National Comprehensive Cancer Network®

2026

NCCN Guidelines for Patients®

Cancer care recommendations from leading experts at the National Comprehensive Cancer Network® (NCCN®)

Neuroendocrine Tumors



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NCCN Guidelines for Patients®

The essential guide for people facing cancer.

Based on care recommendations from leading cancer experts.

Explains high-quality cancer care provided at state-of-the-art cancer centers.

Reviewed and revised every year.

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Because cancer care is always evolving, NCCN develops and frequently updates evidence-based cancer care recommendations used by health care providers worldwide. These recommendations are known as the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

The NCCN Guidelines for Patients plainly explain these expert recommendations, so you can talk with your care team about the best care for you.

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Neuroendocrine and Adrenal Tumors, Version 1.2026 — April 21, 2026.

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1
About neuroendocrine tumors

5 What are NETs?

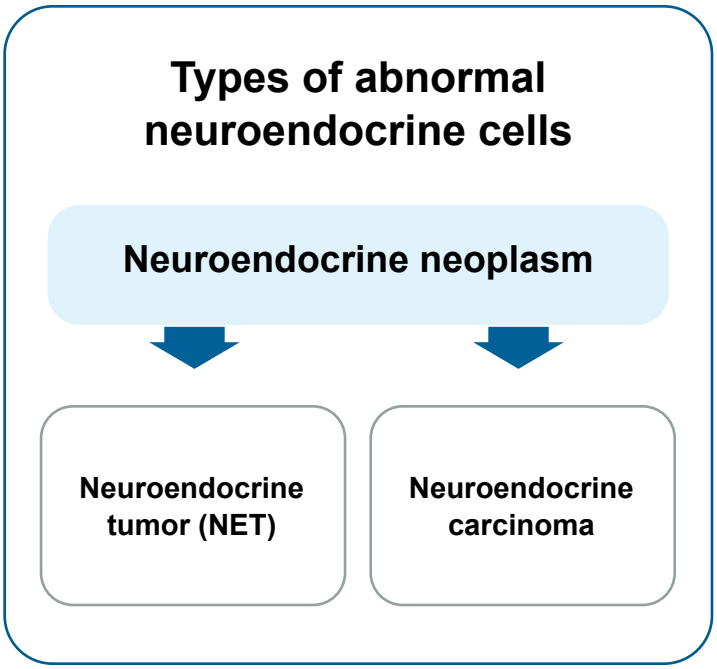
6 What's the neuroendocrine system?

6 How are NETs tested and treated?

8 How can I get the best care?

Neuroendocrine tumors start in neuroendocrine cells that produce and release hormones. Neuroendocrine tumors, called NETs, can develop anywhere in the body. This guide describes the latest treatments for common NET sites.

Neuroendocrine tumors (NETs) are typically found in the lungs, pancreas, stomach, rectum, appendix, and small intestine. NETs may grow slowly or quickly and spread to other parts of the body.



What are NETs?

NETs start as neuroendocrine cells that grow abnormally.

These collections of abnormal cells are called neoplasms. Some neoplasms become:

- Masses, called tumors
- Carcinomas, cancer of the cells that line the inner and outer surfaces of the body

Testing and treatment of the various kinds of NETs are the focus of these guidelines.

Neoplasms are discussed in Chapters 2, 3, and 9 and carcinomas in Chapters 3, 4, and 9.

About neuroendocrine cells

Healthy 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 body functions, including digestion, blood pressure, and heart rate.

When neuroendocrine cells grow abnormally, these body functions may not work as they should.

What's the neuroendocrine system?

The neuroendocrine system manages communication between the body's nervous system and endocrine system.

- The nervous system transmits signals between different parts of the body and the brain.
- The endocrine system produces and releases hormones. It acts as the body's messenger system because hormones regulate how the body uses food to make energy, as well as growth and development and mood.

See the image on page 7 to learn more. The labels indicate several of the glands and organs discussed in these guidelines.

Keep in mind:

- Not all the glands and organs are shown.
- The nervous system includes the spinal cord and nerves (not shown). We have nerves throughout our bodies.
- The endocrine system includes the adrenal glands, ovaries, and testes (not shown).

How are NETs tested and treated?

- Types of tests, including blood and imaging tests, are outlined in Chapter 2.
- Treatment plans are based on what your care team learns from those tests, which includes the information outlined in *Chapter 3: How neuroendocrine tumors are grouped for treatment planning*.

The primary site—where a neoplasm is first found in the body—is one feature that helps cancer care teams make treatment decisions. You can read about NETs of the:

- Gastrointestinal, or GI, tract (stomach, intestines, appendix, and rectum) in Chapter 5
- Lungs and thymus in Chapter 6
- Pancreas in Chapter 7

Treatment for NETs is often a combination of therapies, which may include surgery, radiation therapy, and systemic therapy. For more information about treatment for NETs, read Chapter 4.

Neuroendocrine system

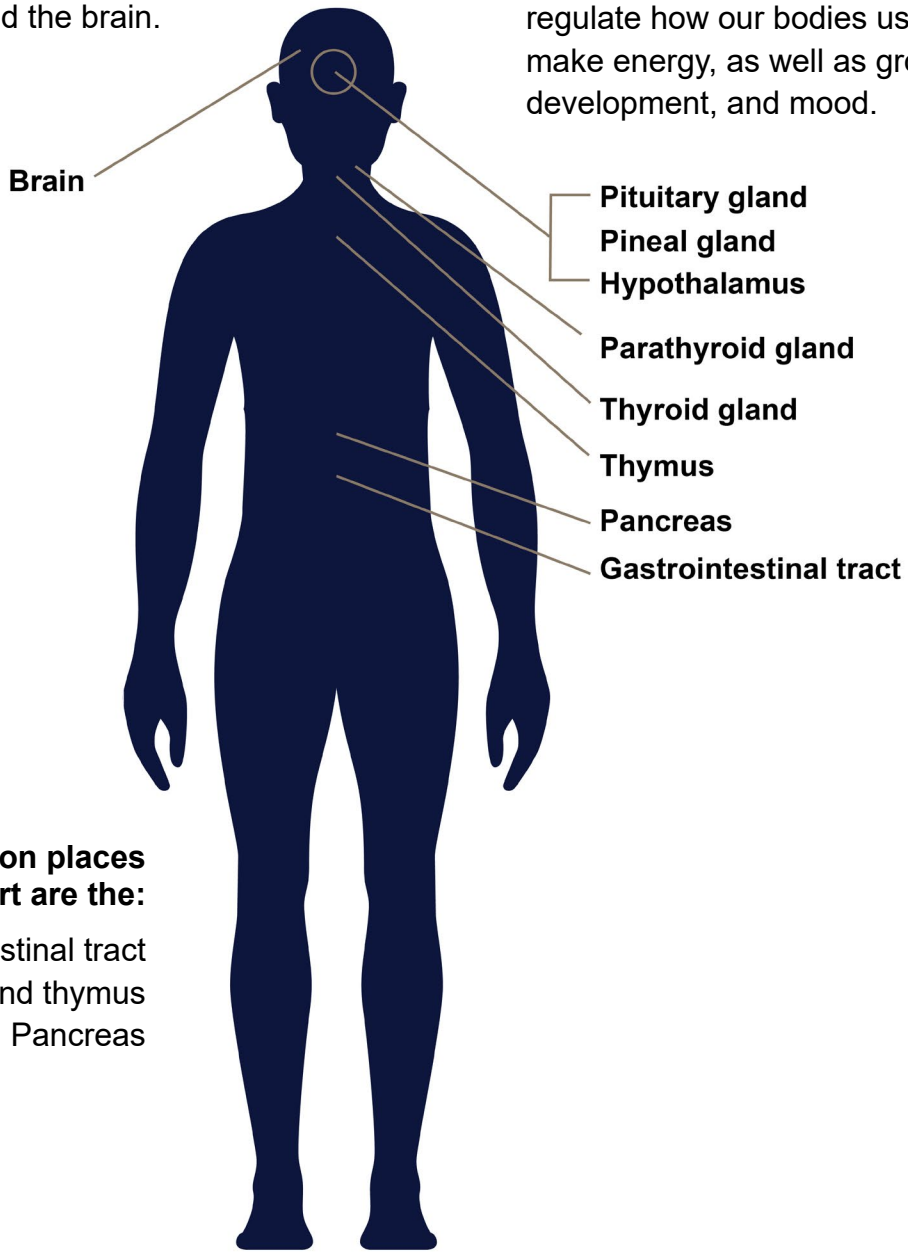
The neuroendocrine system manages communication between our bodies' nervous system and endocrine system.

Nervous system

Nerves are found throughout our bodies. Nerves transmit signals between different parts of the body and the brain.

Endocrine system

The endocrine system is made up of glands and organs that produce and release hormones. Hormones regulate how our bodies use food to make energy, as well as growth and development, and mood.



The most common places where NETs start are the:

Gastrointestinal tract
Lungs (not shown) and thymus
Pancreas

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 chapter.

Keep reading to find the best care for you.

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.

2
Testing for neuroendocrine tumors

10 General health tests

11 Blood and urine tests

11 Genetic tests

12 Imaging tests

13 Tissue sampling and biomarker tests

14 Scoping tests and procedures

15 Key points

15 Questions to ask

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 the NET. This chapter presents an overview of the 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 biopsies, blood and urine tests, and imaging studies are used to determine what treatments are best for the type of neuroendocrine tumor (NET) you have.

Guide 1 offers an overview of the tests you may have. This chapter provides more details on some of these tests.

Guide 1
Neuroendocrine tumors: tests you may have

Medical history, family history, and physical exam
Blood and urine tests
Genetic tests
Imaging tests
Tissue sampling and biomarker tests
Scoping tests and procedures

General health tests

Medical history

A medical or health history is a record of all health issues and treatments you've had in your life. It includes past surgeries and current health conditions.

Family history

Some tumors, cancers, and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives.

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

Blood and urine tests

Blood and urine (pee) 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 the tumor.

- Blood tests require a sample of blood, which is removed through a needle placed into a vein in your arm.
- For a urine (pee) test, you'll be asked to fill a small cup with urine.

Blood and urine samples are sent to a lab for testing. Blood and urine tests you may have are described next.

Complete blood count

A complete blood count measures the red blood cells, white blood cells, and platelets in your blood. It's 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.

Genetic tests

Depending on your family history or other tumor features, your health care team might refer you for genetic testing.

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 (changes in genes) inherited from your biological (birth) parents. Some genetic mutations can put you at risk of more than one type of tumor or cancer. These mutations can be passed on to your children. Other family members may also carry these mutations.

Genetic testing and counseling

Many hereditary, or inherited, syndromes are closely related to NETs. Depending on your family history, you may choose to have a risk assessment and meet with a genetic counselor.



Hereditary cancer risk

Some genetic syndromes put people at risk of certain tumors and cancers. A syndrome is a group of signs or symptoms that suggest the presence or risk of a disease. A hereditary syndrome may also be found in blood (biological) relatives.

A genetic cancer risk assessment will detect 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 may have genetic testing and genetic counseling to see if you have a hereditary syndrome that puts you at risk of NETs.

There are many hereditary syndromes closely related to NETs. One of these—multiple endocrine neoplasia type 1—is explained in *Chapter 9: Other neuroendocrine growths and conditions*.

Imaging tests

Imaging tests take pictures of the inside of your body. They show the primary tumor, or where the cancer started, and look for cancer or tumors in other parts of the body.

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 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 the body.

Contrast material

Contrast is a substance that's sometimes used to improve the quality of imaging tests, such as CT and MRI scans. Contrast might be taken by mouth (oral) or given through a vein (intravenously, or IV). The types of contrast vary and are different for CT and MRI. After the tests:

- Oral contrast is passed with your next bowel movement (poop).
- IV contrast leaves the body in the urine (pee) immediately after the test.

CT or MRI in phases

CTs and MRIs may be done in phases. In these cases, there are 2 scans, one without contrast and one with contrast. The first scan is done without contrast. Then the IV contrast is given, and multiple sets of pictures are taken as the contrast moves through the area of the body near the tumor. This allows your care team to see whether the tumor involves any veins, arteries, or organs.

PET scan

Positron emission tomography (PET) scans use radioactive tracers (or radiotracers) injected into a vein before imaging. Tracers help to see where cancer cells are in the body.

PET scans might be combined with CT or MRI.

FDG and SSRT tracers

A tracer called fluorodeoxyglucose (FDG) is often used with PET scans. FDG-PET scans can help determine if tumors are becoming more aggressive or if cancer has spread.

A tracer that binds to somatostatin receptors (SSTRs) may also be used with PET scans.

- Somatostatin is a hormone that helps control other hormones in the body.
- SSTR tracers can help improve the accuracy of the PET scan and find out if a tumor is positive for SSTRs.
- If the tumor is positive for SSTR, you may benefit from SSTR-focused therapy. You'll read about this therapy in *Chapter 4: Types of treatment*.

Ultrasound

An ultrasound uses high-energy sound waves to form pictures of the inside of the body.

An ultrasound is sometimes used to guide a biopsy.

An echocardiogram (or echo) is a type of ultrasound that shows the structure of the heart and how well the heart is working. It's used to look for carcinoid syndrome.

Tissue sampling and biomarker tests

Biopsy

When a sample of tissue or group of cells is removed for testing, it's called a biopsy. Biopsies are sometimes used to diagnose cancer.

They are also sometimes used to learn things about cancer after it's diagnosed, like to see if the cancer is responding to treatment. Other tests are used to learn more about tumor cells.

Types of biopsies used for NETs include:

- Needle biopsy, guided by imaging (such as ultrasound, CT, or MRI).
- Circulating tumor DNA (ctDNA) biopsy, which tests small pieces of DNA from tumor cells released into the blood.
- Laparoscopic biopsy, in which a scope is guided through small cuts in the belly and a sample is removed.
- Endoscopic biopsy, in which a camera (called a scope or endoscope) is placed into the gastrointestinal (GI) tract to get samples from the stomach, small or large intestine, or rectum.

An endoscopic ultrasound of the gastrointestinal (GI) tract takes samples of the pancreas or suspected lymph nodes.

Tumor biomarker tests

A tissue sample from a biopsy may be tested for biomarkers. Biomarkers are substances that could be hormones, gene mutations (changes), the presence and levels of certain proteins, or other features that could affect treatment decisions.

Some NETs give off specific hormones, such as gastrin, glucagon, insulin, somatostatin, serotonin, and others. Sometimes these extra hormones produce symptoms.

Some kinds of treatments are used only for tumors that make certain hormones. This is discussed in more detail in Chapter 4.

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

Scoping tests and procedures

Some imaging tests use a thin, tube-shaped tool and a camera that's inserted into the body to take pictures that are sent to a television monitor. This minimally invasive procedure is called:

- **Endoscopy**. The scope is guided into the body through a natural opening, such as the mouth, nose, or anus.
- **Laparoscopy**. The scope is inserted through a small surgical cut.

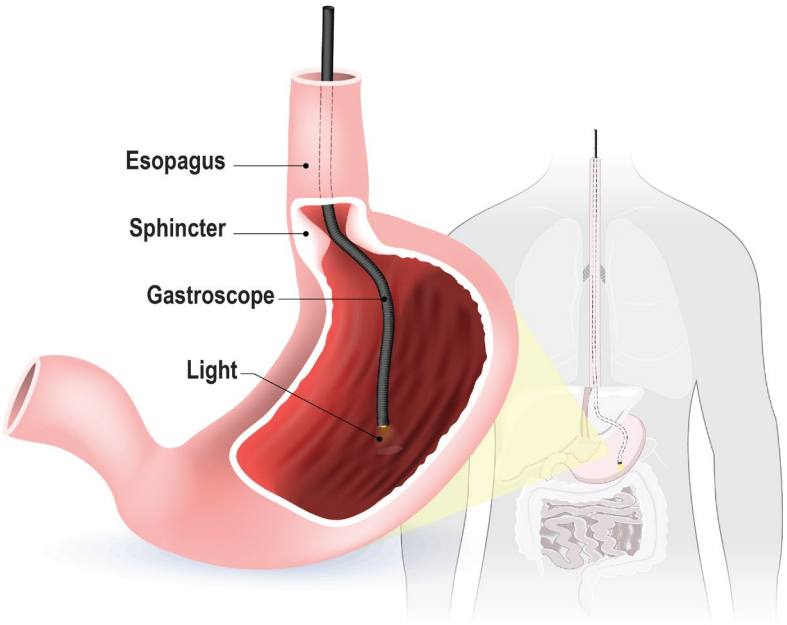
More than one type of scope may be used for testing. A biopsy or surgery might be done during some scoping procedures.

Bronchoscopy

A scope is inserted through the nose or mouth to examine the inside of your airway, including the trachea and bronchi.

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).



Upper GI endoscopy

A scope (camera) is guided down the throat into the esophagus, stomach, and upper parts of the small intestine (duodenum). Also called an esophagogastroduodenoscopy (EGD), this procedure inspects the lining of these organs and looks for any growths or abnormalities, such as abnormal blood vessels or ulcers. Biopsies can be done during an upper GI endoscopy if an abnormal growth is found. Some early cancers and NETs can be removed using this procedure.

Colonoscopy

A scope is guided through the anus, then into the rectum and the colon to inspect the lining of these organs and to look for any growths or abnormalities, such as inflammation. Biopsies can be done if an abnormal growth is found. Some early cancers and NETs can be removed using colonoscopy.

Endoscopic ultrasound

This procedure uses both ultrasound and endoscopy to view pictures of your digestive tract. There are two kinds:

- Upper, which looks at the esophagus, stomach, and duodenum; examines the pancreas; and searches for suspicious lymph nodes
- Lower, which looks at the rectum and any nearby lymph nodes

Tests or a needle biopsy might be done during an endoscopic ultrasound.

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 your organs are working.
- Genetic testing looks for gene mutations inherited from your biological (birth) parents.
- Imaging tests take pictures of the inside of your body and are used to learn more about the type, size, and location of the tumor.
- Some imaging tests use a thin, tube-shaped tool called a scope that's inserted into the body to take pictures.
- A biopsy is the removal of a sample of tissue or group of cells for lab testing.
- A biopsy or surgery might be done during some scoping procedures.

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 genetic testing and counseling? Why or why not?

3

How neuroendocrine tumors are grouped for treatment planning

17 Can the tumors be removed entirely?

17 Do they produce hormones or have hormone receptors?

18 Where did they start?

18 Have they spread to other parts of the body?

19 How quickly will they grow?

20 How big are they?

20 How much cancer is in the body?

20 Key points

20 Questions to ask

There are many differences among neuroendocrine tumors (NETs) that affect treatment planning. A key difference is the organ where the NET started—its primary site. Another important difference is whether the NET has grown or spread.

Based on imaging and the other tests discussed in Chapter 2, cancer care experts put neuroendocrine tumors (NETs) into certain groups that help them make decisions about treatment. The groups are determined by:

- If the NETs can be removed entirely (resectable)
- If the NETs produce hormones (functioning)
- Where they started in the body (primary site)
- If the NETs have grown or spread to other parts of the body
- How quickly they'll grow (grading and differentiation)
- Size of the NET
- How much cancer is in the body (tumor burden)

The answers to the questions in this chapter determine how the NETs will be treated.

Can the tumors be removed entirely?

NETs that:

- Can be removed entirely are called **resectable**.
- Can't be removed entirely are **unresectable**. The surgeon may not be able to remove the tumor entirely if it's near veins, arteries, or organs that make it unsafe to do so.

Do they produce hormones or have hormone receptors?

NETs that:

- Produce hormones are called **functioning** NETs. The extra hormones cause symptoms. Symptoms vary, depending on the location of the tumor and the type of hormone released.

  Hormones produced by NETs include:

  - Gastrin
  - Glucagon
  - Insulin
  - Vasoactive intestinal polypeptide
  - Somatostatin
  - Serotonin

- Don't produce extra hormones are called **nonfunctioning** NETs. They are more common than functioning NETs.

Hormone receptors

Some NETs have a protein, called a receptor, on their surface. This protein attaches to a certain hormone. Some therapies target these kinds of tumors. A lab-made hormone like the one the body makes binds to the receptor.

Where did they start?

NETs are also grouped based on where the abnormal cells start in your body. The most common places are:

- **Gastrointestinal (GI) tract**, which includes your stomach, intestines, rectum, and appendix. (Go to Chapter 5 for more information.) Food is digested in the GI tract.
- **Lungs** or bronchi. Bronchi are tubes that carry air from your windpipe (trachea) to your lungs. (See Chapter 6.)
- **Pancreas**, in its hormone-producing cells. (See Chapter 7.) This cancer is different from what we think of as pancreatic cancer (adenocarcinoma of the pancreas).

Sometimes the primary location of abnormal cells can't be determined. If that's the case, the neoplasm, which may be a tumor or a carcinoma, is treated based on grade and differentiation. This is discussed later in this chapter.

Have they spread to other parts of the body?

NETs that:

- Haven't spread past where they started are called **local**
- Have spread to nearby lymph nodes, tissues, or organs are called **regional**
- Are in the place where they started and have spread nearby are called **locoregional**
- Have spread to distant parts of the body are called **metastatic**

Staging

Sometimes numbered stages are used to describe whether the cancer is local, regional, locoregional, or metastatic. Sometimes the tumor's size plays a role in numbered staging. Here are some things to know about staging:

- Stage 1 cancer is typically small and hasn't spread.
- Stage 4 cancer has typically spread and may be metastatic.
- The way NETs are staged is unique to the organ in which they start. In other words, a NET that starts in the stomach is staged differently from a NET that starts in the appendix or lungs.

Ask your care team about how the stage of the NET that you have affects your treatment plan.

How quickly will they grow?

Cancer researchers can learn about how slowly or quickly abnormal cells grow based on how they look under a microscope. This is referred to as tumor biology. The terms used to describe tumor biology are grading and differentiation.

Grading

Grading is based on how quickly cells grow and spread:

- **Low-grade** (G1) means tumors are growing slowly.
- **Intermediate-grade** (G2) means tumors are growing faster than G1 tumors.
- **High-grade** (G3) tumors tend to grow faster than G1 and G2 tumors.

Neuroendocrine tumors can be G1, G2, or G3. Neuroendocrine carcinomas are G3.

Differentiation

Abnormal cells that look:

- A lot like normal cells are called **well differentiated**. They tend to grow and spread slowly. NETs are well differentiated.
- Very different from normal cells are called **poorly differentiated**. They tend to grow and spread faster than well-differentiated cells. Neuroendocrine carcinomas are poorly differentiated.

Some tumors can have a mix of well- and poorly differentiated cells, or a mix of neuroendocrine and non-neuroendocrine cells. These tumors are called mixed neuroendocrine–non-neuroendocrine neoplasms.

What is tumor biology?

Tumor biology is how abnormal cells look under a microscope. A tumor's biology can help guide treatment planning.



How big are they?

For some GI NETs, the size of the tumor, measured in centimeters, affects treatment decisions.

How much cancer is in the body?

Tumor burden is the amount of cancer in the body, the number of cells, or the size of the cancerous growth(s). It can be high or low. Imaging scans or biomarker tests are used to determine tumor burden.

Key points

- Treatment planning for neuroendocrine tumors (NETs) is based on certain factors, including if the NET can be removed, its size, and if it has spread to other parts of the body.
- A NET that can be entirely removed surgically or endoscopically is called resectable.
- Some NETs produce hormones; some don't.
- Stage 1 cancer is typically small and hasn't spread.
- Stage 4 cancer has typically spread and may be metastatic.
- Looking at tumor cells under a microscope, pathologists can see how quickly they are dividing.
- Tumor burden describes how much cancer is in the body.

Questions to ask

- What type of 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?



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4
Types of treatment

22 Your care team

23 Surgery

23 Systemic therapy

26 Radiation therapy

26 Chemoradiation therapy

27 Other therapies

27 Clinical trials

28 Supportive care

29 Survivorship

30 Key points

30 Questions to ask

In this chapter, you'll learn about the types of treatment recommended for neuroendocrine tumors. Together, you and your care team will choose a treatment plan that's best for you.

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.

Treatment for neuroendocrine tumors (NETs) is usually a combination of therapies starting with surgery and might include systemic therapy or radiation therapy.

Some tumors don't need treatment right away. In these cases, it's called watch and wait, or observation. During this time, you'll have tests to monitor the tumor size. You'll also be watched for symptoms.

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 planning and implementing your treatment. Ask who will coordinate your care.



Your care team

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

- **An oncologist** – A doctor who diagnoses and treats cancer. Types of oncologists include medical, radiation, and surgical oncologists.
- **An endocrinologist** – A doctor who diagnoses and treats conditions of the endocrine system.
- **A gastroenterologist** – A doctor who diagnoses and treats diseases of the digestive tract.
- **A pathologist** – A doctor who analyzes the cells, tissues, and organs removed during a biopsy or surgery.
- **A radiologist** – A doctor who interprets the results of MRIs, CTs, and other imaging tests and performs image-guided needle biopsies as needed.
- **A surgeon** – A doctor who performs surgical procedures.

Surgery

Surgery is an operation or procedure to remove cancer, tissue, or organs from the body.

- It's the main, or primary, treatment for many NETs.
- Surgery plays less of a role in the treatment of neuroendocrine carcinomas because they are often advanced at diagnosis or in a location that makes surgery difficult.

Surgery is sometimes called resection. The goal of surgery is to remove all the cancer.

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

Minimally invasive surgery uses several small incisions (cuts). Small tools are inserted through each cut to perform the surgery.

- One of the tools 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, or laparoscopic, surgery can be done using robotic arms to control the surgical tools.

Endoscopic resection can remove early-stage cancers and precancerous tumors from the gastrointestinal tract during an upper or lower endoscopy.

Endoscopic resection can be the main treatment for early-stage NETs in the stomach, duodenum, and rectum.

Your care team, including a gastroenterologist, can help you decide whether an endoscopic resection may be an option for you.

Specific surgeries you may have are explained in Chapters 5, 6, and 7.

Systemic therapy

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

All systemic 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 maybe 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.

Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells. Some things to know about chemotherapy include:

- When only 1 chemotherapy medicine is used, it's called a single-agent regimen.
- When 2 or more chemotherapy medicines are used, it's called a multi-agent regimen.
- Some chemotherapy medicines are given through a vein (intravenously, or IV) or injected under the skin with a needle. Others may be given as a pill that's swallowed.
- Most chemotherapy is given in cycles of treatment days followed by rest days. This allows the body to recover before the next cycle.

Other chemotherapy medicines that may be given alone or combined include:

- Carboplatin (Kyxata)
- Cisplatin
- Dacarbazine
- Etoposide (Etopophos)
- Irinotecan (Camptosar)

Commonly used abbreviations for some chemotherapy regimens are identified in **Guide 2**.

Guide 2
Common multi-agent chemotherapy regimens for NETs

Abbreviation	Leucovorin calcium	Fluorouracil	Irinotecan (Camptosar)	Oxaliplatin	Capecitabine (Xeloda)
CAPEOX				●	●
FOLFIRI	●	●	●		
FOLFOX	●	●		●	
FOLFIRINOX	●	●	●	●	

Targeted therapy

Targeted therapy focuses on specific or unique features of cancer cells called biomarkers. Targeted therapies seek out how cancer cells grow, divide, and move in the body. These medicines stop or block the action of molecules, like enzymes and proteins, that help cancer cells grow and survive.

Targeted therapy medicines that may be used to treat NETs include:

- Cabozantinib (Cabometyx)
- Dabrafenib (Tafinlar)
- Entrectinib (Rozlytrek)
- Everolimus (Afinitor)
- Larotrectinib (Vitrakvi)
- Repotrectinib (Augtyro)
- Selpercatinib (Retevmo)
- Sunitinib (Sutent)
- Trametinib (Mekinist)

About tumors with somatostatin receptors

Somatostatin is a hormone. Some NETs have a protein on their surface that attaches to somatostatin. These proteins are called somatostatin receptors (SSTRs). Somatostatin binds to these receptors.

This is important because some therapies are recommended only for tumors that have SSTRs. These tumors are called SSTR positive. SSTR-positive tumors release extra hormones that can cause symptoms, like diarrhea and flushing (redness of the face and neck).

Therapies focused on SSTRs include **PRRT**, **SSAs**, or other medicines that bind to SSTRs. They help to control tumor size and symptoms caused by the extra hormones.

Here's how these therapies work:

- **PRRT** is **p**eptide **r**eceptor **r**adionuclide **t**herapy. Peptides are short proteins. With PRRT, lab-made somatostatin peptides work with a radionuclide (a radioactive element).
  - The peptide and radionuclide attach to SSTRs on the tumor. This allows a high dose of radiation to be given directly to the tumor over time.
  - Lutetium Lu 177 dotatate (Lutathera) is a radionuclide used to treat SSTR-positive NETs.
- **SSAs** are **s**omato**s**tatin **a**nalogues. An SSA, which is made in a lab, reduces hormone production just like the somatostatin the body makes. SSAs work for a long time in the body. Possible SSAs are:
  - Octreotide LAR (Sandostatin LAR Depot)
  - Octreotide acetate (Sandostatin, Bynfezia Pen)
  - Lanreotide (Somatuline Depot)

Immunotherapy

Immunotherapy helps your immune system fight cancer cells. It can be given alone or with other types of treatment. Immunotherapies that might be used to treat NETs include:

- Pembrolizumab (Keytruda)
- Nivolumab (Opdivo)
- Ipilimumab (Yervoy)

Immunotherapy can cause side effects. You can learn about the side effects and how they're managed in *NCCN Guidelines for Patients: Immunotherapy Side Effects: Immune Checkpoint Inhibitors*.



Radiation therapy

Radiation therapy uses high-energy x-rays (photons), protons, and other sources to kill cancer cells, shrink tumors, and treat liver 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 (see image below).

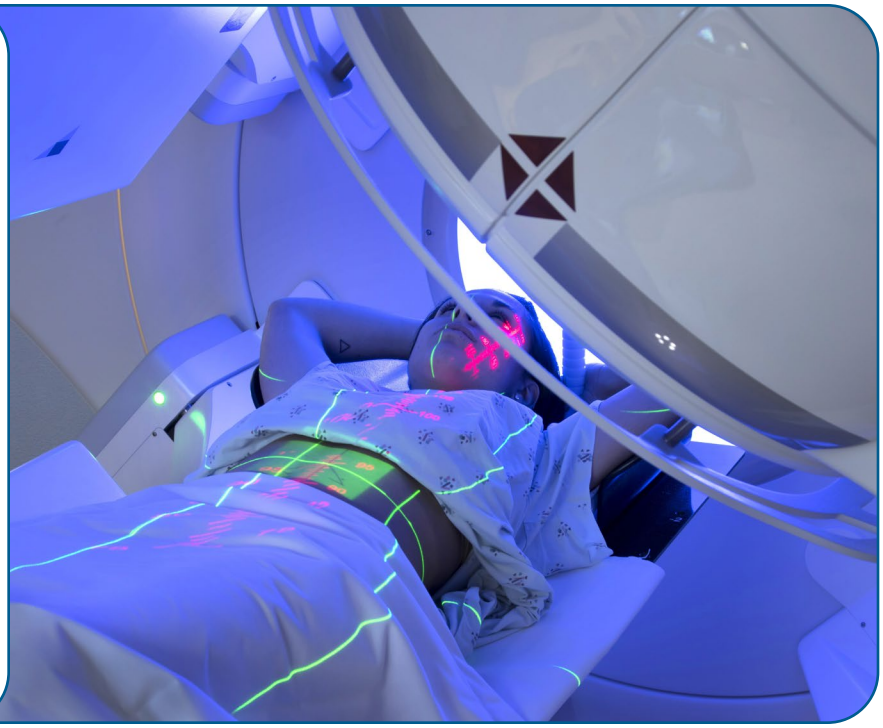
Chemoradiation therapy

Chemoradiation combines lower-dose chemotherapy with radiation therapy. Chemotherapy and radiation therapy can be given at the same time or one after the other. Chemotherapy may improve how well radiation works. That's why they are sometimes used together.

Radiation therapy

External beam radiation therapy (EBRT) uses a machine to aim radiation at the tumor(s) or areas of cancer.

EBRT may be used to treat some types of neuroendocrine tumors (NETs).



Chemoradiation is typically only used for poorly differentiated tumors found outside the lung. For more information, see *Chapter 9: Other neuroendocrine growths and conditions*.

Other therapies

Tumors found in the liver or lung may be treated with 1 or both of the following:

- **Ablation** destroys cancer cells with:
  - Extreme cold or heat
  - Radio waves, microwaves, or sound waves
  - Chemicals
- **Arterially directed therapy**, also called embolization, works by injecting particles, chemotherapy, or radioactive beads directly into the arteries that supply the tumor(s).

“I would recommend getting a second opinion if you are unsure or want reinforcement of a treatment plan.”



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

Clinical trials

You may also be able to obtain 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. 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 is 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.

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.

Supportive care includes a wide range of services. Supportive care prevents or manages the symptoms of cancer 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 advance 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.

Side effects

Cancer treatment can cause unwanted health issues called side effects. Some side effects may just be unpleasant. Others can be very serious.

Possible side effects of treatment include diarrhea, constipation, distress, and fatigue. Your care team can help manage symptoms and offer other resources.

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 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.

Supportive care resources

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



Key points

- Surgery or resection is the main treatment for neuroendocrine tumors (NETs) with limited or no spread.
- Systemic therapy works throughout the body. These types of therapies include chemotherapy, chemoradiation, targeted therapy, and immunotherapy.
- Radiation therapy uses high-energy radiation from x-rays, protons, and other sources to destroy tumors or kill cancer cells.
- Somatostatin analogues (SSAs) are used to slow down hormone production.
- Peptide receptor radionuclide therapy (PRRT) uses a radioactive tracer 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.

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

Neuroendocrine tumors of the gastrointestinal tract

33 Tests and planning for treatment

33 Types of surgeries of the GI tract

34 NETs of the stomach

34 NETs of the duodenum

35 NETs of the jejunum, ileum, and colon

35 NETs and carcinoid syndrome

36 NETs of the appendix

36 NETs of the rectum

37 Advanced GI NETs and metastatic disease

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In this chapter, you'll learn about testing and treating neuroendocrine tumors (NETs) of the gastrointestinal (GI) tract. The GI, or digestive, tract is a common site for NETs. These tumors are often treated with surgery. Radiation therapy or systemic therapy might be given.

This chapter discusses well-differentiated grade 1 or grade 2 neuroendocrine tumors of the gastrointestinal tract (GI NETs).

Treatment for well-differentiated grade 3 NETs can be found in Chapter 8.

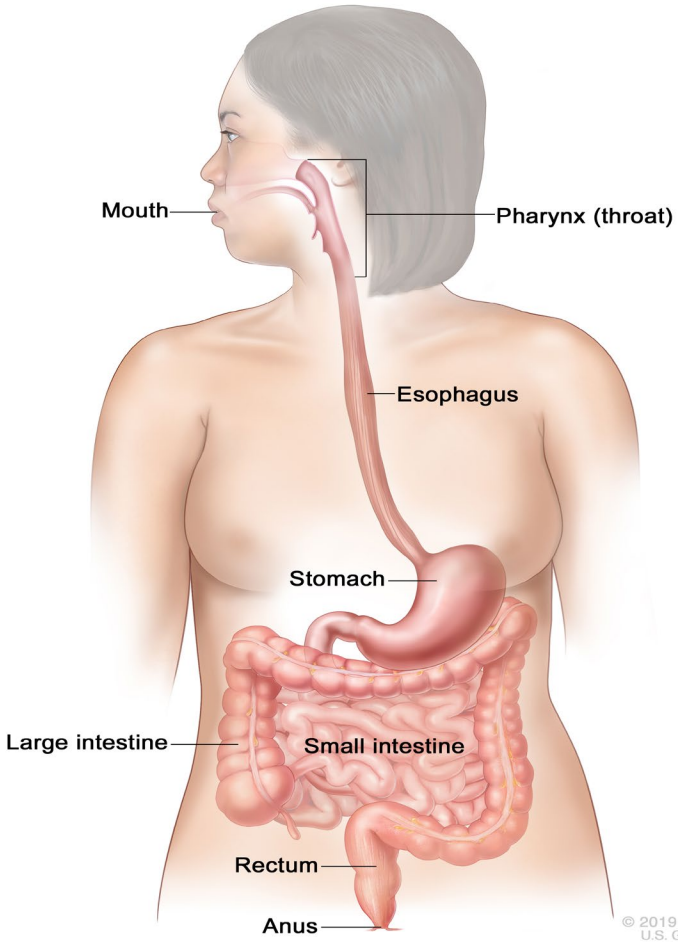
GI NETs are found in the:

- Stomach
- Duodenum
- Jejunum, ileum, and colon
- Appendix
- Rectum

These NETs may produce hormones and proteins that affect blood pressure and blood vessel function.

The GI tract

The gastrointestinal (GI) tract is part of the digestive system. The food we eat passes through the esophagus into the stomach. After being broken down into a liquid, food enters the small intestine. Any unused food enters the large intestine, where it is prepared to leave the body as a bowel movement (poop or stool).



Tests and planning for treatment

Tests for NETs of the GI tract may include CT or MRI scans in phases and somatostatin receptor (SSTR)-PET scans. Depending on the location of the tumor, you might also have scoping procedures, chest CT, or other tests.

Depending on where the NET starts in the GI tract, treatment planning is based on:

- Location
- Size
- If it produces hormones
- If it causes symptoms
- If it has spread to other areas:
  - Near the tumor, such as the lymph nodes
  - Or farther, such as the liver

If NETs have spread

NETs that have spread are often treated with surgery. Systemic therapy and other treatments might also be given.

More details about treatment recommendations for advanced GI NETs and metastatic disease are found at the end of this chapter.

After treatment

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. They may include general health tests, hormone tests, and imaging scans. This monitoring, called surveillance, may last up to 10 years. See **Guide 3**.

Types of surgeries of the GI tract

Your care team can provide information about the surgery specific to your type of NET. Some examples of types of surgery include:

- **Bowel resection**. Part of the small intestine is removed to get rid of the NET. The parts of the small intestine are then reconnected for normal eating and digestion.
- **Endoscopic resection**. An endoscope (scope), a flexible tube, is used to remove tumors and cancer cells from the GI tract. There are several endoscopic resection techniques that may be used for GI NETs, including:
  - Passing the scope down the esophagus, stomach, and duodenum to remove lesions from those organs.
  - Guiding the scope up through the anus to remove lesions from the rectum and colon.
- **Gastrectomy**. Sometimes the part of the stomach with cancer is removed along with nearby lymph nodes and possibly parts of other organs near the tumor. Sometimes the whole stomach, nearby lymph nodes, and parts of the esophagus and small intestine are removed. The esophagus is then reconnected to the small intestine.

- **Hemicolectomy**. Removal of the colon. Once the colon is removed, the remaining parts of the intestine are joined together.
- **Lymphadenectomy**. Removal of lymph nodes or groups of lymph nodes to test for cancer spread. May be called nodal dissection.
- **Appendectomy**. Removal of the appendix.

NETs of the stomach

There are 4 types of stomach (gastric) NETs:

- **Type 1** – Related to atrophic gastritis, an autoimmune condition.
- **Type 2** – Related to Zollinger-Ellison syndrome, a rare condition caused by too much gastrin (discussed later in this chapter).
- **Type 3** – Not related to any conditions.
- **PPI-induced** – Related to long-term use of PPIs, proton pump inhibitors. These are medicines used to treat heartburn caused by reflux and stomach ulcers, among other things.

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

Type 1 and type 2

Treatment is an endoscopic resection to remove the tumor from the stomach. A 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

Treatment may be endoscopic resection for smaller and less-aggressive tumors. Surgery is recommended for larger and more-aggressive tumors. The preferred surgery is gastrectomy with removal of nearby lymph nodes. Follow-up testing can be found in **Guide 3**.

PPI-induced

You'll likely have an endoscopic resection to remove the tumor from your stomach. Your care team will suggest the best treatment available based on current research for NETs caused by PPI use.

NETs of the duodenum

The duodenum is the upper part of the small intestine. Some NETs in this area make and give off the hormone gastrin. They are called duodenal gastrinomas.

Gastrin helps your stomach produce acid. A gastrinoma causes your stomach to produce too much acid and may cause a burning sensation (heartburn) or other symptoms. Treatment depends on whether the NET makes gastrin.

If they produce gastrin (functioning)

Treatment is usually surgery. Your care team will tell you what kind of surgery is recommended. After surgery, you'll have regular endoscopies or other follow-up testing as outlined in **Guide 3**.

If they don't produce gastrin (nonfunctioning)

Smaller nonfunctioning NETs in the duodenum can often be treated with endoscopic resection. Larger or more-aggressive nonfunctioning NETs may be treated with minimally invasive or open surgery. After surgery, you'll have regular endoscopies or other follow-up testing. See **Guide 3**.

NETs of the jejunum, ileum, and colon

The jejunum and ileum are the middle and lower parts of the small intestine. The colon is the large intestine.

Bowel resection is the main treatment for NETs in these areas. The tumor, along with some lymph nodes near the tumor, will be removed. After surgery, you'll have follow-up testing as found in **Guide 3**.

NETs and carcinoid syndrome

Carcinoid syndrome is typically related to small intestine NETs, or in cases where NETs have spread to the liver. This group of symptoms is caused by NETs releasing a lot of serotonin. Serotonin is a hormone and neurotransmitter—a chemical messenger.

Serotonin regulates mood, digestion, and sleep, among other things. Too much serotonin can cause:

- Flushed skin (sudden warmth and redness)
- Diarrhea
- Breathing issues
- Heart problems

Guide 3
GI NETs: Testing schedule after surgery

12 weeks to 1 year and 1 to 10 years (every 1 to 2 years)	• Medical history and physical exam • For hormone-producing tumors, biomarker testing as needed • CT or MRI of abdomen (belly), pelvis, or both, in phases • Chest CT with or without contrast as needed
After 10 years	Testing as needed

Testing for diagnosis may include:

- Biomarker tests
- Echocardiogram (heart ultrasound)
- Imaging scans

Treatment

Treatment is somatostatin analogue (SSA) therapy. If symptoms continue, you might have additional SSA therapy. Telotristat (Xermelo) may be added if you're having diarrhea. Surgery or arterially directed therapy might be used to treat the tumor. Systemic therapy may also be given.

After treatment

Tests may include:

- Echocardiogram every 1 to 3 years or as needed
- Belly and pelvis CT or MRI in phases every 12 weeks to 1 year
- Chest CT with or without contrast as needed

If testing shows cancer has grown or spread, you'll be treated for advanced or metastatic disease.

NETs of the appendix

The appendix is a small, tube-shaped organ attached to the large intestine.

Most NETs of the appendix are found when it is removed because of an infection, called appendicitis. Treatment for this kind of NET is simple appendectomy.

Next steps after surgery depend on the tumor's size and if there's cancer in the lymph nodes.

After the appendix is removed

For a tumor:

- Smaller than 1 cm, no follow-up is needed.
- One cm to 2 cm, watching the tumor for 2 to 5 years is an option.

You might have surgery to remove the right side of the colon (hemicolectomy):

- For a tumor larger than 2 cm.
- If the tumor (of any size) couldn't be removed completely.
- Lymph nodes removed during appendectomy test positive for cancer.

The next step is monitoring. See **Guide 3**.

NETs of the rectum

Small and less-aggressive rectal NETs can often be treated with endoscopic resection. Large and more-aggressive rectal NETs are treated with surgery. Ask your care team what type of surgery is recommended and what side effects to expect.

After endoscopic or surgical resection, decisions for next steps are made based on:

- Whether all the cancer was removed
- Tumor size
- Whether the tumor has grown or spread
- Tumor grade (how likely it is to spread)

For a tumor smaller than 1 cm

No further treatment is typically needed if all the cancer has been removed.

If there may be some remaining cancer, you'll have an endoscopy in 6 to 12 months. If no cancer remains and the tumor is low-grade (not likely to spread), no further treatment is needed.

For all other rectal NETs

You may need further imaging and other tests. Decisions will be made about whether additional surgery is needed (and what kind) based on tumor size and whether cancer is confirmed in lymph nodes. Treatment may also include chemoradiation.

Treatment for advanced GI NETs or metastatic disease is explained next.

Advanced GI NETs and metastatic disease

Advanced disease may be locoregional and involve nearby organs or lymph nodes.

Metastatic disease is cancer that has spread from the primary tumor site to a distant part of the body.

If advanced or metastatic disease is suspected, you'll have testing to confirm.

Testing for treatment planning may include imaging and biomarker tests for serotonin if there are symptoms, or possibly for anyone with metastatic disease.

If possible, you'll have surgery to remove the primary tumor and any areas of cancer that have spread. If your surgeon can't remove all the cancer, next steps are based on the amount of cancer that remains.

If surgery is not possible, next steps are based on tumor burden—how much cancer is in the body. Treatment may include:

- Additional surgery
- Watch and wait
- SSA therapy
- Systemic therapy

If cancer continues to grow and spread

GI NETs that have grown 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.

Systemic therapy recommendations include:

- Cabozantinib (Cabometyx)
- Everolimus (Afinitor)
- Peptide receptor radionuclide therapy
- SSAs

Key points

- The gastrointestinal (GI) tract is a common place for neuroendocrine tumors (NETs).
- GI NETs can start in areas such as the stomach, small intestine, colon, and rectum.
- Treatment is 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.
- For NETs of the stomach, duodenum, and rectum that are small and less aggressive, treatment may be endoscopic resection. Large and more-aggressive NETs are often treated with surgery.
- Treatment for NETs of the jejunum, ileum, appendix, and colon is often surgery.
- There are many possible treatments for a tumor that can't be surgically removed.
- Carcinoid syndrome is a group of symptoms caused when NETs overwhelm your system with hormones (serotonin) and other substances.

Questions to ask

- What type of GI 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?



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

6

Neuroendocrine tumors of the lung and thymus

40 About the lungs and thymus

41 Treatment for local or locoregional NETs

44 Treatment for NETs that have spread

45 Key points

45 Questions to ask

In this chapter, you'll learn about testing and treatment for neuroendocrine tumors (NETs) of the lungs and thymus gland, two common sites for NETs. Treatment is often surgery. If surgery isn't possible, radiation therapy or systemic therapy might be given.

This chapter covers well-differentiated grade 1 or grade 2 neuroendocrine tumors (NETs) of the lungs and thymus. Treatment for well-differentiated grade 3 NETs can be found in Chapter 8.

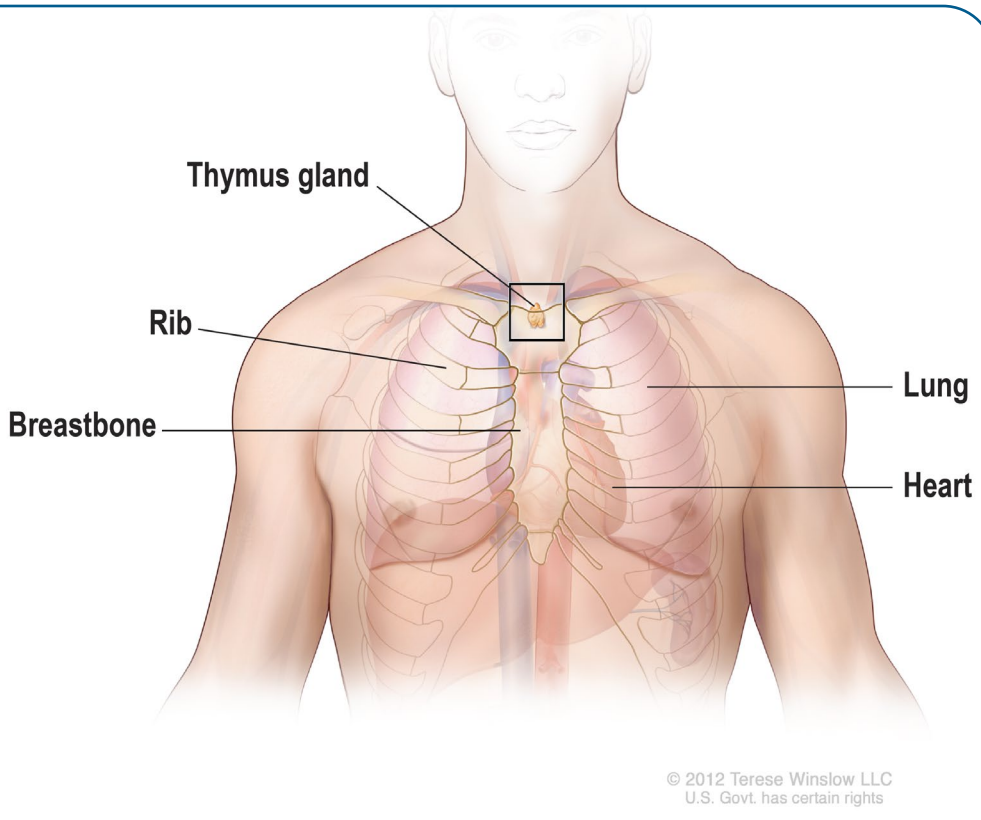
Lung and thymus NETs may secrete hormones and proteins that affect blood pressure and blood vessel function. They can cause Cushing syndrome, a condition where there's too much stress hormone (cortisol) in the body.

About the lungs and thymus

Lungs

There are 2 lungs inside the chest. They supply the body with oxygen and remove carbon dioxide. The lungs help us breathe and are part of the respiratory system.

Lung (pulmonary) NETs often develop in the major bronchi, the large tubes that lead air from the windpipe (trachea) into the lungs.



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).

About lung growths

Growths in the lungs are very common. They are often found on imaging scans. Two kinds of lung growths are:

- Nodules, small areas of abnormal tissue in the lungs. Most are not cancer.
- Tumorlets, very small nodules made up of neuroendocrine cells. Tumorlets are not cancer.

If many lung nodules or tumorlets are found, it may be a sign of a rare lung condition that can cause a cough that lasts for a long time and shortness of breath. If tests confirm this condition, it will be monitored as follows:

- You'll have a chest CT every year to 2 years or as needed.
- You may also have somatostatin analogue (SSA) therapy to control symptoms if other treatments don't help.

To read about SSA therapy, revisit *Chapter 4: Types of treatment*.

Thymus

The thymus is a small gland 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.

Treatment decisions are made, in part, based on where cancer is found. So,

Local means cancer is limited to the site where it started.

Regional means cancer has spread to nearby lymph nodes, tissues, or organs.

Locoregional means cancer is both in the site where it started and has spread nearby.

Metastatic means cancer has spread to distant parts of the body.

Treatment for local or locoregional NETs

For local cancer

- Your lungs are made of distinct, major sections called lobes. The main treatment for lung NETs is lobectomy, removal of the affected lobes. Nearby lymph nodes may also be removed.
- If the thymus is affected, treatment is surgery, if possible.
- Treatment may include thermal ablation, radiation therapy, and systemic therapy if surgery is not an option.

After treatment, you'll have tests on a regular basis to check if the cancer has returned. For a schedule of these tests, see **Guide 4**.

For locoregional cancer

If the entire tumor can be removed, surgery will be followed by monitoring on a regular basis. See **Guide 4**.

Tumor grade

If the tumor can't be removed, treatment is based on whether the tumor is low-grade or intermediate-grade.

- **Low-grade tumors** grow slowly and are not likely to spread beyond the lungs or thymus.
- **Intermediate-grade tumors** are rarer than low-grade tumors and grow more rapidly.

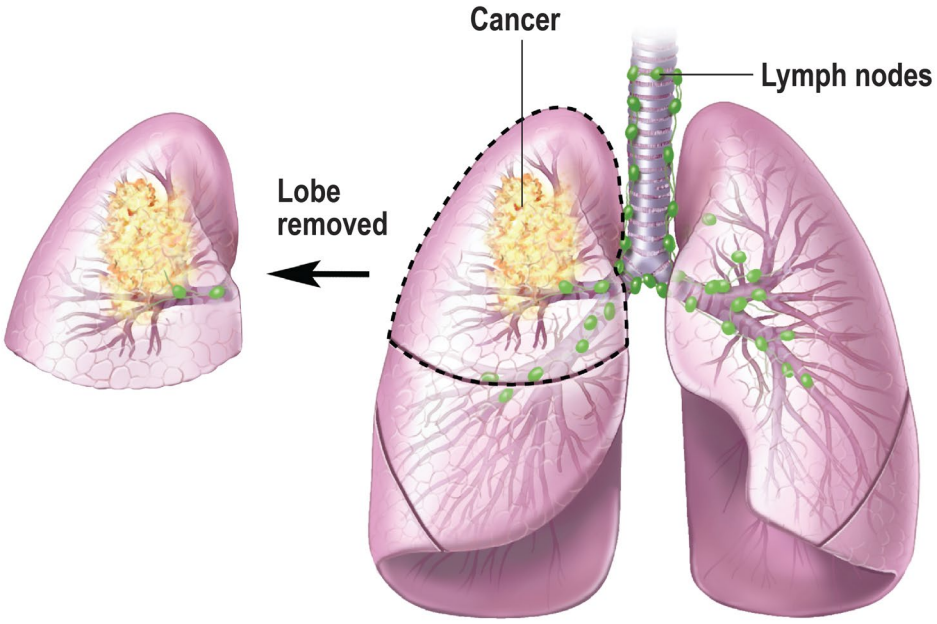
For a low-grade tumor

Treatment may include:

- Watch and wait (observation), if you have no symptoms
- Temozolomide (Temodar) and capecitabine
- Everolimus
- SSA therapy if 1 or both of the following apply:
  - The tumor is somatostatin receptor (SSTR) positive
  - You have hormone-related symptoms
- Radiation therapy

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.



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For an intermediate-grade tumor
Treatment may include:

- Watch and wait (if you have no symptoms and no cancer growth or spread)
- Chemotherapy:
  - Temozolomide and capecitabine
  - Carboplatin with etoposide
  - Cisplatin with etoposide
  - Temozolomide
- Everolimus
- SSA therapy if 1 or both of the following apply:
  - The tumor is SSTR positive
  - You have hormone-related symptoms
- Radiation therapy
- Chemoradiation

If more treatment is needed

It may include:

- Clinical trial (preferred)
- Cabozantinib (a chemotherapy)
- Another therapy based on tumor grade
- Peptide receptor radionuclide therapy (PRRT) if:
  - The tumor is SSTR positive
  - Cancer has grown or spread after SSA therapy

Guide 4
Lung and thymus NETs: Testing schedule after surgery

12 weeks to 1 year and 1 to 10 years (every 1 to 2 years)	• Medical history and physical exam • For hormone-producing tumors, biomarker testing as needed • Chest CT and CT or MRI of abdomen (belly) with contrast, in phases • CT or MRI with contrast of pelvis, as needed
After 10 years	Testing as needed

Treatment for NETs that have spread

NETs of the lung and thymus can spread and form tumors in other parts of the body.

This is called metastatic disease. Treatment recommendations for metastatic disease are based on:

- If the metastases are causing symptoms
- The amount of cancer in the body, called tumor burden
- Tumor grade

See **Guide 5**.

No symptoms, low tumor burden, and low-grade

Cancer that doesn't produce symptoms, has low tumor burden, and is low-grade will be observed. Or you may have SSA therapy if:

- The tumor is SSTR positive
- You have hormone-related symptoms

Possible symptoms, growing or spreading, or other features

Seeking a clinical trial is the preferred treatment for cancer that is any of the following:

- Low-grade with a high tumor burden
- Growing or spreading
- Intermediate-grade
- Causing symptoms

Other treatment options include:

- Watch and wait for people with low tumor burden
- Systemic therapy
- Surgery, thermal ablation, arterially directed therapy, or radiation therapy for liver metastases

Guide 5
Metastatic NETs of the lungs and thymus: Systemic therapy recommendations

Preferred therapies	• Cabozantinib • Everolimus • SSA therapy (for certain tumors)
Therapies used in certain cases	• Carboplatin and Etoposide • Cisplatin and Etoposide • PRRT (for certain tumors) • Temozolomide with or without Capecitabine

Key points

- The lungs and thymus are common sites for neuroendocrine tumors (NETs).
- 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.
- There are many possible treatments for NETs that can't be entirely removed with surgery.
- Somatostatin receptor (SSTR)-positive NETs are often treated with somatostatin analogue (SSA) therapy to help manage symptoms.
- Tests are done after treatment to check if the cancer has returned. These tests can help find cancer early so you can start treatment again, if needed.
- Metastatic NETs are treated based on whether they cause symptoms as well as tumor burden and tumor grade.

Questions to ask

- What type of 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?

7 Neuroendocrine tumors of the pancreas

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48 Making treatment decisions

49 Treatment for PanNETs

51 Treating advanced PanNETs and metastatic disease

52 Key points

52 Questions to ask

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 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 8.

About the pancreas

The pancreas is a large gland found toward the back of the abdomen (belly). It's about 6 inches long, about the size of a dollar bill.

The pancreas has 3 parts:

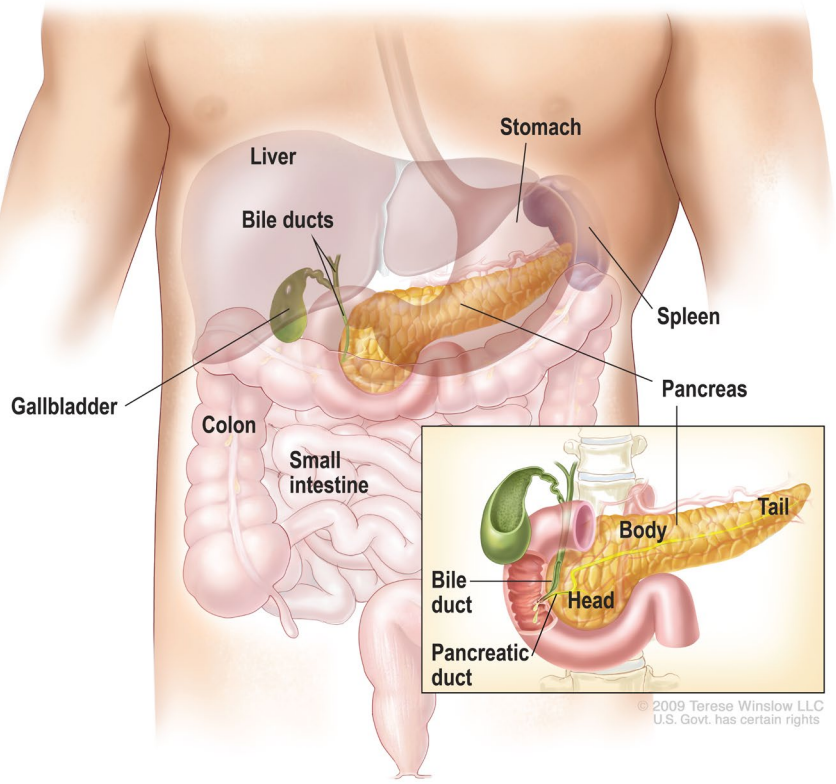
- Wide end, called the head (right side)
- Middle part, called the body
- Narrow end, called the tail (left side)

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.
- **Enzymes** that help digest food in your small intestine.

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.



Testing for treatment

Testing often includes:

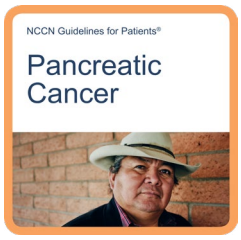
- Imaging tests
- Endoscopic ultrasound with possible biopsy
- Biomarker tests for hormones, proteins, and sugar in blood and urine
- Possible genetic testing and counseling

Locoregional
means cancer is both in the site where it started and has spread nearby.

Metastatic
means cancer is in the site where it started and has spread to distant parts of the body.

PanNETs need different treatment than the more common type of pancreatic cancer.

To learn about 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.



Types of PanNETs

A PanNET starts in the hormone-producing cells of the pancreas. PanNETs are either functioning or, more commonly, nonfunctioning.

- **Functioning PanNETs** produce excess hormones, leading to specific symptoms.
- **Nonfunctioning PanNETs** don't produce enough hormones to cause noticeable symptoms.

Making treatment decisions

In addition to whether the tumor produces hormones and causes symptoms, treatment decisions are based on:

- **Location**. Whether tumors are found in 1 or more areas of the pancreas, and in what part. Cancer can spread to places near the tumor, such as regional lymph nodes. This is called locoregional disease.
- **Metastases**. Whether cancer has spread to distant lymph nodes or new tumors have formed in other parts of the body, such as the liver, lung, or bone. Treatment for tumors that can't be removed with surgery or cancer that metastasized can be found later in this chapter.

Treatment for PanNETs

Standard treatment for PanNETs can include:

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

Types of surgeries

There are many types of surgeries and procedures used to treat PanNETs. The most common are:

- **Enucleation**. Only the tumor or tumor cells are removed from the pancreas. Enucleation is often used for insulinomas because they are rarely cancer.
- **Pancreatoduodenectomy**. Removes the head of the pancreas, gallbladder, 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.
- **Distal pancreatectomy**. Removes part of the pancreas, and sometimes the spleen. The left adrenal gland might also be removed. This surgery can be open or minimally invasive.
- **Total pancreatectomy**. Removes the whole pancreas, part of the small intestine, part of the stomach, the common bile duct, gallbladder, spleen, and nearby lymph nodes. It's usually done as open surgery.

Other procedures include:

- **Duodenotomy**, removal of the upper part of the small intestine (called the duodenum). This is often done for gastrinomas.
- **Liver resection** to remove part of the liver.
- **Peripancreatic lymphadenectomy**, surgery that removes lymph nodes near the pancreas to look for cancer.
- **Splenectomy**, surgery that removes part or all of the spleen.

After surgery

Tests are done at specific times to check if the cancer has returned. These tests help find cancer early so you can start treatment again, if needed. Tests may include general health tests, biomarker tests, and imaging scans. CT or MRI scans are often done. A testing schedule may last up to 10 years. See **Guide 6**.

Treatment for PanNETs that don't produce hormones

Nonfunctioning PanNETs may have hormone levels that are higher than normal, but not high enough to cause symptoms.

Treatment for nonfunctioning PanNETs is based on if the cancer can be removed with surgery.

- If it can be removed, next steps are based on tumor size and whether tumors have spread locoregionally.
- If the tumor can't be removed, additional tests will be done to decide next steps.

Treatment for hormone-producing PanNETs

The following explains the 4 different types of functioning (hormone-producing) PanNETs and how they are treated.

Gastrinoma

A gastrinoma is usually found in the upper part of the small intestine or in the head of the pancreas. Gastrinomas make too much gastrin. Gastrin helps your body control stomach acid and digest food. Too much acid can cause ulcers.

Gastrinomas are treated with:

- High-dose proton pump inhibitors (PPIs) and somatostatin analogues (SSAs)
- Surgery

Glucagonoma

A glucagonoma is usually found in the tail of the pancreas. Glucagonomas make too much glucagon. Glucagon is a hormone that helps the body control glucose (sugar) levels in the blood.

Glucagonomas are treated with:

- SSAs to control hormone-related symptoms
- Surgery

Insulinoma

An insulinoma makes more insulin than your body can use. They can cause low blood sugar.

Treatment starts with getting your glucose (sugar) levels stable. This can be done by doing 1 or more of the following:

- Changing what you eat
- Taking diazoxide (Proglycem) or everolimus (Afinitor)
- Treating with an SSA, if the tumor is SSTR positive

Insulinomas are the most common type of functioning PanNET. They are typically noncancerous.

Guide 6
PanNETs: Testing schedule after surgery

12 weeks to 1 year and 1 to 10 years (every 6 to 12 months)	• Medical history and physical exam • For hormone-producing tumors, biomarker testing as needed • CT or MRI, in phases • Chest CT (with or without contrast) as needed
After 10 years	Testing as needed

VIPoma

A VIPoma secretes vasoactive intestinal peptide (VIP). VIP is a hormone that helps the body release sodium, chloride, potassium, and water in the small intestine. Too much VIP can cause chronic, watery diarrhea.

VIPomas are treated with:

- SSAs to control hormone-related symptoms
- Surgery

Treating advanced PanNETs and metastatic disease

Treatment for locoregionally advanced or metastatic disease may include surgery to remove tumors and metastases. Additional treatment is based on other factors, including:

- Whether the tumor was entirely removed by surgery
- The amount of cancer found in the body (tumor burden)
- Whether the tumor is SSTR positive
- Rate of growth, spread, or both

For stable cancer with low tumor burden that's not causing symptoms

Treatment may include therapy with an SSA. It may also involve observation (watch and wait). Testing will include a chest CT (with or without contrast) and CT or MRI in phases every 3 to 6 months.

For cancer that's growing or spreading, causing symptoms, and has high tumor burden

Treatment will be given to manage symptoms. It may include an SSA. It may also include systemic therapy. See **Guide 7**.

About systemic therapy for metastatic disease

SSA therapy and PRRT are only used for tumors that are SSTR positive. PRRT may be used in cases of high tumor burden. It may also be used for SSTR-positive tumors that don't respond to SSA therapy.

Guide 7
Advanced or metastatic PanNETs: Recommended systemic therapy

Preferred therapies	• Cabozantinib • Everolimus • Sunitinib • SSA therapy* • PRRT in certain cases • Temozolomide with Capecitabine
Other recommended therapies	• FOLFOX • CAPEOX
Therapies used in certain cases	• SSA therapy • Belzutifan • Chemoradiation

*If SSTR-positive.

If PanNETs grow or spread after treatment, additional treatment might include:

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

Medicines in abbreviated systemic therapy regimens are found in Chapter 4, Guide 2.

Key points

- The pancreas is a large gland found in your abdomen, behind your stomach.
- A pancreatic neuroendocrine tumor is called a PanNET.
- Functioning PanNETs give off excess hormones, leading to specific symptoms.
- Nonfunctioning PanNETs do not produce enough hormones to cause noticeable symptoms.
- Treatment for PanNETs depends, in part, on whether the tumors are causing symptoms and where in the body they are found.
- Treatment often includes surgery.
- Next steps after surgery are based on whether all the cancer was removed.
- Treatment may also include systemic therapy and treatment to manage symptoms.

Questions to ask

- What type of 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 from pancreatic cancer?

8

Neuroendocrine tumors, well-differentiated grade 3

54 What is a well-differentiated grade 3 NET?

54 Testing and treatment decision-making

54 Treating locoregional disease

55 Treating locally advanced or metastatic disease

58 Key points

58 Questions to ask

This chapter discusses treatment recommendations 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.

What is somatostatin?

A hormone that regulates many body functions. Some neuroendocrine tumors have a protein on their surface that attaches to the somatostatin. These proteins are called somatostatin receptors (SSTRs).

What is a well-differentiated grade 3 NET?

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.

High-grade tumors are more likely to spread to other areas of the body. They are diagnosed with a tumor biopsy that shows a high amount of a certain protein in the tumor cells.

Testing and treatment decision-making

Testing might include CT or MRI in phases 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 may be recommended.

Treatment decisions are based on:

- Whether the cancer is locoregional or metastatic
- Whether the tumor(s) can be surgically removed
- Whether the tumor has a certain protein that suggests it is fast or slow growing (tumor biology)
- Whether the tumor tests positive for SSTR

The protein Ki-67 is sometimes found on a NET. A high level of this protein suggests a faster-growing tumor. This may be used to help guide treatment decisions.

Treating locoregional disease

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

For a tumor with favorable biology, treatment is surgery to remove the tumor and nearby lymph nodes. Favorable biology means the tumor cells are growing slowly.

Favorable biology:
Low level of Ki-67
Slower growing
SSTR positive

Unfavorable biology:
High level of Ki-67
Faster growing
SSTR negative

For a tumor with unfavorable (faster-growing) biology:

- Treatment in a clinical trial is preferred.
- Treatment is surgery to remove the tumor and nearby lymph nodes (if appropriate).
  - Systemic therapy may be given before surgery. See **Guide 8**.

After treatment, you'll 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.

Treating 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 decisions for a locally advanced or metastatic grade 3 NET is based on tumor biology and if the tumor can be removed with surgery (resectable) or can't be removed with surgery (unresectable).

For tumors with favorable biology

If the tumor has been removed

After removal of the primary tumor and any metastatic sites, you'll be monitored to see if the disease returns. You can 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.

Guide 8
Locoregional well-differentiated NETs with unfavorable biology: Neoadjuvant systemic therapy recommendations

Clinical trial is the preferred treatment. If surgery is planned, the systemic therapies listed here may be given beforehand (neoadjuvant).

Preferred therapies	• Carboplatin and Etoposide • Cisplatin and Etoposide
Other recommended therapies	• Capecitabine and Temozolomide • FOLFOX or CAPEOX • Temozolomide

If the tumor can't be removed

People with high tumor burden or tumors that have spread or gotten worse receive treatment different from those with no symptoms and low tumor burden.

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

- Clinical trial (preferred).
- Systemic therapy. See **Guide 9**.
- Chemoradiation. A certain type of chemotherapy, called an antimetabolite, may be used.
- Treatment for metastases, such as radiation therapy, ablation, or arterially directed therapy.

Medicines in abbreviated systemic therapy regimens are found in Chapter 4, Guide 2.

Guide 9
Locally advanced or metastatic disease with favorable biology: Systemic therapy recommendations

Clinical trial is the preferred treatment for well-differentiated grade-3 NETs that can't be removed entirely and have high tumor burden or cancer has grown or spread.

Preferred therapies	• Cabozantinib • Capecitabine and Temozolomide • PRRT (if SSTR-positive) • Temozolomide
Other recommended therapies	• CAPEOX • Everolimus • FOLFOX • SSA therapy*
Therapies used in certain cases	• Carboplatin and Etoposide • Cisplatin and Etoposide • SSA therapy* (high dose) • Pembrolizumab (for tumors with certain genetic traits) • Sunitinib (for PanNETs) • Chemoradiation

*If SSTR-positive, hormonal symptoms, or both.

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

- Observation (watch and wait), in some cases
- Somatostatin analogue (SSA) therapy if 1 or both of the following apply:
  - The tumor is SSTR positive
  - You're having hormonal symptoms
- Peptide receptor radionuclide therapy (PRRT), if the tumor is SSTR positive
- Radiation therapy to treat metastases

After treatment, you can expect tests every 12 to 24 weeks for the first 2 years and then every 6 to 12 months for up to 10 years.

For tumors with unfavorable biology

These tumors are treated in a clinical trial (preferred) or with systemic therapy. See **Guide 10**.

Treatment may also include:

- Radiation therapy.
- Chemoradiation. A certain type of chemotherapy, called an antimetabolite, may be used.
- Radiation therapy, ablation, or arterially directed therapy (for metastases).
- Surgery.

Guide 10
Locally advanced or metastatic well differentiated NETs with unfavorable biology: Systemic therapy recommendations

Clinical trial is the preferred treatment for well-differentiated grade-3 NETs that can be removed and have high tumor burden or cancer has grown or spread.

Preferred therapies	• Carboplatin and Etoposide • Cisplatin and Etoposide • CAPEOX, FOLFIRINOX, or FOLFIRI
Other recommended therapies	• Capecitabine and Temozolomide • Cisplatin and Irinotecan or FOLFIRI • Temozolomide • Ipilimumab and Nivolumab
Therapies used in certain cases	• Pembrolizumab (for tumors with certain genetic traits) • Chemoradiation

After treatment

You'll be monitored for signs that cancer has returned, grown, or spread. You can expect imaging tests and possibly biomarker tests every 12 to 24 weeks for tumors with favorable biology and every 8 to 12 weeks for tumors with unfavorable biology. Tell your care team about any changes in your health.

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, in part, on tumor location and if the tumor can be removed with surgery (resectable) or can't be removed with surgery (unresectable).
- Systemic therapy is often used to treat these tumors.
- A tumor with unfavorable biology may be treated with systemic therapy before surgery.
- Locally advanced or metastatic cancer may be treated with radiation therapy, chemoradiation, ablation, or arterially directed therapy.
- You'll be monitored after treatment for signs that cancer has returned, grown, or spread.

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?

9

Other neuroendocrine growths and conditions

60 What neuroendocrine growths and conditions are discussed in this chapter?

60 Neuroendocrine neoplasms: Primary site unknown

61 Extrapulmonary poorly differentiated tumors

62 Tumors related to multiple endocrine neoplasia type 1

65 Key points

65 Questions to ask

This chapter describes treatment recommendations for certain neuroendocrine neoplasms, extrapulmonary poorly differentiated tumors, and tumors related to multiple endocrine neoplasia type 1 (MEN1).

What neuroendocrine growths and conditions are discussed in this chapter?

Neuroendocrine neoplasms

Neoplasms are collections of abnormal growths. Neuroendocrine neoplasms may or may not be cancer. They are treated based on where they are found, but sometimes tests aren't able to detect where they started (their primary site).

Neuroendocrine carcinomas

Carcinoma is cancer of the cells that line the inner and outer surfaces of the body. Neuroendocrine carcinomas are poorly differentiated. Poorly differentiated means they tend to grow and spread faster than well-differentiated cells.

MEN1

Multiple endocrine neoplasia type 1 (MEN1) is a rare, inherited condition that can put a person at increased risk of tumors in the endocrine glands or tissues. These neoplasms tend to occur in the:

- Parathyroid glands
- Pituitary gland
- Pancreas
- Stomach
- Duodenum (upper portion of the small intestine)
- Thymus
- Lungs

Neuroendocrine neoplasms: Primary site unknown

A neuroendocrine neoplasm is an abnormal neuroendocrine growth that may start in the pancreas. It may also start in the gastrointestinal (GI) tract, lungs, or other sites. These neoplasms may or may not be cancer.

Sometimes a neuroendocrine neoplasm is found and confirmed by a biopsy, but it isn't clear where in the body the growth started (called primary site).

Testing for primary site

Your care team will do imaging studies and possibly biomarker testing to try to learn where the growth began.

If testing identifies where the growth started, your treatment will be based on that information.

If testing is unable to detect where the growth started

A well-differentiated grade 1 or 2 growth is treated as locoregional advanced or metastatic disease of the GI tract. See *Chapter 5: Neuroendocrine tumors of the gastrointestinal tract*.

A well-differentiated grade 3 growth is treated based on:

- Whether cancer is locoregional or metastatic
- Whether the cancer can be removed
- Tumor biology

See *Chapter 8: Neuroendocrine tumors, well-differentiated grade 3* for treatment recommendations.

For a poorly differentiated tumor, treatment follows recommendations explained in the next section.

Extrapulmonary poorly differentiated tumors

Extrapulmonary poorly differentiated tumors are aggressive, fast-growing, abnormal growths found outside the lungs. Treatment is based on tumor location and may include a combination of surgery, chemotherapy, and radiation therapy.

Types of extrapulmonary poorly differentiated tumors include:

- Neuroendocrine carcinoma
- Large or small cell neuroendocrine carcinoma
- Mixed neuroendocrine–non-neuroendocrine neoplasm, a mix of neuroendocrine and non-neuroendocrine cells, such as adenocarcinoma or squamous cell carcinoma

Your care team can explain more about the type of cells found in your tumor. Imaging and other tests will be done to learn more about the type of tumor. Treatment will be based on the location of the tumor and if it can be removed with surgery.

Treatment

If the tumor can be removed

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

Treatment may include 1 or more of the following:

- Surgery
- Chemotherapy
- Radiation therapy
- Chemoradiation

Systemic therapy recommendations include:

- Carboplatin and etoposide
- Cisplatin and etoposide
- FOLFIRI
- FOLFOX
- Temozolomide

Medicines in abbreviated systemic therapy regimens are found in Chapter 4, Guide 2.

After treatment, you'll 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.

If the tumor can't be removed

If the tumor has spread to nearby lymph nodes

Treatment may include radiation therapy and systemic therapy. Preferred systemic therapy options include:

- Carboplatin and etoposide
- Cisplatin and etoposide

Capecitabine (an antimetabolite) may also be used in certain circumstances.

After treatment, you'll 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 imaging scans.

If the tumor has spread to distant sites

Metastatic disease is cancer that has spread to distant organs or lymph nodes. It's treated with systemic therapy, which may include:

- Chemotherapy
- Immunotherapy
- Targeted therapy

Systemic therapy recommendations for metastatic disease can be found in **Guide 11**.

Most of the medicines used in certain cases are targeted therapies used for very specific types of tumors with certain gene mutations (changes).

After treatment, you'll 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 imaging scans.

If cancer grows or spreads during or after treatment, you'll have systemic therapy.

Tumors related to multiple endocrine neoplasia type 1

MEN1 is a rare, inherited condition that can put a person at increased risk of developing neoplasms in the endocrine glands. These include the parathyroid glands, pancreas, thymus, and pituitary gland.

Anyone who might have MEN1 should receive genetic counseling and screening for inherited genetic conditions.

The *MEN1* gene provides instructions for making a protein called menin. This protein keeps cells in the body from growing and dividing too fast or in an uncontrolled way. However, when there's an abnormal change (or mutation) in the *MEN1* gene, tumors can grow.

In MEN1, endocrine glands grow tumors that create an overload of hormones. The tumors are usually benign (not cancer). MEN1 is also referred to as Wermer syndrome.

Screening for MEN1

Screening depends on where the tumor is found. It usually includes biomarker and imaging tests. It's important to have genetic counseling and screening if you're diagnosed with MEN1.

Treatment for tumors related to MEN1

Treatment is based on where the tumor is located or where it started.

Guide 11
Metastatic extrapulmonary poorly differentiated tumors: Systemic therapy recommendations

Preferred therapies	• Carboplatin and Etoposide • Cisplatin and Etoposide • Cisplatin and Irinotecan
Other recommended therapies	• Capecitabine and Temozolomide • Carboplatin and Irinotecan • FOLFIRI • FOLFOX • FOLFIRINOX • Temozolomide • Ipilimumab and Nivolumab
Therapies used in certain cases	• Pembrolizumab (for tumors with certain genetic traits) • Dabrafenib and Trametinib • Entrectinib • Larotrectinib • Repotrectinib • Selpercatinib

Parathyroid glands

Surgery is the main treatment. You may have:

- A parathyroidectomy, surgery to remove one or more of the parathyroid glands or a tumor that's affecting a parathyroid gland
- A thymectomy to remove the thymus gland

Cryopreservation of parathyroids might also be done. Cryopreservation removes part of a healthy parathyroid gland and freezes it so it can be put back in the body later, if needed.

Pancreas

If a tumor is found in your pancreas, you'll be treated as discussed in *Chapter 7: Neuroendocrine tumors 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. Treatment is based on tumor size, if it's producing hormones, or both. It may include surgery.

Lung and thymus

Treatment for tumors of the lung and thymus can be found in Chapter 6.

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. Testing will likely include blood tests and imaging scans. The timing of the tests varies depending on the location of the MEN1 tumor and if you have any symptoms.

What is MEN1?

A rare, inherited condition that can put a person at increased risk of developing neoplasms in the endocrine glands.



Key points

- Extrapulmonary poorly differentiated tumors are fast-growing tumors found outside the lungs.
- Surgery, systemic therapy, chemoradiation, or a combination of these treatments may be used for these tumors.
- Metastatic disease is treated with chemotherapy, immunotherapy, or targeted therapy (depending on certain tumor features).
- Multiple endocrine neoplasia type 1 (MEN1) is a rare, inherited condition that can increase a person's risk of tumors in the endocrine glands.
- Testing and treatment for MEN1 are based on where the tumor is located, such as the parathyroid glands, pancreas, pituitary gland, lungs, or thymus.
- After treatment, tests are done to check if the cancer has returned.
- Anyone with suspected MEN1 should receive genetic counseling and screening over time for inherited genetic conditions.

Questions to ask

- What type of tumor do I have and is there more than one tumor?
- Is there cancer in any lymph nodes or distant organs?
- Can the tumor(s) be removed with surgery?
- What therapies do you recommend for treatment?
- Should my children or other family members related by blood be tested for MEN1?

10
Other resources

67 What else to know

67 What else to do

67 Where to get help

68 Questions to ask

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

What else to know

This guide 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
- Making treatment decisions
- The details of treatment and its side effects
- 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

Cancer*Care*
cancercare.org

Imerman Angels
imermanangels.org

My Faulty Gene
myfaultygene.org

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?



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NCCN.org/patients/feedback



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 cheeks of the buttocks through which stool passes out of the body.

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

biomarker
A substance in the body that provides information about a tumor. Biomarkers include hormones and proteins, as well as gene mutations (changes). The presence of biomarkers can affect treatment planning.

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

bronchoscopy
A minimally invasive procedure that's done to examine the airways.

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 occur when carcinoid tumors release serotonin and other chemicals into the blood.

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 food turns from a liquid into a solid form.

computed tomography (CT)
A test that uses x-rays from many angles to take pictures of the inside of the body.

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

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. Also called the digestive tract.

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

genetic testing
A lab test (usually done on blood or saliva) to identify abnormal genes (coded instructions in cells 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.

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 takes pictures (images) of the inside of the body.

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

immunotherapy
Drug treatment 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; has 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 take pictures of the inside 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
Cancer that starts in neuroendocrine cells. Usually fast growing.

neuroendocrine neoplasm
A collection of abnormal neuroendocrine cells. Types include neuroendocrine tumors and neuroendocrine carcinomas.

neuroendocrine system
A complex network that manages 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.

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

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

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 place in the body in which a tumor or cancer develops.

radiation therapy (RT)
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 and nervous systems.

somatostatin analogues (SSAs)
Treatment that slows down or stops 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.

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

targeted therapy
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 inside 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 take pictures of the inside of the body.

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This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Neuroendocrine and Adrenal Tumors, Version 1.2026. It was adapted, reviewed, and published with help from the following people:

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