Keep reading to find the best care for you.

We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer. Take our survey to let us know what we got right and what we could do better.
NCCN.org/patients/feedback

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Testing for NETs

Each neuroendocrine tumor (NET) is unique. Treatment planning starts with testing. Your care team will want to gather as much information as they can about your NET. This chapter presents an overview of the possible tests you might receive and what to expect.

Tests are used to find cancer, plan treatment, and see how your cancer is responding to treatment. Results from a tumor biopsy, blood and urine tests, and imaging studies will be used to determine what treatments are best for your type of neuroendocrine tumor (NET). This chapter provides a general overview some of tests you might have.

General health tests

Medical history

A medical history is a record of all health issues and treatments you've had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter (OTC) medicines, herbals, or supplements you take. Some supplements interact with and affect medicines that your care team may prescribe. Tell your care team about any symptoms you have. A medical or health history will help determine which treatment is best for you.

Family history

Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer, where the cancer started, if it's in multiple locations, and if they had genetic testing.

Physical exam

During a physical exam, your health care team may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and weight
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched
- Feel for enlarged lymph nodes in your neck, underarm, and groin

Performance status

Performance status (PS) is a rating of a person's general level of fitness and ability to perform daily tasks.

Blood and urine tests

Blood and urine tests check for signs of disease and how well organs are working. They are also used to look for hormones and other chemicals produced by your tumor. Blood tests require a sample of blood, which is removed through a needle placed into a vein in your arm. For a urine test, you will be asked to fill a small container with urine (pee in a cup). You might be asked to collect your urine at home for 24 hours using a special container. Blood and urine samples are sent to a lab for testing.

Some possible blood and urine tests are described next.

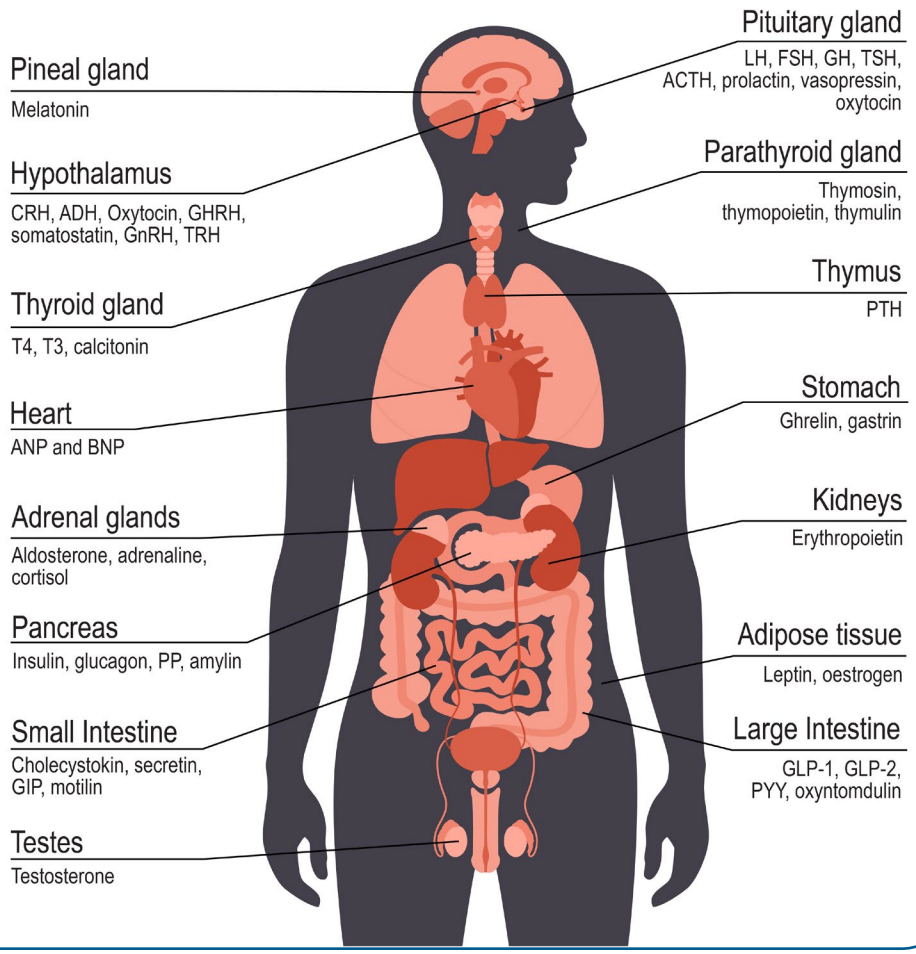
Biochemical tests

There are many types of biochemical tests. They measure substances such as hormones, proteins, and sugar (glucose) in blood and urine. You might be asked to fast (not eat) for a fasting blood glucose test or to collect your urine for a 24-hour urine test.

Some NETs can secrete specific hormones such as gastrin, glucagon, somatostatin, serotonin, and others. Hormonal testing is guided by the symptoms of the excess hormone.

Hormones

The endocrine system produces and releases hormones. Hormones are chemicals that carry messages throughout your body. This image shows the different hormones found in the body. The ovaries (not shown) also produce hormones.



Neuroendocrine tumors (NETs) develop from cells that produce hormones. This means the tumor can also produce hormones.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. A CBC is a key test that gives a picture of your overall health.

Comprehensive metabolic panel

A comprehensive metabolic panel measures substances in your blood. It provides important information about how well your kidneys and liver are working, among other things.

5-HIAA test

A 5-HIAA test is a biochemical test that measures the amount of 5-hydroxyindoleacetic acid in the body. 5-HIAA is a breakdown product or byproduct of a hormone called serotonin. Some types of NETs can cause too much serotonin in the body. This test often involves collecting a 24-hour urine sample.

Imaging tests

Imaging tests take pictures of the inside of your body. Imaging tests show the primary tumor, or where the cancer started, and look for cancer in other parts of your body. A radiologist, a medical expert, will interpret the test and send a report to your doctor. The following imaging tests are in alphabetical order and not in order of importance. You will likely have a combination of these tests.

Contrast material

Contrast material is a substance used to improve the quality of imaging tests such as CT and MRI scans. It's used to make the pictures clearer. Not all imaging tests require contrast, but many do.

Contrast might be taken by mouth (oral) or given through a vein (intravenously or IV). Oral contrast will be passed with your bowel movements. IV contrast will leave your body in your urine immediately after the test. The types of contrast vary and are different for CT and MRI.

Tell your care team if you've had allergic reactions to contrast in the past. This is important. You might be given medicines to avoid the effects of those allergies. Contrast might not be used if you have a serious allergy or if your kidneys aren’t working well.

CT scan

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles.

Other less common types of CT scans such as a single-photon emission CT (SPECT) and 4D-CT may be used in very specific cases.

MRI scan

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of your body. It doesn't use x-rays, which means there's no radiation delivered to your body during the test. Because of the very strong magnets used in the MRI machine, tell the technologist if you have any metal or a pacemaker in your body. During the test, you'll likely be asked to hold your breath for 10 to 20 seconds as the technician collects the images.

A closed MRI has a capsule-like design where the magnet surrounds you. The space is small and enclosed. An open MRI has a magnetic top and bottom, which allows for an opening on each end. Closed MRIs are more common than open MRIs, so if you have claustrophobia (a dread or fear of enclosed spaces), be sure to talk to your care team about it. MRI scans take longer to perform than CT scans.

Multiphasic CT or MRI

In a multiphasic CT or MRI there are 2 scans, one without contrast and one with contrast. First, a scan is done without contrast. Then, contrast is injected into a vein and multiple sets of pictures are taken as the contrast moves through the body area near the tumor. This allows your care team to see whether the tumor involves any veins, arteries, or organs.

PET scan

A PET (positron emission tomography) scan uses a radioactive substance called a tracer. A tracer is a substance injected into a vein to see where cancer cells are in your body and how much sugar is being taken up by the cancer cells. This gives an idea about how fast the cancer cells are growing. Cancer cells show up as bright spots on PET scans. However, not all tumors will appear on a PET scan. Also, not all bright spots found on the PET scan are cancer. It's normal for the brain, heart, kidneys, and bladder to be bright on PET. Inflammation or infection can also show up as bright spots.

A PET scan can be combined with a CT, MRI, or somatostatin receptor (SSTR).

The following are types of PET scans that might be used for NETs:

- **FDG-PET** uses a radiotracer called fluorodeoxyglucose (FDG). It's made of fluoride and a simple form of sugar called glucose. FDG-PET scans can help determine if NETs are becoming more aggressive or when there's cancer in the bones. An FDG-PET might be combined with an SSTR-PET to provide more detailed information about the tumor. FDG-PET scans are usually done in more aggressive tumors such as a grade 3 NET or NEC.
- **SSTR-PET** uses a tracer that binds to somatostatin receptors (SSTRs). Somatostatin is a hormone that helps to control other hormones in the body. Since NETs tend to have higher levels of SSTRs, this test is used to determine if you'll benefit from SSTR-focused therapy.
- **SSTR-PET/CT or SSTR-PET/MRI** adds CT or MRI to an SSTR-PET to help improve accuracy and find out if a tumor tests positive or negative for SSTRs.

"A second opinion from a NET specialist changed my life and the trajectory of my cancer treatment. I was properly diagnosed, provided additional treatment options, and given sufficient information to make an informed decision about next steps. Above all, my NET specialist was kind, caring, patient, and filled me with hope."

Ultrasound

An ultrasound uses high-energy sound waves to form pictures of the inside of the body. This is similar to the sonogram used for pregnancy. A wand-like probe (transducer) will be held and moved on your bare skin using gel. Ultrasound doesn't use x-rays, so it can be repeated as needed. Sometimes, an ultrasound is used to guide a biopsy.

- **An echocardiogram** (or echo) is a type of ultrasound that shows the structure (valves and muscle thickness) and function of your heart (or ejection fraction). It's used to test for carcinoid syndrome.

Scoping tests and procedures

Some imaging tests use a thin, tube-shaped tool called a scope that's inserted into the body to take pictures. One end of the scope has a small light and camera lens to see inside your body. The image is sent to a television monitor. The scope is guided into the body through a natural opening, such as the mouth, nose, or anus. It may also be inserted through a small surgical cut.

More than one type of scope may be used for testing. A biopsy or surgery might be done during some scoping procedures. Ask your carte team for more information.

Bronchoscopy

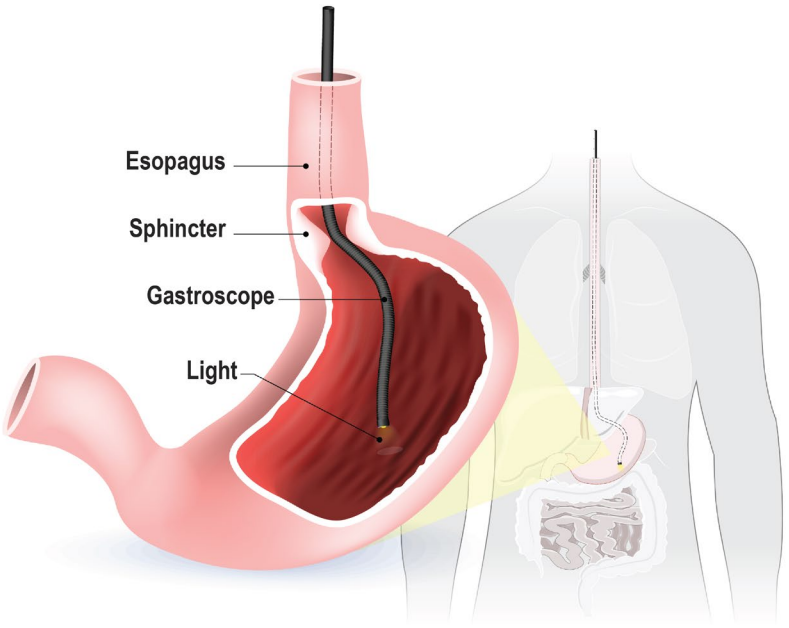
During a bronchoscopy, a device is inserted through the nose or mouth to examine the inside of your airway, including the trachea and bronchi.

Upper GI endoscopy or EGD

In an upper gastrointestinal (GI) endoscopy or esophagogastroduodenoscopy (EGD), a device is guided down the throat into the esophagus, stomach, and upper parts of the small intestine (duodenum). An EGD is used to inspect the lining of these organs and to look for any signs of cancer or other abnormalities such as dilated blood vessels or ulcers. Biopsies are usually performed during an EGD. After the endoscopy, your throat may feel sore, and you may feel some swelling.

Upper endoscopy

In an upper gastrointestinal (GI) endoscopy or esophagogastroduodenoscopy (EGD), a device is guided down the throat into the esophagus, stomach, and upper parts of the small intestine (duodenum).



Colonoscopy

In a colonoscopy, an endoscope is used to examine the inside of the colon. A colonoscope has a light and a lens for viewing and may have a tool to remove tissue. It's guided through the anus, then into the rectum and the colon. A colonoscopy is usually done under sedation, so you'll be comfortable during the procedure and won't remember it after it's over.

Endoscopic ultrasound

Endoscopic ultrasound (EUS) uses both imaging and an endoscope. An endoscope is a flexible tube with a light and camera attached. It's used to view pictures of your digestive tract. The endoscope can be inserted through the mouth during an upper endoscopy procedure to look at the esophagus, stomach, or duodenum, or it can be inserted through the anus during a lower endoscopy procedure to look at the rectum and prostate. Tests or a biopsy might be done during an endoscopy.

Biopsy

A biopsy is the removal of a sample of tissue or group of cells for testing. It's an important part of an accurate diagnosis. A pathologist, a medical expert, will examine the biopsy and note the overall appearance and the size, shape, and type of cells. This is called histology or histopathology. Lab tests will be done on the biopsied cells.

There are different types of biopsies. Some biopsies are guided using imaging, such as ultrasound or MRI, or they're done during scoping procedures.

Some types of biopsies may include:

- **Fine-needle aspiration (FNA) or core biopsy (CB)** uses needles of different sizes to remove a sample of tissue or fluid.
- **Brushings or washings** remove tumor or cell samples with a small brush at the end of an endoscope.
- **Liquid biopsy** uses a sample of blood for testing.

Laparoscopy

Laparoscopy (key-hole surgery or minimally invasive surgery) is a surgical procedure that inserts a camera and various instruments (laparoscope) through small cuts (ports) in the abdomen. During the procedure, a tool can take tissue samples or remove tumors. Laparoscopy is done under general anesthesia. This is a loss of feeling and a complete loss of awareness that feels like a very deep sleep.

Genetic testing

Depending on your family history or other features of your tumor, your health care provider might refer you for hereditary genetic testing to learn more about your tumor. A genetic counselor or trained provider will speak with you about the results.

Genetic testing is done using blood or saliva (spitting into a cup or taking a cheek swab). The goal is to look for gene mutations inherited from your biological (birth) parents called germline mutations. Some mutations can put you at risk for more than one type of tumor or cancer. You can pass these genes on to your children. Also, other family members might carry these mutations. Tell your care team if there's a family history of cancer.

Hereditary cancer predisposition syndromes

Certain genetic (inherited) syndromes may put someone at risk for developing certain tumors and cancers. A syndrome is a group of signs or symptoms that occur together and suggest the presence of or risk for a disease. A hereditary syndrome is found in blood (biological) relatives.

A genetic cancer risk assessment will identify if you have a genetic risk factor for tumors or cancer, and if you may benefit from genetic testing, additional screening, or preventive interventions. Depending on the genetic risk assessment, you might undergo genetic testing and genetic counseling to see if you have a hereditary syndrome that puts you at risk for developing NETs.

Hereditary syndromes closely related to NETs include:

- Multiple endocrine neoplasia type 1 (MEN1)
- Multiple endocrine neoplasia type 4 (MEN4)
- Neurofibromatosis type 1 (NF1)
- Tuberous sclerosis complex (TSC1 and TSC2)
- Von Hippel-Lindau (VHL) syndrome

Biomarker testing

A sample from a biopsy of your tumor may be tested to look for gene mutations, protein levels, or other molecular features. It's sometimes called molecular testing or tumor profiling, tumor sequencing, gene expression profiling, or genomic testing. Your treatment team will recommend the best types of biomarker testing that are important for you.

Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process used to study cells from a biopsy or tumor sample. Examples of biomarkers found with IHC that might relate to NETs include synaptophysin, chromogranin A, keratin, Ki-67 (or MIB-1), and INSM1.

For example, keratins are proteins that have predictable patterns. Patterns that look different than expected or the presence or absence of certain keratins can help tell the difference between types of tumors and predict how aggressive a tumor might be. Keratins help tell the difference between NETs and adrenal tumors called pheochromocytoma (PCC) or paraganglioma (PGL). The Ki-67 proliferation index measures dividing cells and is an indicator of the tumor growth rate.

NETest

A NETest, or Neuroendocrine Tumor Expression Test, is a blood test that measures gene expression in NETs.

Tumor mutation testing

A sample of your tumor or blood may be used to see if the cancer cells have any specific DNA mutations. This is a different type of DNA testing than the genetic testing for mutations you may have inherited from your birth parents. In tumor mutation testing, only the tumor is tested and not the rest of your body.

Key points

- Tests are used to find cancer, plan treatment, and check how your cancer is responding to treatment.
- Blood and urine tests check for signs of disease and how well the organs are working. These tests are also used to look for hormone, blood sugar (glucose), and protein levels.
- Imaging tests take pictures of the inside of your body and are used to learn more about the type, size, and location of your tumor. Some imaging tests use a thin, tube-shaped tool called a scope that's inserted into the body to take pictures. A biopsy or surgery might be done during some scoping procedures.
- A biopsy is the removal of a sample of tissue or group of cells for testing. Lab tests will be done on the biopsied cells.
- Genetic testing looks for gene mutations inherited from your biological (birth) parents called germline mutations. Some germline mutations can put you at risk for neuroendocrine tumors (NETs) or more than one type of cancer.

Questions to ask

- What tests will I have?
- What tests will be done on the tumor?
- Who will explain the test results to me?
- What other information do you need to gather before starting treatment?
- Do you recommend I have genetic testing and counseling for inherited cancer risk or predisposition syndromes? Why or why not?

3
NET staging

Cancer staging is used to reflect the course your cancer will likely take and to guide treatment decisions. It describes the size and location of the tumor and if cancer has spread to lymph nodes, organs, or other parts of the body.

How are NETs staged?

A cancer stage is a way to describe the cancer at the time you're first diagnosed. Based on testing, your cancer will be assigned a stage. Staging helps to predict prognosis and is needed to make treatment decisions. A prognosis is the course your cancer will likely take.

Information gathered during staging:

- **The size and location of the tumor (T)**: Where is the tumor located? How large is the tumor? Has it grown into nearby areas?
- **The spread to nearby lymph nodes (N)**: Has the cancer spread to nearby lymph nodes? If so, how many? Where?
- **The spread (metastasis) to distant sites (M)**: Has the cancer spread to distant organs such as the lungs or liver?
- **Tumor or cancer grade (G)**: How likely and how quickly are the tumors cells to grow and spread?
- **Differentiation**: How much do the cancer cells look like normal cells?
- **Biomarker testing**: Does the cancer have any genes, proteins, hormones, markers, or mutations that might suggest treatment?

Staging is based on a combination of information to reach a final numbered stage. Often, not all information is available at the initial evaluation. More information can be gathered as treatment begins.

TNM scores

The tumor, node, metastasis (TNM) system is used to stage many neuroendocrine tumors (NETs). In this system, the letters T, N, and M describe different areas of cancer growth. Based on test results, a score or number will be assigned to each letter. The higher the number, the larger the tumor or the more the cancer has spread. These scores will be combined to assign the cancer a stage. A TNM example might look like this: T2N1M0 or T2, N1, M0.

- **T (tumor)** – Size of the main (primary) tumor. It's usually measured in centimeters (cm).
- **N (node)** – If cancer has spread to nearby (regional) lymph nodes. Lymph node involvement is uncommon in NETs.
- **M (metastasis)** – If cancer has spread to distant parts of the body or metastasized. Cancer that has metastasized is written as M1.

Numbered stages

Numbered stages are based on TNM scores. Stages range from stage 0 to stage 4, with 4 being the most advanced. They might be written as stage 0, stage I, stage II, stage III, and stage IV.

Other terms might be used instead of numbered cancer stages. These include the following:

- **Resectable** – Tumor can be removed completely with surgery.
- **Unresectable** – Tumor can't be removed with surgery. It might involve nearby veins, arteries, or organs making it unsafe to remove.
- **Locoregional or locally advanced** – Tumor might be in nearby lymph nodes, organs, and tissues.
- **Metastatic** – Cancer has spread to other parts of the body, including distant lymph nodes.

How are NETs classified?

Classification focuses on how tumor cells look under a microscope.

Grade

Another factor used in staging is the tumor grade or how quickly these cells are likely to grow and spread. Higher-grade tumors tend to grow and spread faster than lower-grade tumors. The letter G stands for the grade. GX means the grade can't be determined, followed by G1, G2, and G3. G3 is the highest grade for NETs.

What's the difference between a NEN, NET, and NEC?

- **Neuroendocrine neoplasm (NEN)** is the general term for all types of neuroendocrine tumors (NETs) and cancers. NEN includes NETs and neuroendocrine carcinomas (NECs).
- **Neuroendocrine tumor (NET)** is a type of NEN. It's well-differentiated and can be grade 1, 2, or 3.
- **Neuroendocrine carcinoma (NEC)** is a type of NEN. It's poorly differentiated and grade 3. Examples include small-cell NEC, large-cell NEC, and mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN).

- **GX** – Grade can't be determined
- **G1** – Low grade
- **G2** – Intermediate grade
- **G3** – High grade

For tumors of the gastrointestinal (GI) tract or pancreas, grade is often determined by mitotic rate and Ki-67 index. Mitotic rate and Ki-67 index measure how quickly the tumor cells divide (proliferate). A higher Ki-67 index suggests a faster-growing tumor and can be used to help determine prognosis and guide treatment decisions.

Differentiation

Differentiation describes how much tumor cells look like normal cells when viewed under a microscope (histology). This is important information for treatment planning. It also explains the difference between a NET and a neuroendocrine carcinoma (NEC), which are types of neuroendocrine neoplasms (NENs).

- **Well-differentiated** tumor cells look like normal cells and tend to grow and spread more slowly. NETs are well-differentiated.
- **Poorly differentiated** tumor cells look very different compared to normal cells and tend to grow and spread faster. Poorly differentiated cells are also divided into large-cell and small-cell types. All poorly differentiated NECs are grade 3.

Differentiation depends on the tumor type and location. Some tumors can have a mix of well and poorly differentiated cells or a mix of neuroendocrine and nonendocrine cells. These tumors are called mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs).

NETs of the gastrointestinal tract

NETs of the gastrointestinal (GI) tract (also known as GI NETs) can start in the stomach, small intestine, appendix, colon, or rectum. While staging for each of these organs is slightly different, they all have stages 1 through 4. The following staging is for well-differentiated NETs that are grade 1, 2, or 3.

Stomach

The stomach is a muscular, hollow organ located between the esophagus and the small intestine. It secretes enzymes and acid that convert what you eat and drink into a liquid. The stomach wall has 5 main layers: mucosa, submucosa, muscularis propria, subserosa, and serosa.

Here are general stages for well-differentiated NETs of the stomach, also called gastric NETs:

- **Stage 1** – Tumor is less than or equal to 1 cm wide.
- **Stage 2** – Tumor is larger than 1 cm wide or has grown into other layers of tissue.
- **Stage 3** – Tumor has grown into the outermost layer of the stomach, or into nearby structures or organs. It may have spread to lymph nodes, but not distant parts of the body.
- **Stage 4** – Cancer has spread to distant parts of the body. This is metastatic disease.

Duodenum and ampulla of Vater

The duodenum is the first part of the small intestine. It connects to the stomach. The ampulla of Vater is a small conelike structure where the common bile duct and the main pancreatic duct join before emptying into the duodenum.

Here are general stages for well-differentiated NETs of the duodenum and ampulla of Vater:

- **Stage 1** – Tumor is less than or equal to 1 cm wide. Tumor is confined to a small area and hasn't spread to any lymph nodes.
- **Stage 2** – Tumor is larger than 1 cm wide and has begun to grow into other layers of the duodenum or may be in the pancreas. Cancer hasn't spread to lymph nodes or distant body parts.
- **Stage 3** – Tumor is bigger and affects nearby organs or the outermost layer of the duodenum. It may have spread to nearby lymph nodes or the pancreas, but hasn't spread to distant parts of the body.
- **Stage 4** – Tumor can be any size. Cancer may be in the lymph nodes. Cancer has spread to distant parts of the body. This is metastatic disease.

The digestive tract

The stomach, small intestine, appendix, colon, and rectum are part of the digestive tract.

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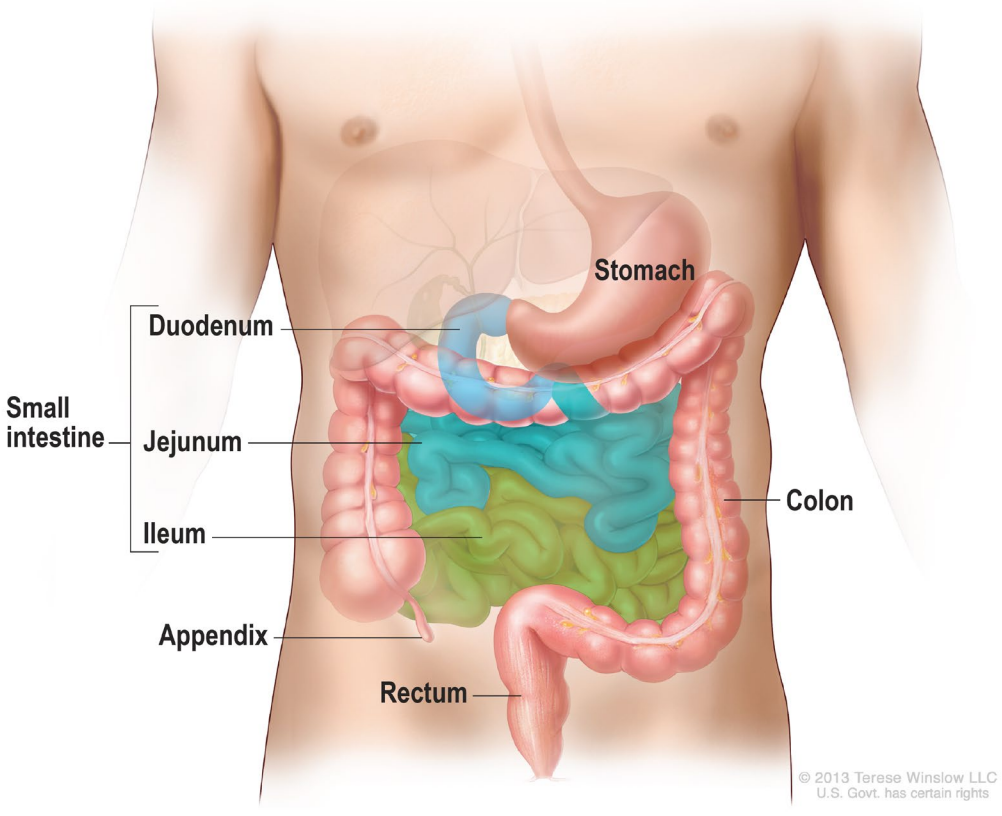


Jejunum and ileum

The jejunum is the middle part of the small intestine. The ileum is the last section of the small intestine. The jejunum and ileum help digest food coming from the stomach and absorb nutrients (vitamins, minerals, carbohydrates, fats, and proteins) and water from food.

Here are general stages for well-differentiated NETs of the small intestine:

- **Stage 1** – Tumor is less than or equal to 1 cm wide. It hasn't spread to any lymph nodes or outside the small intestine.
- **Stage 2** – Tumor is larger than 1 cm wide and has begun to grow into other layers of the small intestine. It hasn't spread to lymph nodes or distant body parts.
- **Stage 3** – Tumor is bigger and affects nearby organs or the outermost covering of the small intestine. It may have spread to nearby lymph nodes but hasn't spread to other parts of the body.
- **Stage 4** – Tumor can be any size. Cancer may be in the lymph nodes. Cancer has spread to distant parts of the body. This is metastatic disease.

Appendix

The appendix is a small, fingerlike pouch that sticks out near the end of the small intestine. It produces and stores healthy bacteria and helps with the immune system. The appendix has 4 main layers: mucosa, submucosa, muscularis externa, and serosa.

Here are general stages for well-differentiated NETs of the appendix:

- **Stage 1** – Tumor is 2 cm wide or less and hasn't spread to any lymph nodes.
- **Stage 2** – Tumor is between 2 cm and 4 cm wide. It may be growing into other tissue layers around the appendix. It hasn't spread to any lymph nodes or distant parts of the body.
- **Stage 3** – Tumor may have spread to nearby lymph nodes, or may be growing into the outermost layer of tissue of the appendix. Cancer may have spread to nearby lymph nodes.
- **Stage 4** – Tumor can be any size. Cancer may be in the lymph nodes, but also has spread to distant parts of the body. This is metastatic disease.

Colon and rectum

The wall of the colon (large intestine) and rectum are made up of 4 main layers: mucosa, submucosa, muscularis propria, and serosa.

Here are general stages for well-differentiated NETs of the colon and rectum:

- **Stage 1** – Tumor is 2 cm wide or less and has grown into the mucosa or submucosa.
- **Stage 2A** – Tumor is greater than 2 cm wide. The tumor might have grown into the muscularis propria layer of the colon or rectum.
- **Stage 2B** – Tumor has grown into one of the outer layers of the wall of the colon or rectum.
- **Stage 3A** – Tumor has grown into the outer layer of the intestine or nearby organs. It has not spread to nearby lymph nodes.
- **Stage 3B** – Tumor has spread to nearby lymph nodes. It has not yet spread (metastasized) to distant parts of the body.
- **Stage 4** – Tumor can be any size. Cancer may be in the lymph nodes, but also has spread to distant parts of the body. This is metastatic disease.

NETs of the lung

There are 2 lungs. Together, they supply the body with oxygen and remove carbon dioxide from the body. The lungs are part of the respiratory system. NETs of the lung are different than lung cancer.

Here are very general stages for well-differentiated NETs of the lung:

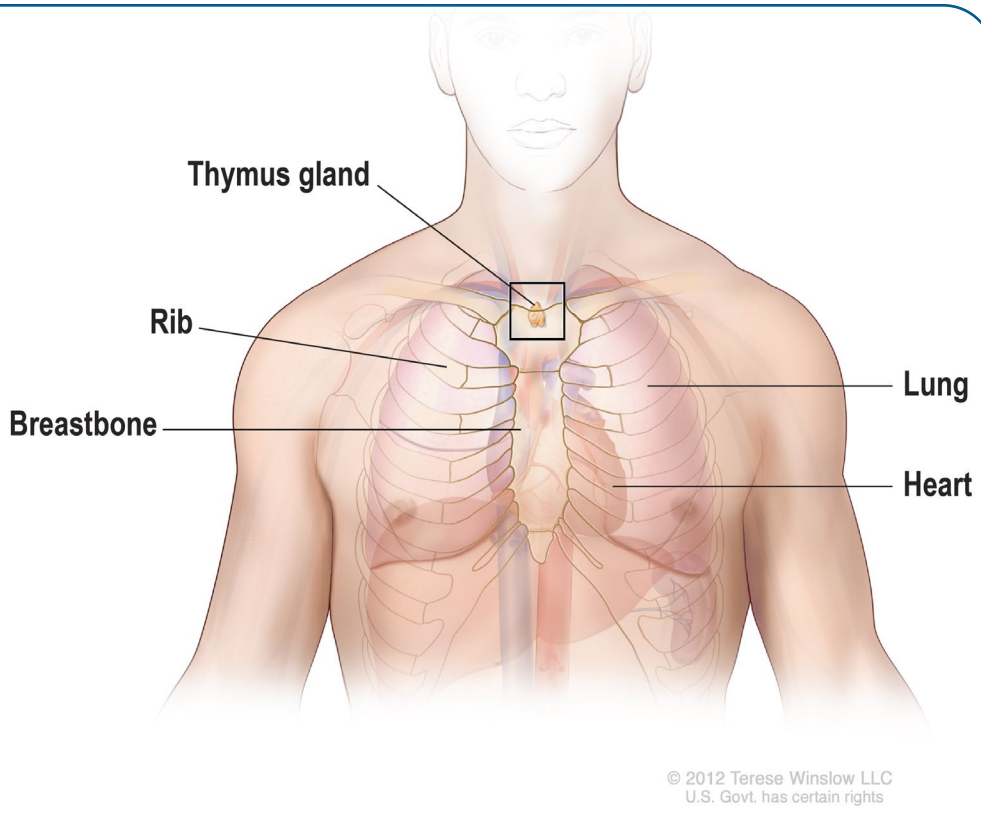
- **Stage 1** – Tumor is 3 cm or less.
- **Stage 2** – Tumor is between 3 cm and 5 cm.
- **Stage 3** – Tumor is 5 cm or larger. The tumor has spread to nearby lymph nodes.
- **Stage 4** – Tumor is any size and has grown into lymph nodes and organs. This is metastatic disease.

NETs of the thymus

The thymus gland is a small organ found in the upper chest behind the breastbone (sternum). It makes white blood cells, called lymphocytes, which protect the body against infections. The thymus is part of the lymphatic system, which is part of the immune system.

Here are general stages for well-differentiated NETs of the thymus:

- **Stage 1** – Tumor is in the thymus or might have grown slightly outside the thymus.
- **Stage 2** – Tumor has grown into the lung, phrenic nerve, or lining around the heart. The phrenic nerve plays a role in breathing.
- **Stage 3A** – Tumor has grown into major veins and arteries in the chest, or into the chest wall.
- **Stage 3B** – Tumor has grown into major vessels of the heart or lung, or organs such as the esophagus or trachea.
- **Stage 4A** – Tumor is any size. Cancer might be in nearby lymph nodes or very small cancer cells might be in the area around the lung or heart.
- **Stage 4B** – Tumor is any size. Cancer might have spread to lymph nodes in the neck, lungs, or distant parts of the body.



Lungs and thymus

The lungs are a pair of organs found inside the ribcage. The thymus is a gland found inside the chest behind the breastbone (sternum).

Neuroendocrine neoplasms of unknown primary

Neuroendocrine neoplasms of unknown primary refer to tumors that do not have a known original tumor site. A neoplasm is an abnormal growth of cells. A neoplasm can grow into a tumor.

Imaging tests will be used to try to identify the original tumor site. If the original tumor site is found, then you will be treated based on tumor type and its location. If the main tumor site can't be found, then you will be treated based on tumor differentiation and grade listed below.

- **For poorly differentiated tumors**, see *Chapter 8: Extrapulmonary poorly differentiated NECs*.
- **For well-differentiated grade 1 and 2 tumors**, see the section on *Advanced or metastatic disease - GI NETs* in *Chapter 5: NETs of the GI tract, lung, and thymus*.
- **For well-differentiated grade 3 tumors**, see *Chapter 7: Well-differentiated, grade 3 NETs*.

NETs of the pancreas

The pancreas is a large gland found in your abdomen (belly). NETs of the pancreas or PanNETs are different from pancreatic cancer. However, staging is similar.

Here are general stages for well-differentiated PanNETs:

- **Stage 1** – Tumor is less than 2 cm across and found only in the pancreas.
- **Stage 2** – Tumor is 2 cm or more and may have spread to the duodenum, ampulla of Vater, or common bile duct.
- **Stage 3** – Tumor has grown into nearby organs or large arteries or veins. It may be in nearby lymph nodes.
- **Stage 4** – Tumor can be any size. Cancer may be in the nearby lymph nodes. Cancer has spread (metastasized) to parts of the body such as the liver, lung, ovary, or bone. This is metastatic disease.

Key points

- Staging helps to predict prognosis and is needed to make treatment decisions. A prognosis is the course your cancer will likely take.
- The tumor, node, metastasis (TNM) system is used to stage many neuroendocrine tumors (NETs). Other information such as grade and differentiation is also used in staging.
- Grade describes how quickly tumor cells are likely to grow and spread. Higher-grade tumors tend to grow and spread faster than lower-grade tumors.
- Differentiation describes how much tumor cells look like normal cells when viewed under a microscope (histology). Differentiation depends on the tumor type and location.

Questions to ask

- What type of neuroendocrine tumor (NET) do I have?
- How long have I had the tumor?
- Do I have more than one tumor?
- What's the tumor stage, grade, and differentiation?
- Is the tumor in one place or has it spread?

4
Types of treatment

There's more than one treatment for neuroendocrine tumors (NETs). This chapter describes treatment options and what to expect. Together, you and your care team will choose a treatment plan that's best for you.

Overview

Results from blood, urine, tumor, and imaging tests will guide your treatment plan. Many factors play a role in how a tumor or cancer responds to treatment. It's important to have regular talks with your care team about your goals for treatment and your treatment plan.

Treatment for neuroendocrine tumors (NETs) is usually a combination of therapies starting with surgery and might include systemic (drug) therapy or radiation therapy. Some tumors don’t need treatment right away. This is called watch and wait, surveillance, or observation. During this time, you'll have blood, imaging, and other tests to monitor the tumor size as well as you for symptoms. Observation is not an option for everyone.

Your care team

Depending on the type and location of your neuroendocrine tumor (NET), your care team might include the following specialists.

- **Oncologist** is a doctor who diagnoses and treats cancer. Types of oncologists include medical, radiation, and surgical oncologists.
- **Endocrinologist** is a doctor who diagnoses and treats disorders of the endocrine system.
- **Gastroenterologist** is a doctor who diagnoses and treats diseases of the digestive tract.
- **Pathologist** is a doctor who analyzes the cells, tissues, and organs removed during a biopsy or surgery.
- **Radiologist** is a doctor who interprets the results of CT scans, MRIs, and other imaging tests, and performs needle biopsies as needed.

Your care team

Treating cancer takes a team approach. Treatment decisions should involve a multidisciplinary team of health care and psychosocial care professionals from different professional backgrounds who have knowledge and experience in your type of cancer. This team is united in the planning and implementing of your treatment. It may include a pathologist, endocrinologist, radiologist, and a medical, radiation, or surgical oncologist. Ask who will coordinate your care.

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and help them get to know you.

Surgery

Surgery is an operation or procedure to remove cancer from the body. It's the main or primary treatment for many NETs, but has less of a role in the treatment of neuroendocrine carcinomas (NECs) because NECs are often advanced at diagnosis or in a challenging location.

When preparing for surgery, seek the opinion of a surgeon who is an expert in performing your type of surgery. Hospitals that perform many surgeries often have better results. You can ask for a referral to a hospital or cancer center that has experience in treating your type of cancer.

Surgery is sometimes called resection or excision. Ask your care team what will be removed during surgery and what to expect.

Goal of surgery

The goal of surgery is to remove all the cancer. To do so, the tumor is removed along with a rim of normal-looking tissue around its edge called the surgical margin. The surgical margin may look normal during surgery, but cancerous cells may be found when viewed under a microscope by a pathologist. A clear or negative margin (R0) is when no cancer cells are found in the tissue around the edge of the tumor. In a positive margin, cancer cells are found in normal-looking tissue around the tumor.

Some examples of surgical procedures are described next. Your care team can provide more information about surgery specific to your type of cancer.

Bowel resection

In a bowel resection, part of the small intestine is removed to get rid of the NET. The parts of the small intestine are then reconnected so normal eating and digesting can happen again. The small intestine includes the duodenum, jejunum, and ileum.

Endoscopic resection

An endoscopic resection (ER) uses an endoscope to remove tumors and cancer cells from the gastrointestinal (GI) tract. During the procedure, a flexible tube (endoscope) is passed down the esophagus, stomach, upper part of the small intestine (duodenum), or lung. The tube may be guided up through the anus to remove lesions from the colon. This procedure is used to remove tumors without surgery. It's also referred to as an endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD).

Gastrectomy

In a partial gastrectomy or gastric resection, the part of the stomach with cancer is removed along with nearby lymph nodes (regional lymphadenectomy), and possibly parts of other organs near the tumor.

In a total gastrectomy, the whole stomach, nearby lymph nodes, and parts of your esophagus and small intestine are removed. The esophagus is reconnected to the small intestine. You'll have a working digestive system that allows swallowing, eating, and digesting food, but in a much different way.

Hemicolectomy

A hemicolectomy removes the part of your large intestine called the colon. Once the colon is removed, the remaining parts of the intestine are joined together.

Lobectomy

A lobectomy is the removal of part of the lung. The right lung has 3 lobes. The left lung has 2 lobes.

Lymph node surgery

The removal of lymph nodes or groups of lymph nodes to test for cancer spread is called lymph node or nodal dissection. It might be referred to as a lymphadenectomy. A regional lymphadenectomy is surgery to remove 1 or more lymph nodes near the tumor.

Minimally invasive surgery

Minimally invasive surgery (key-hole surgery) uses several small incisions. Small tools are inserted through each incision to perform the surgery. One of the tools, called a videoscope, is a long tube with a video camera at the end. The camera lets your surgeon see the area near the tumor. Other tools are used to remove the tumor. Minimally invasive surgery, also called laparoscopic surgery, can be done using robotic arms to control surgical tools. This is called robot-assisted or robotic surgery.

Open surgery

Open surgery or laparotomy removes tissue through one large surgical cut. The large cut lets your surgeon directly view and access the tumor in your adrenal gland. This procedure is often done when the tumor might be in lymph nodes or other nearby organs, of if cancer is suspected.

Pancreatic surgery

There are many types of pancreatic surgery. For more information, see *Chapter 6: NETs of the pancreas*.

Simple appendectomy

An appendectomy is surgery to remove the appendix. The appendix is a small tube attached to the large intestine.

Systemic therapy

Systemic therapy is drug therapy that works throughout the body. Some types of systemic therapy include chemotherapy, targeted therapy, and immunotherapy.

All systemic (drug) treatments listed in this guide are recommended and appropriate. When helpful, NCCN experts also assign a level of preference to their recommendations for systemic therapies:

- **Preferred therapies** have the most evidence they may work better and may be safer than other therapies.
- **Other recommended therapies** can provide effective results but may have less evidence, more side effects, or may not work quite as well as preferred therapies.
- **Therapies used in certain cases** work best for individuals with specific cancer features or health circumstances.

For a general list of systemic therapies, **see Guide 1**.

Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells. More than one chemotherapy may be used to treat NETs. When only one drug is used, it's called a single agent. A combination or multi-agent regimen is the use of 2 or more chemotherapy drugs.

Some chemotherapy drugs are liquids given through a vein (intravenously or IV) or injected under the skin with a needle. Other chemotherapy drugs may be given as a pill that's swallowed.

Most chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next cycle. Cycles vary in length depending on which drugs are used. The number of treatment days per cycle and the total number of cycles given also vary.

Chemoradiation

Chemoradiation combines lower-dose chemotherapy with radiation therapy (RT). The chemotherapy and RT can be given at the same time (concurrent) or one after the other (sequential). Chemotherapy may improve how well radiation works, and that's why they are sometimes used together. Chemoradiation is typically only used for poorly differentiated tumors found outside the lung. For more information, see *Chapter 8: Extrapulmonary poorly differentiated NECs.*

Targeted therapy

Targeted therapy is drug therapy that focuses on specific or unique features of cancer cells. Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop or inhibit the action of molecules that help cancer cells grow and/or survive. Some target a specific tumor (gene) mutation, such as *NTRK*. There are many types of targeted therapies used to treat NETs such as mTORs, tyrosine kinase inhibitors (TKIs), and those explained on the next page.

Somatostatin analogs

Somatostatin analogs (SSAs) and somatostatin receptor (SSTR) therapy are used to slow down or stop tumor hormone production. This helps reduce symptoms such as diarrhea and flushing and to control tumor growth. SSAs work for a long time in the body. Treatment focused on SSTRs could include SSAs, peptide receptor radionuclide therapy (PRRT), or other drugs that bind to SSTRs.

Octreotide LAR or lanreotide can be used if the tumor is SSTR-positive and/or you're

Guide 1
Systemic therapy examples

Chemotherapy	• Capecitabine (Xeloda) • Carboplatin • Cisplatin • Dacarbazine • Etoposide (Etopophos)	• Fluorouracil • Irinotecan (Camptosar) • Oxaliplatin • Temozolomide (Temodar)
Targeted therapy	• Belzutifan (Welireg) • Cabozantinib (Cabometyx) • Dabrafenib (Tafinlar) • Entrectinib (Rozlytrek) • Everolimus (Afinitor)	• Larotrectinib (Vitrakvi) • Repotrectinib (Augtyro) • Selpercatinib (Retevmo) • Sunitinib (Sutent) • Trametinib (Mekinist)
Immunotherapy	• Pembrolizumab (Keytruda) • Nivolumab (Opdivo) • Ipilimumab (Yervoy)	
PRRT	• Lutetium Lu 177 dotatate (Lutathera)	
Somatostatin analogs (SSAs)	• Octreotide LAR (Sandostatin LAR Depot) • Lanreotide (Somatuline Depot) • Octreotide acetate (Sandostatin, Bynfezia Pen)	

having hormone-related symptoms. Octreotide acetate might be added to octreotide LAR or lanreotide.

PRRT

Peptide receptor radionuclide therapy (PRRT) combines a protein that binds to the tumor cell receptors with a radioactive element called a radionuclide. PRRT with lutetium Lu 177 dotatate may be used to slow down or stop tumor growth in SSTR-positive tumors. The treatment works by attaching to SSTRs found on the tumor. This allows a high dose of radiation to be delivered directly to the tumor. Typically, this involves a series of 4 treatments given 8 weeks apart.

Immunotherapy

The immune system has many on and off switches. Tumors take advantage of off switches. Immunotherapy can block these off switches, which helps turn the immune system back on. Immunotherapy can be given alone or with other types of treatment. Pembrolizumab nivolumab, and ipilimumab are examples of immunotherapy. Immunotherapy is only used in very specific cases to treat NETs. Examples include pembrolizumab, nivolumab, and ipilimumab.

Standard of care is the best-known way to treat a particular disease based on past clinical trials. There may be more than one treatment regimen that's considered standard of care. Ask your care team what treatment options are available and if a clinical trial might be right for you.

Radiation therapy

In addition to PRRT, other forms of radiation therapy are sometimes given to treat a NET or NEC. Radiation therapy uses high-energy radiation from x-rays (photons), protons, and other sources to kill cancer cells, shrink tumors, or treat metastases. Radiation is typically delivered from outside the body by a computerized device, which can shape the treatment to closely fit the location and size of the tumor. Treatment is given in small daily doses on weekdays, with weekends off.

At least once a week, you will meet with your radiation oncologist to review treatment results and to check for side effects, such as sunburn-like rash. Ask your care team which radiation option(s) are best for your situation, if RT will be combined with chemotherapy, and what side effects to expect.

A four-dimensional (4D) CT scan might be used to plan RT. A 4D-CT records multiple images over time. It allows playback of the scan as a video, so that internal movement can be tracked and observed.

Other therapies

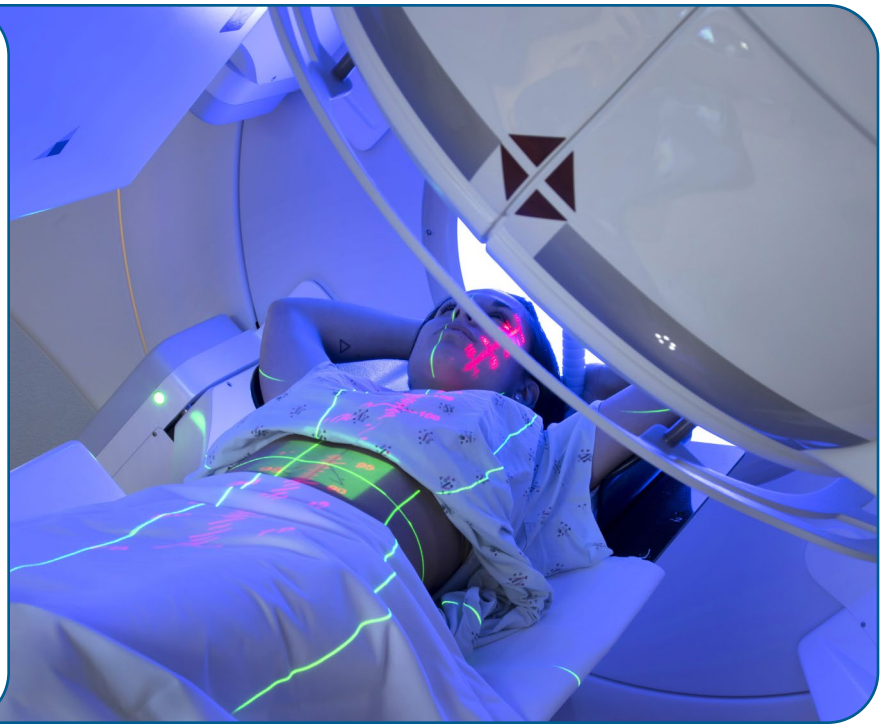
Tumors found in the liver or lung may be treated with one or more of the following therapies.

Ablation

Ablation uses extreme cold, extreme heat, radio waves, microwaves, or chemicals to destroy cancer cells. It can destroy small tumors and metastases with little harm to nearby tissue. Ablation might be used if you aren't healthy enough for surgery. Tumors in the liver or lung might be treated with ablation.

Radiation therapy

External beam radiation therapy uses a machine outside of the body to aim radiation at the tumor(s) or specific areas of the body. It may be used to treat some types of neuroendocrine tumors (NETs).



It might take multiple treatments to destroy the tumor or metastasis.

Types of ablation include:

- **Chemical** – Uses ethanol or acetic acid injections to kill cancer cells.
- **Thermal** – Uses high-energy radio waves or microwaves to kill cancer cells. Metastases in the liver might be treated with thermal ablation.
- **Cryoablation** – Freezes cancer cells with a very cold substance.
- **Histotripsy** – Uses focused ultrasound energy (sound waves) to destroy tumors or metastases in the liver.

Arterially directed therapy

Arterially directed therapy or embolization treats tumors by injecting particles, chemotherapy, or radioactive beads directly into the blood vessels that supply the tumor(s). First, a small catheter is inserted into the artery and is guided to the tumor. Once in place, the particles, chemotherapy, or beads are injected. Tumors or metastases in the liver might be treated with arterially directed therapy.

Clinical trials

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

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

Phases

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

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the safety and benefit of an FDA-approved treatment.

Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

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

Will I get a placebo?

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

Are clinical trials free?

There's no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by insurance.

Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

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

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

Supportive care

Supportive care is an important part of cancer care. The goal is to improve your quality of life during and after cancer treatment. Supportive care is for everyone with cancer and their families, not just for those at the end of life. It's also known as palliative care.

Supportive care includes a wide range of services. Supportive care prevents or manages the symptoms of cancer and the side effects of cancer treatment, like pain and cancer-related fatigue. It also addresses the mental, social, emotional, and spiritual concerns faced by people with cancer.

Supportive care provides help with additional needs, such as:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advanced care and end of life

Read more about the types of support you may receive in *NCCN Guidelines for Patients: Palliative Care*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app. Palliative care is appropriate for anyone, regardless of age, cancer stage, or the need for other therapies. It focuses on physical, emotional, social, and spiritual needs that affect quality of life.

Side effects

Cancer treatment can cause unwanted health issues called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may just be unpleasant. Others may be harmful to one's health. Treatment can cause several side effects. Some are very serious. Tell your care team about any new or worsening symptoms.

Some possible side effects of treatment are described next.

Supportive care resources

More information on supportive care is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Diabetes

Diabetes is a condition where the amount of glucose (a type of sugar) in your blood is too high. The amount of glucose in your blood is called your blood sugar level or blood glucose level. If you have diabetes or early-onset diabetes, a pancreatic tumor can change how the diabetes is managed. Diabetes can also happen when part or all of your pancreas is removed. Each type of diabetes is different and treated differently.

Diarrhea or constipation

Diarrhea is frequent and watery bowel movements. Your care team will tell you how to manage diarrhea. It's important to drink lots of fluids. Constipation is also common, especially if taking certain pain medicines. Drinking fluids, staying active, and taking medicines for constipation are often recommended.

Distress

Depression, anxiety, and sleeping issues are common and are a normal part of cancer diagnosis. Talk to your care team and with those whom you feel most comfortable about how you are feeling. There are services, people, and medicine that can help relieve your distress.

Fatigue

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. Let your care team know how you're feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, acupuncture, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

Survivorship

A person is a cancer survivor from the time of diagnosis until the end of life. After treatment, your health will be monitored for side effects of treatment and the return of cancer. This is part of your survivorship care plan. It's important to keep any follow-up care and imaging test appointments. Seek routine medical care, including regular doctor visits for preventive care and cancer screening.

A personalized survivorship care plan will contain a summary of possible long-term effects of treatment called late effects and a list of follow-up tests. Find out how your primary care provider will coordinate with specialists for your follow-up care.

Key points

- Surgery is the main or primary treatment for neuroendocrine tumors (NETs) with limited or no spread. The type of surgery depends on where the tumor is located, the size of the tumor, and how far the disease has spread. Surgery has less of a role in the treatment of neuroendocrine carcinomas (NECs) because they are often advanced at diagnosis or in a challenging location.
- Systemic therapy is drug treatment that works throughout the body. Types include chemotherapy, chemoradiation, targeted therapy, immunotherapy, and others.
- Radiation therapy uses high-energy radiation from x-rays (photons, electrons), protons, and other sources to destroy tumors or kill cancer cells.
- Somatostatin analogs (SSAs) are used to slow down or stop tumor hormone production.
- Peptide receptor radionuclide therapy (PRRT) uses a radioactive molecule to deliver high doses of radiation to tumors.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.
- Supportive care is health care that relieves symptoms and improves quality of life. It might include pain relief (palliative care), emotional or spiritual support, financial aid, or family counseling.

Questions to ask

- What are my treatment options?
- What treatment(s) do you recommend and why?
- What are the treatment side effects?
- Does the order of treatments matter?
- How long will treatment take?

5

NETs of the GI tract, lung, and thymus

This chapter gives testing and treatment information for the most common sites for neuroendocrine tumors (NETs). These are NETs of the gastrointestinal tract (GI NETs), lung, and thymus. Treatment is often surgery. Radiation therapy or systemic (drug) therapy might be given.

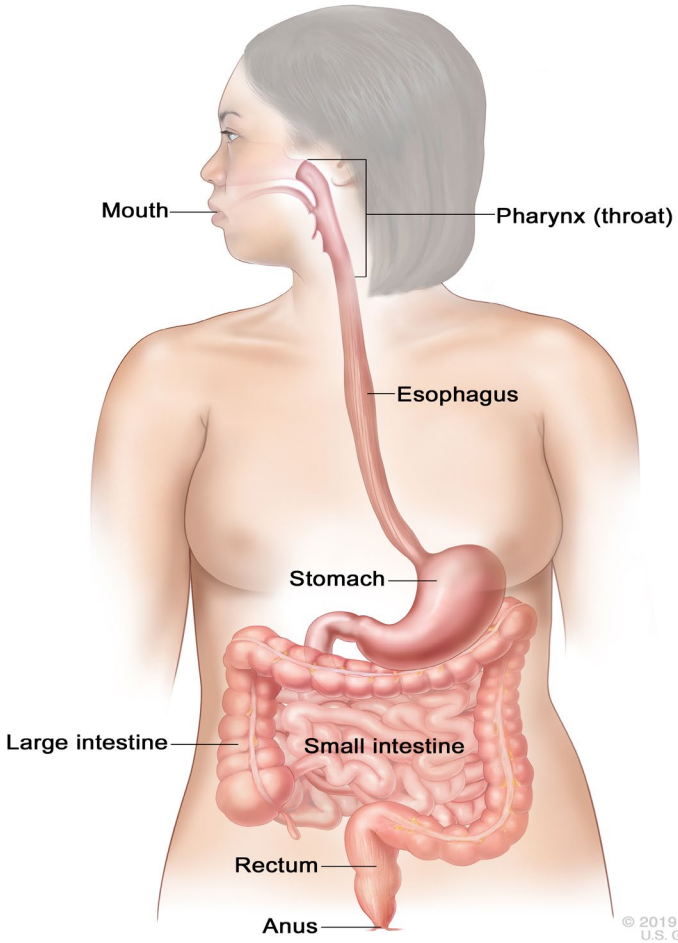
This chapter is for well-differentiated grade 1 or grade 2 neuroendocrine tumors of the gastrointestinal tract (GI NETs), lung, and thymus. Treatment for well-differentiated, grade 3 NETs can be found in *Chapter 7: Well-differentiated, grade 3 NETs*.

NETs of the GI tract, lung, and thymus are the most common sites for NETs. These NETs may secrete hormones and proteins that affect blood pressure and blood vessel function.

NETs of the lungs and thymus are also a cause of Cushing syndrome, a condition where there is too much stress hormone (cortisol) in the body.

The digestive tract

The digestive or gastrointestinal (GI) tract is part of the digestive system. Food enters the mouth and passes through the esophagus into the stomach. After being broken down into a liquid, food enters the small intestine. The large intestine prepares unused food to be moved out of the body.



Diagnosis and treatment overview

GI tract

The GI tract is the main part of the digestive system. It starts at the mouth and ends at the anus. Main functions include digesting food and liquid and processing food waste. The most common places to find GI NETs are in the small intestine or rectum. However, they can also start in the stomach, appendix, colon, and other areas of the GI tract.

Lungs

There are 2 lungs found inside the chest. Together, they supply the body with oxygen and remove carbon dioxide from the body. The lungs help us breathe and are part of the respiratory system. Lung (pulmonary) NETs often develop in the major bronchi. These are large tubes that lead air from the windpipe (trachea) into the lungs.

Thymus

The thymus gland is a small organ found between the lungs in the upper chest, behind the breastbone (sternum). It's part of the lymphatic system, which is part of the immune system. The thymus makes white blood cells, called lymphocytes, which protect the body against infections.

Tests

Tests for NETs of the GI tract, lung, and thymus might include multiphasic CT or MRI and somatostatin receptor (SSTR)-PET/CT or SSTR-PET/MRI. Depending on the locationof the tumor, you might also have scoping procedures, chest CT, or other tests.

NETs of the gastrointestinal tract (well-differentiated grade 1 or 2), lung, and thymus

These NETs are grouped as follows:

- Jejunal (middle part of small intestine), ileal (last part of small intestine), colon (large intestine)
- Duodenal (first part of small intestine)
- Appendix
- Rectal
- Stomach (gastric)
- Lung
- Thymus
- Carcinoid syndrome

Treatment

Treatment options are based on the location of the NET and if it has spread to other areas near the tumor, such as the lymph nodes, or farther such as the liver.

The following terms are used to describe the location of NETs:

- **Locoregional or locally advanced disease** is the spread of cancer to places near the primary tumor such as regional lymph nodes. The disease has not spread far within the body. Treatment is often surgery. A tumor that can be removed with surgery is called resectable. A tumor that can't be removed with surgery is called unresectable.
- **Metastatic disease** is the spread of cancer from the primary tumor to a new (often distant) site in the body. When possible, treatment is surgery to remove the tumor and metastases. System therapy and other treatments might be given.

Surveillance

Surveillance tests are done at specific times such as every 12 months after treatment to check if the cancer has returned. These tests help find cancer early so you can start treatment again, if needed. Surveillance tests may include general health tests such as a medical history, physical exams, biochemical tests, and imaging scans. CT or MRI scans are common. Surveillance might last up to 10 years. **See Guide 2**.

Stomach

There are 4 types of stomach (gastric) NETs or G-NETs:

- Type 1 - associated with chronic atrophic gastritis or high gastric pH
- Type 2 - associated with antrum-sparing type A Zollinger-Ellison syndrome
- Type 3 - sporadic and unifocal
- Other

Tests such as upper endoscopy and a biopsy will be done to pinpoint your type of stomach NET. Once the type has been identified, you may receive additional testing to determine treatment options.

Type 1 and type 2

Treatment for type 1 and type 2 is an endoscopic resection. An endoscopic resection uses an endoscope to remove the tumor from the stomach. One year after completing treatment, you'll have an upper endoscopy to check for any new tumors. You might have this test every 1 to 3 years or if you develop symptoms.

Type 3

The preferred treatment for type 3 is surgery to remove part or all of the stomach (gastrectomy) and nearby lymph nodes. An endoscopic resection or other surgery is possible. Follow-up testing can be found in **Guide 2**.

Other

Your care team will suggest the best treatment available based on current research for a G-NET classified as other.

Duodenum

Treatment for NETs in the duodenum (first part of the small intestine) is broken up into 3 categories:

- Nonfunctioning NET
- Duodenal gastrinoma
- Metastatic disease

Nonfunctioning NET

A nonfunctioning NET is a tumor that does not make enough hormones to cause symptoms. Treatment is surgery. Ask your care team what surgery they recommend for you. After surgery, you might have regular endoscopies and other follow-up testing as found in **Guide 2**.

Duodenal gastrinoma

Duodenal gastrinoma is a gastrin-secreting tumor. Gastrin is a hormone that helps your stomach produce acid. A gastrinoma secretes large amounts of gastrin, which causes your stomach to produce too much acid and may cause a burning sensation or other symptoms.

Guide 2
NETs of GI, lung, and thymus: Surveillance

12 weeks to 1 year after surgery	• Medical history and physical exam • For functioning tumors, biochemical testing as needed • Multiphasic CT or MRI for primary GI NETs and as needed for lung and thymic NETs • Chest CT with CT or MRI of abdomen with contrast for primary lung and thymic NETs and as needed for primary GI tumors
1 to 10 years after surgery	Every 12 to 24 months • Medical history and physical exam • For functioning tumors, biochemical testing as needed • Multiphasic CT or MRI for primary GI NETs and as needed for lung and thymic NETs • Chest and abdomen CT with contrast for primary lung and thymic NETs and as needed for primary GI tumors
After 10 years	• Continue surveillance as needed

Treatment is surgery. Ask your care team what surgery they recommend for you. After surgery, you might have regular endoscopies and other follow-up testing as found in **Guide 2**.

Metastatic disease

Treatment for a duodenal NET that has spread to other parts of the body can be found under the section on *Advanced and metastatic disease – GI NETs*.

Jejunum, ileum, and colon

Surgery called bowel resection is the main treatment for NETs found in the jejunum, ileum, or colon. During surgery, the tumor along with some lymph nodes near the tumor will be removed. After surgery you will have follow-up testing as found in **Guide 2**.

Treatment for metastatic disease and tumors that can't be removed with surgery can be found under the section on *Advanced and metastatic disease – GI NETs*.

Appendix

Most NETs of the appendix are found when the appendix is removed because of appendicitis, an infection of the appendix. Treatment for an appendiceal NET is surgery called a simple appendectomy.

After surgery,

- For a tumor smaller than 1 cm, no follow-up is needed.
- For a tumor 1 cm to 2 cm, surveillance for 2 to 5 years is an option.
- If you have a tumor larger than 2 cm, there is cancer in your lymph nodes, or your surgeon wasn't able to remove all of the cancer, you might have a right hemicolectomy. This is surgery to remove the right side of your colon. The next step is surveillance to monitor for the return of cancer. **See Guide 2**.

Rectum

Rectal NETs need different treatments than other more common types of bowel cancer. Rectal NETs are treated with surgery. Ask your care team what type of surgery you might have and what side effects to expect.

After surgery,

- For a tumor smaller than 1 cm, no follow-up is usually needed.
- For a tumor 1 cm to 2 cm, follow-up tests might include endoscopy with rectal MRI or endorectal ultrasound at 6 to 12 months or as needed.
- For a tumor larger than 2 cm or cancer in the lymph nodes, **see Guide 3**.

Advanced and metastatic disease - GI NETs

Advanced disease may be locally or regionally advanced and involve nearby organs or lymph nodes. It might include cancer that can't be removed with surgery (unresectable). Metastatic disease refers to cancer that has spread from the primary tumor site to a distant part of the body. If advanced or metastatic disease is suspected, you will have testing to confirm.

Testing may include:

- Multiphasic CT or MRI
- Chest CT with or without contrast
- SSTR-PET/CT or SSTR-PET/MRI
- Biochemical tests

If possible, you'll have surgery to remove the primary tumor and any areas of metastases. Treatment might also include octreotide LAR (Sandostatin LAR Depot) or lanreotide (Somatuline Depot) or other systemic therapies to treat symptoms or to reduce the amount of cancer in the body. Metastases in the liver might be treated with radiation therapy, ablation, or arterially directed therapy. You will be monitored during and after treatment.

Disease progression

Grade 1 or grade 2 GI NETs that have progressed or spread during or after treatment are often treated with systemic therapy. Radiation therapy or chemoradiation might be used in some cases. Metastases in the liver might be treated with radiation therapy ablation, or arterially directed therapy.

"My doctor reminded me that stress cannot help me, but it can hurt me! It helped me remember to control those things I could control and relax in front of those that I could not control."

For disease progression, the preferred systemic therapy options include:

- Cabozantinib (Cabometyx)
- Everolimus (Afinitor)
- PRRT with lutetium Lu 177 dotatate (Lutathera)
- Octreotide LAR or lanreotide

Lung and thymus

NETs of the lung and thymus are treated similarly. Lung (pulmonary) NETs often develop in the major bronchi. These are large tubes that lead air from the windpipe into the lungs. The thymus gland sits in your upper chest between the lungs.

There are 2 types of lung and thymic NETs described next:

- **Typical carcinoid (low grade)** – slow growing and less likely to spread beyond the lungs or thymus
- **Atypical carcinoid (intermediate grade)** – rarer and grow more rapidly than typical tumors

Stage 1, 2, or 3

The main treatment for a thymic NET is surgery.

Treatment for lung NETs may include:

- Surgery to remove part of the lung (lobectomy) and nearby lymph nodes
- Thermal ablation or radiation therapy

After surgery, you'll have surveillance tests to check if the cancer has returned. These tests can help find cancer early so you can start treatment again, if needed. For a list of tests and time frames, **see Guide 2**.

Stage 3 (unresectable)

A tumor that can be removed with surgery is called resectable. A tumor that can't be removed with surgery is called unresectable. Treatment for an unresectable tumor is systemic therapy or radiation therapy as described below.

For a low-grade (typical carcinoid) tumor, treatment options are:

- Observation (if you have no symptoms)
- Everolimus
- Octreotide LAR or lanreotide (if tumor is SSTR-positive and/or you have hormone-related symptoms)
- Temozolomide (Temodar) with or without capecitabine
- Radiation therapy

For an intermediate-grade (atypical carcinoid) tumor, treatment options are:

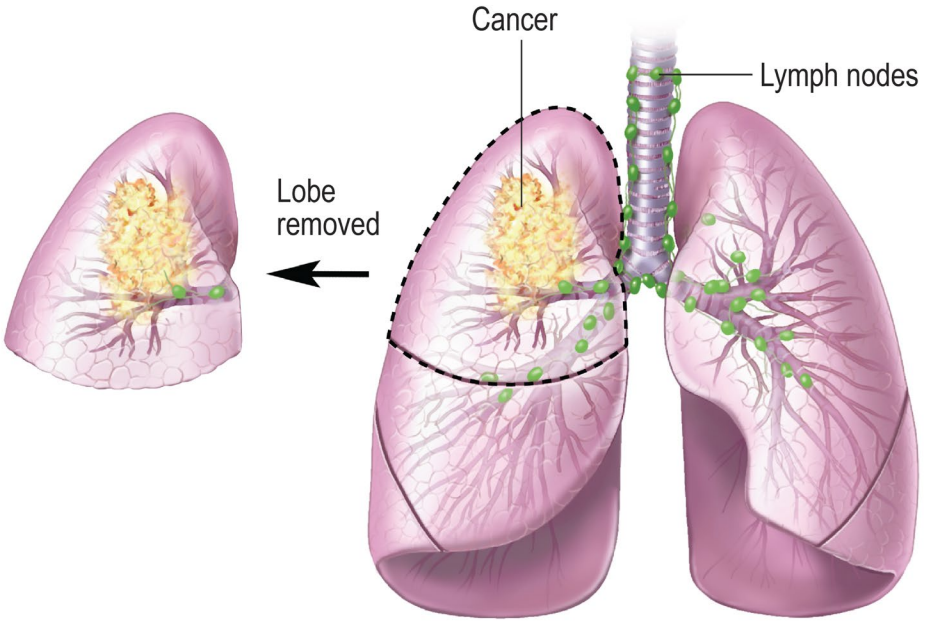
- Observation (if you have no symptoms)
- Chemotherapy such as cisplatin with etoposide, carboplatin with etoposide, or temozolomide with or without capecitabine
- Everolimus (a targeted therapy)
- Octreotide LAR or lanreotide (if tumor is SSTR-positive and/or you have hormone-related symptoms)
- Radiation therapy
- Chemoradiation

Next therapy options

- Clinical trial (preferred)
- Cabozantinib (a chemotherapy)
- Another therapy based on tumor grade
- Peptide receptor radionuclide therapy (PRRT) with lutetium Lu 177 dotatate (if tumor is SSTR-positive and cancer has progressed on octreotide LAR or lanreotide)

Lobectomy

During a lobectomy, part of the lung is removed. The right lung has 3 lobes. The left lung has 2 lobes. Here, 1 of the lobes of the right lung has been removed.



Stage 4 (metastatic)

NETs of the lung and thymus can spread and form tumors in other parts of the body. This is called metastatic disease. Treatment options for metastatic disease are based on if the metastases are causing symptoms, the amount of cancer called tumor burden, and the tumor grade (typical carcinoid or atypical carcinoid).

For no symptoms, low tumor burden, and low grade (typical carcinoid), or multiple lung nodules or tumorlets and evidence of a condition called DIPNECH (diffuse idiopathic pulmonary neuroendocrine cell hyperplasia), the options are:

- Observation (watch and wait)
- Octreotide LAR or lanreotide

With observation, you should expect to have a chest CT with contrast and abdomen and pelvis multiphasic CT or MRI every 3 to 6 months to monitor the disease.

For high tumor burden and low grade (typical carcinoid), or disease progression, or intermediate grade (atypical carcinoid), or symptoms, then the options are:

- Clinical trial (preferred)
- Observation (in some cases)
- Systemic therapy, **see Guide 3**
- For metastases in the liver, treatment might include surgery, thermal ablation, arterially directed therapy, or radiation therapy.

Guide 3
NETs of lung and thymus: Systemic therapy options for distant metastases

Preferred therapies	• Cabozantinib • Everolimus • Octreotide LAR or lanreotide if SSTR-positive and/or hormone symptoms
Therapies used in certain cases	• Carboplatin and etoposide (Etopophos) • Cisplatin and etoposide • PRRT with lutetium Lu 177 dotatate (if SSTR-positive and progression on octreotide LAR or lanreotide) • Temozolomide with or without capecitabine (Xeloda)

Carcinoid syndrome

Carcinoid syndrome refers to a group of symptoms caused when NETs release unusually large amounts of serotonin and other substances such as histamine or tachykinin. This overwhelms your body and can cause a range of symptoms. Flushed skin (sudden warmth and redness) and watery diarrhea are the most common symptoms, but this syndrome can also thicken heart valves or cause breathing issues. Carcinoid syndrome is most commonly associated with small bowel NETs.

Possible tests to see if you have carcinoid syndrome include:

- Biochemical tests with 24-hour urine or 5-HIAA
- Echocardiogram (heart ultrasound)
- Imaging scans

Treatment for carcinoid syndrome is octreotide LAR or lanreotide. If your symptoms continue, then you might have systemic (drug) therapy such as telotristat (Xermelo) to help treat diarrhea. Surgery or arterially directed therapy might be used to treat your tumor.

Surveillance

After treatment, follow-up tests may include:

- Echocardiogram every 1 to 3 years or as needed
- Abdomen and pelvis multiphasic CT or MRI every 12 weeks to 12 months
- Chest CT with or without contrast as needed

If testing shows cancer has grown or spread, you will be treated based on if the advanced or metastatic disease is in the GI tract, lung, or thymus.

Key points

- The most common sites for neuroendocrine tumors (NETs) are the gastrointestinal tract (GI), lung, or thymus.
- GI NETs start in areas such as the stomach, small intestine, colon, and rectum.
- Treatment options are based on the location of the NET and if it has spread to other areas near the tumor, such as the lymph nodes, or farther such as the liver.
- Treatment for NETs is often surgery. A resectable tumor can be removed with surgery. An unresectable tumor can't be removed with surgery. There are many possible treatments for an unresectable NET.
- Carcinoid syndrome refers to a group of symptoms caused when NETs overwhelm your system with hormones (serotonin) and other substances. This syndrome is most commonly associated with small bowel NETs.
- Surveillance tests are done to monitor your health and check if the cancer has returned. These tests can help find cancer early so you can start treatment again, if needed.

Questions to ask

- What type of neuroendocrine tumor (NET) do I have?
- Where is the tumor located?
- What treatment(s) do you recommend and why?
- What should I expect from treatment?
- What are the treatment side effects?

6
NETs of the pancreas

A pancreatic neuroendocrine tumor (PanNET) is a type of cancer of the pancreas. There is more than one type of PanNET. Treatment often includes surgery and systemic (drug) therapy.

This chapter is about well-differentiated grade 1 and grade 2 neuroendocrine tumors of the pancreas (PanNETs). Treatment for well-differentiated, grade 3 NETs can be found in *Chapter 7: Well-differentiated, grade 3 NETs*.

About the pancreas

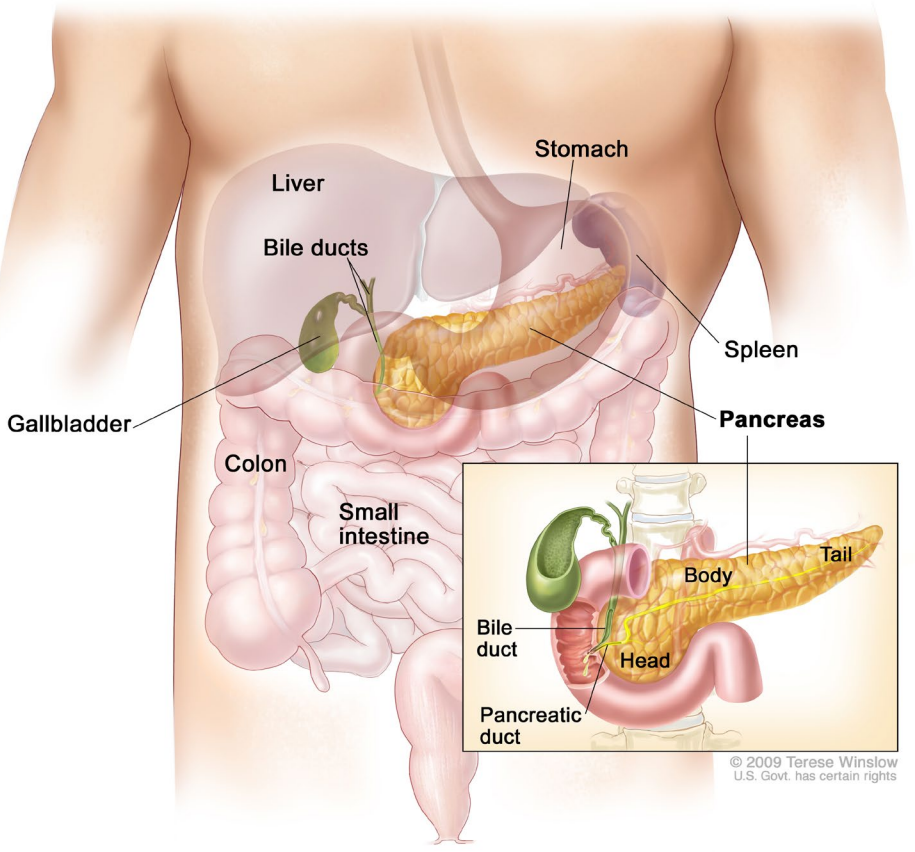
The pancreas is a large gland found in your abdomen. It's about 6 inches long and lies behind the stomach and across the spine. The small intestine wraps along the wide end (head) of the pancreas. The liver and gallbladder are found nearby. The spleen is found at the tail end of the pancreas.

The pancreas has 3 parts:

- Wide end called the head (includes neck and uncinate)
- Middle part called the body
- Narrow end called the tail

The pancreas

The pancreas is located behind the stomach and next to the spleen. The small intestine wraps around the wide end of the pancreas. The liver and gallbladder are found nearby.



The pancreas does 2 important things:

- **It makes hormones** (such as insulin and glucagon) that control the amount of sugar (glucose) in your blood. This helps your body use and store energy from food. Removing part of the pancreas might put you at risk for diabetes. If you have diabetes, it might make it worse.
- **It makes pancreatic enzymes** that help digest food in your small intestine. Removing part of the pancreas can decrease the amount of these enzymes. This can cause oily diarrhea (watery stool), stools that float, abdominal pain, bloating, gas, and weight loss.

Where does a pancreatic NET start?

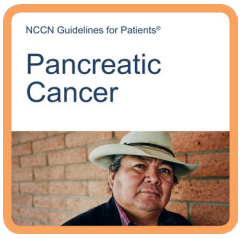
A pancreatic neuroendocrine tumor (PanNET) is thought to start in the hormone-producing cells of the pancreas called islet cells. PanNETs are either functioning or, more commonly, nonfunctioning. Functioning PanNETs secrete excess hormones, leading to specific symptoms, while nonfunctioning PanNETs don't produce enough hormones to cause noticeable symptoms.

Types of functioning PanNETs

There are 4 types of functioning pancreas NETs:

- **Gastrinoma** – This type of tumor makes too much gastrin. Gastrin is a hormone that causes acid production in the stomach. Too much stomach acid can cause severe ulcers (referred to as Zollinger-Ellison syndrome).
- **Glucagonoma** – This type of tumor makes too much glucagon. Glucagon is a hormone that increases glucose (sugar) levels in the blood. Too much blood glucose is called hyperglycemia.
- **Insulinoma** – This type of tumor makes too much insulin, which can rapidly lower blood sugar (referred to as hypoglycemia or low blood sugar). Insulinomas are typically noncancerous. Insulinoma is the most common type of functioning PanNET.
- **VIPoma** – This type of tumor starts in the cells of the pancreas that make vasoactive intestinal peptide (VIP). VIP is a hormone that helps move water into the intestines. Too much VIP can cause chronic, watery diarrhea. This is referred to as Verner-Morrison syndrome.

PanNETs need different treatment than the more common type of pancreatic cancer. For more information on pancreatic cancer and pancreatic adenocarcinoma, see *NCCN Guidelines for Patients: Pancreatic Cancer* at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Testing and treatment overview

Testing

Testing often includes:

- Imaging tests such as multiphasic CT or MRI and somatostatin receptor (SSTR)-PET/CT or SSTR-PET/MRI
- Endoscopic ultrasound (EUS) with possible biopsy
- Biochemical tests to measure substances such as hormones, proteins, and sugar (glucose) in blood and urine
- Possible genetic testing and counseling

Locoregional disease

Locoregional disease is cancer limited to the pancreas. It might have spread to nearby lymph nodes. Treatment is often surgery. After surgery you will enter surveillance to monitor changes in your health.

Metastatic disease

Treatment for tumors that can't be removed with surgery (unresectable) or cancer that has spread to distant parts of the body can be found under the section on *Advanced and metastatic disease* on page 62.

NETs of the pancreas (well-differentiated grade 1 or 2)

PanNETs are grouped like this:

- Nonfunctioning pancreatic tumors
- Gastrinoma
- Insulinoma
- Glucagonoma
- VIPoma

Treatment

Treatment for PanNETs is based on the following:

- **Hormones** – if the tumor produces hormones and causes symptoms (functioning) or doesn't cause symptoms (nonfunctioning).
- **Location** – if tumors are found in one or more areas of the pancreas, and if the tumors are in the tail or head of the pancreas. Cancer can spread to places near the tumor such as regional lymph nodes.
- **Metastases** – whether the cancer has spread to distant lymph nodes or new tumors have formed in other parts of the body such as the liver, lung, peritoneum, or bone.

Standard treatment for PanNETs includes:

- Observation, sometimes called watch and wait, for small tumors
- Surgery – the type depends on the size and location of the tumor.
- Systemic therapy

Types of surgeries

There are many types of pancreatic surgeries that might be used to treat PanNETs. The most common types are described next.

Enucleation

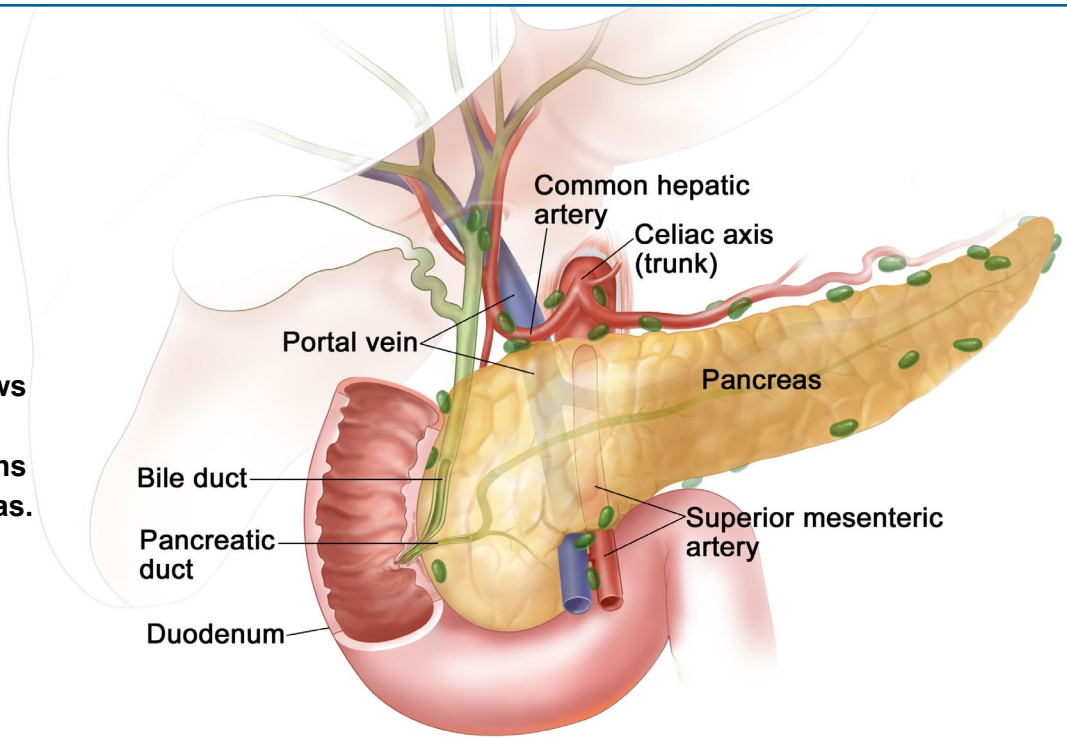
In an enucleation, only the tumor or tumor cells are removed from the pancreas. Other pancreatic surgeries remove the tumor with a section of the pancreas. Enucleation is often used for insulinomas because they are rarely cancer.

Pancreatoduodenectomy

Pancreatoduodenectomy refers to surgery that removes the head of the pancreas, gallbladder, duodenum (first part of the small intestine), part of the bile duct, nearby lymph nodes, and often part of the stomach. This is known as a Whipple procedure. This surgery can be open or minimally invasive.

A closer look

This image shows arteries, veins, ducts, and organs near the pancreas.



Distal pancreatectomy

A distal pancreatectomy is surgery that removes the body and tail of the pancreas, and sometimes the entire spleen (splenectomy). The left adrenal gland might also be removed. This surgery can be open or minimally invasive.

Total pancreatectomy

A total pancreatectomy is surgery that removes the whole pancreas, part of the small intestine, part of the stomach, the common bile duct, the gallbladder, the spleen, and nearby lymph nodes. It's usually done as open surgery.

Other procedures

- **Duodenotomy** – surgery that removes the first part of the small intestine called the duodenum. It's often performed for gastrinomas in or near the duodenum.
- **Liver resection** – surgery to remove part of the liver.
- **Peripancreatic lymphadenectomy** – surgery that removes lymph nodes near the pancreas to look for cancer.
- **Splenectomy** – surgery that partially or completely removes the spleen.

Nonfunctioning PanNETs

Nonfunctioning PanNETs do not cause hormone-related symptoms. Hormone levels may or may not be higher than normal (elevated), but not high enough to cause symptoms. Treatment for nonfunctioning PanNETs is based on if the cancer is localized or metastatic.

Functioning PanNETs

Functioning PanNETs make extra hormones causing symptoms. The following explains treatment for different types of functioning PanNETs.

Gastrinoma

A gastrinoma is usually found in the duodenum (first part of the small intestine) or head of the pancreas, near the pancreatic ducts. Gastrinomas make too much gastrin. Gastrin helps your body control the amount of acid in your stomach and helps to digest food. Too much acid can cause ulcers in your stomach or duodenum. To prevent this, gastrinomas are treated with high-dose proton pump inhibitors (PPIs) and octreotide LAR (Sandostatin) or lanreotide (Somatuline Depot). Surgery is also part of treatment. The type of surgery is based on the location of the tumor and if it can be removed with surgery.

Glucagonoma

A glucagonoma is usually found in the tail of the pancreas. Glucagonomas make too much of the hormone glucagon. Glucagon is a hormone that helps the body control glucose (sugar) levels in the blood. Treatment is octreotide LAR (Sandostatin) or lanreotide (Somatuline Depot), which controls symptoms caused by increased hormone levels produced by the tumor. If you have hyperglycemia (high blood sugar) or diabetes it will also be treated. Surgery is also part of treatment. The type of surgery is based on the location of the tumor and if it can be removed with surgery.

Insulinoma

An insulinoma makes more insulin than your body can use. Insulinomas are known to cause hypoglycemia (low blood sugar). Treatment starts with getting your glucose (sugar) levels stable. This can be done with a change in what you eat (including adding cornstarch to your diet) and taking diazoxide (Proglycem) or everolimus (Afinitor). Octreotide LAR or lanreotide might be considered **only** if the tumor expresses SSTRs. Otherwise, these drugs can make hypoglycemia much worse.

VIPoma

A VIPoma secretes vasoactive intestinal peptide (VIP). VIP is a hormone that helps the body to release sodium, chloride, potassium, and water in the small intestine. Treatment is octreotide LAR or lanreotide, which controls symptoms caused by increased hormone levels produced by the tumor. Surgery is also part of treatment. The type of surgery is based on the location of the tumor and if it can be removed with surgery.

Surveillance after surgery

Surveillance tests are done at specific times after treatment to check if the cancer has returned. These tests help find cancer early so you can start treatment again, if needed. Surveillance tests may include general health tests such as medical history, physical exams, biochemical tests, and imaging scans. CT or MRI scans are common. Surveillance might last up to 10 years. **See Guide 4**.

Advanced and metastatic disease

Locoregionally advanced disease is cancer that has spread or progressed near the tumor area. It might be cancer in the lymph nodes or cancer that's causing symptoms. Metastatic disease is cancer that has spread to form tumors in distant parts of the body. Treatment options for metastatic disease are based on tumor burden, SSTR expression, rate of growth (and/or proliferation rate), and whether the tumor could be removed by surgery. Tumor burden is the amount of cancer found in the body.

No symptoms, low tumor burden, and stable disease

Treatment for tumors not causing symptoms, low tumor burden, and stable disease includes:

- Surgery to remove tumor and metastases, if possible and needed
- Observation (watch and wait)
- Octreotide LAR or lanreotide

With observation, you should expect to have a chest CT with contrast and multiphasic CT or MRI every 3 to 6 months to monitor the disease.

Guide 4
PanNET: Surveillance after surgery

12 weeks to 1 year after surgery	• Medical history and physical exam • For functioning tumors, biochemical testing as needed • Multiphasic CT or MRI of the abdomen and maybe pelvis • Chest CT as needed
1 to 10 years after surgery	Every 6 to 12 months • Medical history and physical exam • For functioning tumors, biochemical testing as needed • Multiphasic CT or MRI of the abdomen and maybe pelvis • Chest CT as needed
After 10 years	• Continue surveillance as needed

Symptoms, high tumor burden, or disease progression

Treatment for tumors causing symptoms, high tumor burden, and disease that's growing or spreading includes:

- Surgery to remove tumor and metastases, if possible and needed
- Treatment to manage symptoms
- Observation (watch and wait)
- Octreotide LAR or lanreotide
- Systemic therapy, **see Guide 5**.

Treatment for disease progression might include:

- Clinical trial
- Systemic therapy
- Radiation therapy
- Therapies to treat metastases such as ablation or arterially directed

Guide 5
PanNET advanced or metastatic disease: Systemic therapy options

Preferred therapies	• Cabozantinib (Cabometyx) • Everolimus (Afinitor) • Sunitinib (Sutent) • Octreotide LAR or lanreotide if SSTR-positive • First-line PRRT with lutetium Lu 177 dotatate • PRRT with lutetium Lu 177 dotatate (if SSTR-positive and progression on octreotide LAR or lanreotide) • Temozolomide (Temodar) with capecitabine (Xeloda)
Other recommended therapies	Chemotherapy • FOLFOX, which is fluorouracil, leucovorin, and oxaliplatin • CAPEOX, which is capecitabine and oxaliplatin
Therapies used in certain cases	• Octreotide LAR or lanreotide if SSTR-negative • Belzutifan (Welireg) • Chemoradiation

Key points

- The pancreas is a large gland found in your abdomen. The pancreas lies behind the stomach and across the spine. The pancreas has 3 parts: the head, the body, and the tail.
- A pancreatic neuroendocrine tumor (PanNET) forms tumors in the pancreas. PanNETs are either functioning or, more commonly, nonfunctioning.
- Functioning PanNETs secrete excess hormones, leading to specific symptoms, while nonfunctioning PanNETs do not produce enough hormones to cause noticeable symptoms.
- Gastrinoma is a functioning PanNET that makes too much gastrin. Gastrin helps your body control the amount of acid in your stomach and helps to digest food.
- Glucagonoma is a functioning PanNET that occurs when your body makes too much of the glucagon hormone.
- Insulinoma is a functioning PanNET that makes more insulin than your body can use.
- VIPoma is a functioning PanNET that secretes a hormone called vasoactive intestinal peptide (VIP). VIP helps the body to release sodium, chloride, potassium, and water in the small intestine.

Questions to ask

- What type of pancreatic neuroendocrine tumor (PanNET) do I have?
- Where is the tumor located in the pancreas?
- Is the tumor making excess hormones and if so, what does this mean?
- What treatment(s) do you recommend and why?
- How is PanNET different than pancreatic cancer?

7

Well-differentiated, grade 3 NETs

This chapter discusses treatment options for well-differentiated, grade 3 neuroendocrine tumors (NETs). Treatment is often surgery to remove any tumors, including metastases. Other treatments might be used to reduce the amount of cancer in the body.

Overview

Well-differentiated neuroendocrine tumor (NET) cells look like normal neuroendocrine cells. A well-differentiated, grade 3 NET is considered high grade. This means the tumor has normal-looking neuroendocrine cells that divide relatively quickly (fast-growing). High-grade tumors are more likely to spread to other areas of the body and are diagnosed through a tumor biopsy that shows a Ki-67 index or more than 20 percent (20%) (or a high mitotic rate).

Ki-67 index measures the amount of the Ki-67 protein found in tumor cells. A higher Ki-67 index suggests a faster growing tumor and can be used to help determine prognosis and guide treatment decisions. Your care team can answer any questions you may have about tumor biology and what this means for treatment.

Testing might include multiphasic CT or MRI and somatostatin receptor (SSTR)-PET/CT or SSTR-PET/MRI. Depending on the location of the tumor, you might also have scoping procedures, chest CT, FDG-PET/CT, or other tests. Genetic testing and counseling are possible.

“Connecting with other neuroendocrine cancer survivors—virtually and in-person—is vital to my well-being. This journey can feel lonely at times, and it helps so much to share thoughts and experiences with people who also struggle sometimes and understand!”

Treatment for well-differentiated, grade 3 NETs is based on tumor location and tumor biology.

A tumor with:

- **Favorable biology** typically has a Ki-67 index of less than 55 percent, is slower-growing, and has a positive SSTR-based PET result.
- **Unfavorable biology** typically has a Ki-67 index of 55 percent or greater, is faster-growing, and has a negative SSTR-based PET result.

Locoregional disease

Locoregional disease is cancer limited to a small area. It might include nearby lymph nodes.

Slower-growing, SSTR-positive tumors are treated with surgery to remove the tumor and nearby lymph nodes (regional lymphadenectomy).

Faster-growing, SSTR-negative tumors are treated with one of the following:

- Clinical trial (preferred)
- Surgery to remove the tumor and nearby lymph nodes
- Chemotherapy before surgery (in some cases), **see Guide 6**

After treatment you will be monitored to see if the disease returns. You should expect imaging tests every 12 to 24 weeks for the first 2 years and then every 6 to 12 months for up to 10 years.

Locally advanced or metastatic disease

In locally advanced disease, the tumor has spread to a nearby area. In metastatic disease, tumors are found in distant parts of the body. Treatment for a locally advanced or metastatic grade 3 NET is based on if the tumor can be removed with surgery (resectable) or can't be removed with surgery (unresectable). However, tumor biology also plays a key role in treatment options. Tumor biology can be favorable or unfavorable.

Resectable tumors

Resectable tumors are treated with surgery to remove the primary tumor and any metastatic sites. After surgery, you should expect tests every 12 to 24 weeks for the first 2 years and then every 6 to 12 months for up to 10 years.

Unresectable tumors

Unresectable tumors with high tumor burden or disease progression receive different treatment than those with no symptoms and low tumor burden.

If you have high tumor burden or your disease has grown or spread, the options are:

- Clinical trial (preferred)
- Systemic therapy, **see Guide 6**
- Chemoradiation
- Treatment for metastases such as radiation therapy, ablation, or arterially directed therapy

If you have no symptoms and low tumor burden you will be treated with one of the following:

- Observation (in some cases)
- Octreotide LAR or lanreotide (if SSTR-positive and/or hormonal symptoms)
- PRRT with lutetium Lu 177 dotatate
- Radiation therapy to treat metastases

Surveillance

After treatment for unresectable disease, you will be monitored for signs that cancer has returned, grown, or spread. You should expect imaging tests every 12 to 24 weeks for tumors with favorable biology and 8 to 12 weeks for tumors with unfavorable biology. Tell your care team about any changes in your health.

Guide 6
Well-differentiated, grade 3 NETs: Systemic therapy options

Favorable biology (unresectable with high tumor burden or disease progression)	• Clinical trial (preferred) • Cabozantinib (Cabometyx) • Chemotherapy • Everolimus (Afinitor) • Octreotide LAR (Sandostatin LAR Depot) or lanreotide (Somatuline Depot) if SSTR-positive and/or hormone symptoms • Pembrolizumab (Keytruda) only in some cases • PRRT with lutetium Lu 177 dotatate (if SSTR-positive • Sunitinib (for NET in pancreas only) • Chemoradiation
Unfavorable biology (resectable, locoregional disease)	• Clinical trial (preferred) • Cisplatin or carboplatin with etoposide (Etopophos) • FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CAPEOX (capecitabine and oxaliplatin) • Temozolomide with or without capecitabine (Xeloda)
Unfavorable biology (locally advanced or metastatic disease)	• Clinical trial (preferred) • Cisplatin or carboplatin with etoposide • Irinotecan (Camptosar)-based therapy • Oxaliplatin-based therapy • Pembrolizumab • Temozolomide with or without capecitabine • Nivolumab (Opdivo) with ipilimumab (Yervoy) • Chemoradiation

Key points

- Well-differentiated grade 3 neuroendocrine tumor (NET) cells look like normal neuroendocrine cells.
- Well-differentiated, grade 3 tumors are considered high grade. High-grade tumors are more likely to spread to other areas of the body.
- Treatment is based on tumor location and if the tumor can be removed with surgery (resectable) or can't be removed with surgery (unresectable). However, tumor biology also play a key role in treatment options. Tumor biology can be favorable or unfavorable.
- A tumor with favorable biology typically has a Ki-67 index of less than 55 percent, (55%) is slower-growing, and has a positive SSTR-based PET result.
- A tumor with unfavorable biology typically has a Ki-67 index of 55 percent or greater, is faster-growing, and has a negative SSTR-based PET result.
- You will be monitored after treatment for signs that cancer has returned, grown, or spread. You should expect imaging tests every 12 to 24 weeks for tumors with favorable biology and 8 to 12 weeks for unfavorable tumor biology.
- Tell your care team about any new or worsening symptoms.

Questions to ask

- What tests will I have and who will explain the results to me?
- Is there more than one tumor?
- Can the tumor(s) be removed with surgery? Why or why not?
- What treatment(s) do you recommend and why?
- How can I prepare for treatment?

8

Extrapulmonary poorly differentiated NECs

Extrapulmonary poorly differentiated tumors are aggressive, fast-growing tumors found outside of the lungs. These tumor types include neuroendocrine carcinoma (NEC), large cell neuroendocrine carcinoma (LCNEC) or small cell neuroendocrine carcinoma (SCNEC), and mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN). Treatment is based on tumor location and may include a combination of surgery, chemotherapy, and radiation therapy.

Overview

Poorly differentiated tumor cells look very different compared to normal cells. Because of their aggressive nature, these tumors tend to spread to other areas of the body very early in the disease course. This chapter explains treatment for poorly differentiated neuroendocrine carcinomas (NECs) found outside of the lung (extrapulmonary).

Poorly differentiated NECs are always grade 3 (G3) and often have a very high Ki-67 proliferation index. The Ki-67 proliferation index measures dividing cells and is a an indicator of the tumor growth rate. NECs also may have a mix of neuroendocrine and nonendocrine cells such as adenocarcinoma or squamous cell carcinoma.

Types of extrapulmonary poorly differentiated tumors include:

- Poorly differentiated neuroendocrine carcinoma (PDNEC)
- Large cell neuroendocrine carcinoma (LCNEC) or small cell neuroendocrine carcinoma (SCNEC)
- Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN)

Your care team can explain more about the type of cells found in your type of tumor.

Imaging and other tests will be done to learn more about your type of NEC. Treatment will be based on the location of the tumor and if it can be removed with surgery (resectable).

Resectable disease

A resectable tumor can be removed with surgery. Treatment options depend on where your tumor cells are found. Depending on the tumor location, chemotherapy or chemoradiation might be used to treat a resectable tumor instead of surgery, or before or after surgery.

Treatment may include:

- Surgery to remove the tumor followed by chemotherapy with or without radiation therapy
- Chemotherapy with or without radiation therapy, followed by surgery to remove the tumor
- Chemotherapy alone
- Chemoradiation with cisplatin and etoposide or chemoradiation with carboplatin and etoposide

Chemotherapy options include:

- Carboplatin with etoposide
- Cisplatin with etoposide
- FOLFIRI (fluorouracil, leucovorin, and irinotecan)
- FOLFOX (fluorouracil, leucovorin, and oxaliplatin)
- Temozolomide with or without capecitabine

After treatment you will be monitored to see if the disease returns. You should expect tests every 12 weeks to 1 year, then every 6 months. You might have tests sooner if you have symptoms. Follow-up testing will include CT or MRI scans.

Locoregional, unresectable disease

Locoregional cancer might be in nearby lymph nodes or organs. An unresectable tumor can't be removed with surgery.

Treatment options for locoregional, unresectable disease include:

- Chemoradiation
- Chemotherapy

Chemotherapy options include:

- Capecitabine
- Carboplatin with etoposide
- Cisplatin with etoposide

After treatment, you will be monitored to see if the disease returns. You should expect tests every 6 to 16 weeks, but you might have tests sooner if you have symptoms. Follow-up testing will include CT or MRI scans.

If the tumor grows during or after treatment (called progression), then you may have chemotherapy, immunotherapy, or targeted therapy. **See Guide 7**.

Metastatic disease

Metastatic disease is cancer that has spread to distant organs or lymph nodes. It's treated with chemotherapy. Chemotherapy options can be found in **Guide 7**.

After treatment, you will be monitored to see if the disease returns. You should expect tests every 6 to 16 weeks, but you might have tests sooner if you have symptoms. Follow-up testing will include CT or MRI scans.

If the tumor grows during or after treatment, then you may have chemotherapy, immunotherapy, or targeted therapy. Focused radiation is also used to treat symptoms caused by brain and bone metastases. For systemic therapy options, **see Guide 7**.

“Being diagnosed with cancer is scary. Remember that you are not alone; there are tens of thousands of people living and thriving with NETs. Connect with a NET support group to find comfort in meeting others with NETs, share your story, hear about the newest treatment options, and to fill you with hope.”

Guide 7
Locoregional unresectable or metastatic: Systemic therapy options

Chemotherapy	• Carboplatin with etoposide (Etopophos) • Cisplatin with etoposide • Carboplatin with irinotecan (Camptosar) • Cisplatin with irinotecan • FOLFIRI, which is fluorouracil, leucovorin, and irinotecan • FOLFIRINOX, which is fluorouracil, leucovorin, oxaliplatin, and irinotecan • FOLFOX, which is fluorouracil, leucovorin, and oxaliplatin • Temozolomide (Temodar) with or without capecitabine (Xeloda)
Immunotherapy	• Pembrolizumab (Keytruda) • Nivolumab (Opdivo) with ipilimumab (Yervoy)
Targeted therapy	• Dabrafenib (Tafinlar) with trametinib (Mekinist) • Entrectinib (Rozlytrek) • Larotrectinib (Vitrakvi) • Repotrectinib (Augtyro) • Selpercatinib (Retevmo)

Key points

- Extrapulmonary poorly differentiated neuroendocrine carcinomas (NECs) are aggressive, fast-growing tumors found outside of the lungs.
- Extrapulmonary poorly differentiated NECs sometimes contain a mix of neuroendocrine and nonendocrine cells such as adenocarcinoma or squamous cell carcinoma.
- These tumors are grade 3 (high grade). NECs are more likely to spread to other areas of the body and are frequently metastatic at diagnosis.
- A resectable tumor can be removed with surgery. Depending on the tumor location, chemotherapy or chemoradiation might be used to treat a resectable tumor instead of surgery, or before or after surgery.
- An unresectable tumor is often treated with chemoradiation or chemotherapy.
- Metastatic disease is cancer that has spread to distant organs or lymph nodes. It's treated with chemotherapy, immunotherapy, or targeted therapy (depending on the tumor's molecular features).

Questions to ask

- What type of neuroendocrine carcinoma (NEC) do I have and is there more than one tumor?
- Is there cancer in any lymph nodes or distant organs? What does this mean in terms of treatment options?
- Can the tumor(s) be removed with surgery? Why or why not?
- What systemic therapies do you recommend to treat this NEC?
- Will you use radiation therapy or chemoradiation to treat the NEC?

9

Multiple endocrine neoplasia type 1

Multiple endocrine neoplasia type 1 (MEN1) is a rare, inherited condition that can put one at increased risk for developing tumors in the endocrine glands. Anyone who might have MEN1 should receive genetic counseling and screening for inherited genetic conditions.

Overview

The *MEN1* gene provides instructions for making a protein called menin. This protein acts as a tumor suppressor, which means that it keeps cells from growing and dividing too fast or in an uncontrolled way. However, when there's an abnormal change (or mutation) in the *MEN1* gene, such as what's found in multiple endocrine neoplasia type 1 (MEN1), tumors can grow.

MEN1 is a rare, inherited condition that can put one at increased risk for developing tumors in the endocrine glands. Endocrine glands include the parathyroid glands, pancreas, thymus, and pituitary gland. In MEN1, endocrine glands grow tumors that create excessive amounts of hormones. The tumors are usually benign (not cancer). MEN1 is also referred to as Wermer syndrome.

“It's important to understand what you are going through. If your care team starts explaining things that are hard to understand, don’t hesitate to ask questions. Ask them to slow down and re-explain, and don’t feel bad about it. This is an important way of advocating for yourself.”

Screening for MEN1

Screening for MEN1 is specific to where the tumor is found, such as the parathyroid glands, pancreas, pituitary gland, lung, or thymus gland. Screening usually includes biochemical and imaging tests. Anyone who might have MEN1 should receive genetic counseling and screening over time for inherited genetic conditions.

Treatment for MEN1

Treatment for MEN1 is based on tumor location.

Parathyroid glands

Surgery is the main treatment for a tumor in the parathyroid glands. A parathyroidectomy is surgery to remove one or more of the parathyroid glands or a tumor that's affecting a parathyroid gland. Cryopreservation of parathyroids and thymectomy might also be done. Cryopreservation removes part of the parathyroids and freezes it so it can be put back in the body later. A thymectomy removes the thymus gland.

Pancreas

If a tumor is found in your pancreas, you will be treated as discussed in *Chapter 6: NETs of the pancreas*.

Pituitary gland

Treatment for a tumor located in the pituitary gland will begin with a referral to an endocrinologist for more testing.

Lung and thymus

Treatment for tumors of the lung and thymus can be found in *Chapter 5: NETs of the GI tract, lung, and thymus.*

Surveillance

After treatment, surveillance tests are done to check if the cancer has returned. These tests can help find cancer early so you can start treatment again, if needed. Surveillance tests will likely include blood and imaging tests. The timing of the tests varies depending on the location of the MEN1 tumor and if you have any symptoms.

Key points

- Multiple endocrine neoplasia type 1 (MEN1) is a rare, inherited condition that can put one at increased risk for developing tumors in the endocrine glands. The endocrine glands include the parathyroids, pancreas, pituitary, and thymus.
- In MEN1, endocrine glands grow tumors that create excessive amounts of hormones.
- Testing and treatment for MEN1 is based on where the tumor is located, such as the parathyroid glands, pancreas, pituitary gland, lungs, or thymus.
- Anyone with suspected MEN1 should receive genetic counseling and screening over time for inherited genetic conditions.
- After treatment, surveillance tests are done to check if the cancer has returned. These tests can help find cancer early so you can start treatment again, if needed.

Questions to ask

- Should my children or other family members related by blood be tested for multiple neuroendocrine neoplasia type 1 (MEN1)?
- What's the difference between a neuroendocrine tumor (NET) and a tumor caused by MEN1?
- Is this tumor cancer or not cancer (benign)?
- How will the tumor be treated?
- How often will I have follow-up tests to look for any new tumors?

10
Other resources

Want to learn more? Here's how you can get additional help.

What else to know

This book helps you know your options so you can make informed decisions and improve your cancer care. But it’s not the only resource that you have.

Ask for as much information and help as you need. Many people are interested in learning more about:

- Finding an oncologist or doctor who's an expert in neuroendocrine tumors (NETs)
- The details of treatment and its side effects
- Making treatment decisions
- Getting financial help
- Coping with other health challenges

What else to do

Your health care center can help you with next steps. It often has on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself.

Where to get help

Look through the list below and visit the provided websites to learn more about these organizations.

Bone Marrow & Cancer Foundation
Bonemarrow.org

CancerCare
Cancercare.org

Imerman Angels
Imermanangels.org

My Faulty Gene
Myfaultygene.org

MedlinePlus
medlineplus.gov

National Cancer Institute (NCI)
cancer.gov

Neuroendocrine Cancer Awareness Network
Netcancerawareness.org

Neuroendocrine Cancer Foundation
Ncf.net

Neuroendocrine Tumor Research Foundation
Netrf.org

TargetCancer Foundation
Targetcancer.org

The Healing NET Foundation
thehealingnet.org

Triage Cancer
triagecancer.org

Questions to ask

- Who can I talk to about help with housing, food, and other basic needs?
- What help is available for transportation, childcare, and home care?
- What other services are available to me and my caregivers?
- How can I connect with others and build a support system?
- Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?

Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.
NCCN.org/patients/response

Words to know

adrenal gland
A small organ on top of each kidney that makes hormones.

anus
The opening of the intestinal tract between the legs through which stool passes out of the body.

appendix
A small tube-like organ attached to the first section of the large intestine.

biochemical test
A test to measure the level of chemicals in the body.

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

bronchoscopy
A procedure to work inside the airways with a device that's guided down the throat.

cancer grade
A rating of how much cancer cells look like normal cells.

cancer stage
A rating of the outlook for people with cancer based on the cancer's growth and spread.

carcinoid syndrome
A group of symptoms that happen when carcinoid tumors release serotonin and other chemicals into the blood.

carcinoid tumor
A neuroendocrine tumor found most commonly in the gastrointestinal tract, lungs, bronchi, thymus, and other areas in the body. It may secrete the hormone serotonin and other chemicals.

carcinoma
A cancer of cells that line the inner or outer surfaces of the body.

chemoradiation
Treatment with a combination of chemotherapy and radiation therapy.

chemotherapy
Drugs that kill cancer cells by damaging or disrupting the making of the genetic code.

clinical trial
A type of research that assesses health tests or treatments.

colon
The hollow organ in which eaten food turns from a liquid into a solid form.

computed tomography (CT)
A test that uses x-rays from many angles to make a picture of the insides of the body.

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

cortisol
A hormone that controls blood sugar, metabolism, and other functions in the body.

duodenum
A part of the digestive tract that receives food from the stomach and mixes it with digestive juices.

endocrine system
A complex network of glands and organs. It uses hormones to regulate your metabolism,

energy level, growth and development, and mood.

endoscope
A device that's passed through a natural opening in the body, such as the nose, mouth, or anus.

enucleation
Removal of an organ or tumor in such a way that it comes out clean and whole, like a nut from its shell.

gastrin
A hormone made and released by the stomach.

gastrointestinal (GI) tract
The group of organs through which food passes after being eaten. Also called digestive tract.

gene
Coded instructions in cells for making new cells and controlling how cells behave.

genetic testing
A lab test (usually performed on blood or saliva) to identify abnormal genes (coded instructions in cells that are passed down within a family) that impact your risk of developing cancer.

glucagon
A hormone made by the pancreas that works with insulin to control blood sugar levels. It raises the blood sugar levels.

hereditary
Passed down from parent to child through coded information in cells.

histology
The structure of cells, tissue, and organs as viewed under a microscope.

hormone
A chemical in the body that triggers a response from cells or organs.

hypothalamus
A part of the brain that works with the nervous system and glands that make hormones in the body.

ileum
The last section of the small intestine.

imaging
A test that makes pictures (images) of the insides of the body.

immune system
The body's natural defense against infection and disease.

immunotherapy
A treatment with drugs that help the body find and destroy cancer cells.

insulin
A chemical that controls the amount of sugar in the blood. It lowers the blood sugar levels.

jejunum
The middle section of the small intestine.

liver
The largest organ and gland in the body with many vital functions.

lung
One of a pair of organs that consists of airways and air sacs.

lymph node
A small, bean-shaped disease-fighting structure.

magnetic resonance imaging (MRI)
A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

medical history
A report of all your health events and medications.

metastasis
The spread of cancer cells from the first (primary) tumor to a new site.

multiple endocrine neoplasia (MEN)
An inherited syndrome that causes tumors to grow in the glands of the endocrine system. The 2 main types are MEN1 and MEN2.

mutation
An abnormal change in cells.

nervous system
The body's communication network, responsible for transmitting signals between different parts of the body and the brain.

neuroendocrine cell
A cell that receives signals from the nervous system to make and release hormones into the blood.

neuroendocrine carcinoma (NEC)
Cancer that starts in neuroendocrine cells. Usually fast growing.

neuroendocrine neoplasm (NEN)
General term for all types of neuroendocrine tumors and cancers. Types include neuroendocrine tumors and neuroendocrine carcinomas.

neuroendocrine system
Complex network that manages the communication between the body's nervous system and endocrine system.

neuroendocrine tumor (NET)
A tumor that starts in neuroendocrine cells. Usually slow growing.

observation
A period of testing for changes in cancer status while not receiving treatment. Also called surveillance.

palliative care
Health care that includes symptom relief but not cancer treatment. Also sometimes called supportive care.

pancreas
An organ that makes fluids that help digest food and hormones that control blood sugar.

peptide receptor radionuclide therapy (PRRT)
A treatment that combines a protein that binds to the tumor cell receptors with a radioactive element.

pineal gland
A small gland in the cerebrum of the brain.

pituitary gland
An organ in the brain that controls certain body functions and other hormone glands. Also called the “master gland.”

positron emission tomography (PET)
A test that uses radioactive material to see the shape and function of body parts.

primary treatment
The main treatment used to rid the body of cancer.

primary tumor
The first mass of cancer cells.

progression
The growth or spread of cancer after being tested or treated.

radiation therapy (RT)
A treatment that uses high-energy rays or related approaches to kill cancer cells.

rectum
An organ that holds stool until expelled from the body.

serotonin
A hormone that sends signals between nerve cells and controls things like mood, sleep, and memory.

somatostatin
A hormone that attaches to receptors and controls the endocrine system and nervous system.

somatostatin analogs (SSAs)
A treatment used to slow down or stop tumor hormone production.

somatostatin receptor (SSTR)
A protein found on some types of tumors that causes the tumor to release extra hormones.

stomach
An organ of the digestive system that turns solid food into a more liquid form.

supportive care
Health care that includes symptom relief but not cancer treatment. Also called palliative care or best supportive care.

surgery
An operation to remove or repair a part of the body.

surgical margin
The normal-looking tissue around the edge of a tumor that's removed during surgery.

targeted therapy
A drug treatment that impedes the growth process specific to cancer cells.

thymus
A gland found behind the breastbone inside the chest.

ulcer
A sore on the skin or mucous membrane in the body.

ultrasound
A test that uses sound waves to take pictures of the insides of the body.

vasoactive intestinal polypeptide (VIP)
A hormone that controls the amount of water and minerals absorbed into the small intestine during digestion.

x-ray
A test that uses small amounts of radiation to make pictures of the insides of the body. Also called a plain radiograph.

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NCCN Cancer Centers

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

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

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

Dana-Farber/Brigham and Women's Cancer Center |
Mass General Cancer Center
Boston, Massachusetts
877.442.3324 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

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

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

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

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

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • healthcare.utah.edu/huntsmancancerinstitute

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

Johns Hopkins Kimmel Cancer Center
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

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

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

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

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

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

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

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

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

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

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

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

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

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

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • uclahealth.org/cancer

UCSF Helen Diller Family Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital
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855.4.SMILOW • yalecancercenter.org

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