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FOR PATIENTS®

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Neuroendocrine Tumors

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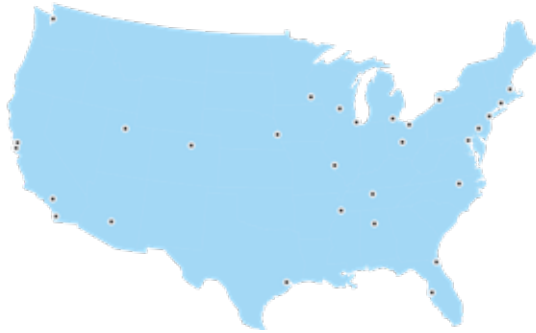
LEARNING that you have cancer can be overwhelming.

The goal of this book is to help you get the best care. It explains which cancer tests and treatments are recommended by experts in neuroendocrine tumors.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 27 of the world's leading cancer centers. Experts from NCCN® have written treatment guidelines for doctors who treat neuroendocrine tumors. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of neuroendocrine tumors in adults. Key points of the book are summarized in the related [NCCN Quick Guide™](#). NCCN also offers patient resources on lung, melanoma, and many other cancer types. Visit [NCCN.org/patients](https://www.nccn.org/patients) for the full library of patient books, summaries, and other resources.

About



These patient guidelines for cancer care are produced by the National Comprehensive Cancer Network® (NCCN®).

The mission of NCCN is to improve cancer care so people can live better lives. At the core of NCCN are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). NCCN Guidelines® contain information to help health care workers plan the best cancer care. They list options for cancer care that are most likely to have the best results. The NCCN Guidelines for Patients® present the information from the NCCN Guidelines in an easy-to-learn format.

Panels of experts create the NCCN Guidelines. Most of the experts are from NCCN Member Institutions. Their areas of expertise are diverse. Many panels also include a patient advocate. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors.

For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

Dorothy A. Shead, MS
*Director, Patient
Information Operations*

Laura J. Hanisch, PsyD
*Medical Writer/Patient
Information Specialist*

Erin Vidic, MA
Medical Writer

Alycia Corrigan
Medical Writer

Rachael Clarke
*Guidelines Data and
Layout Coordinator*



NCCN Foundation was founded by NCCN to raise funds for patient education based on the NCCN Guidelines. NCCN Foundation offers guidance to people with cancer and their caregivers at every step of their cancer journey. This is done by sharing key information from leading cancer experts. This information can be found in a library of NCCN Guidelines for Patients® and other patient education resources. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of cancer research, education, and progress of cancer therapies.

For more information about NCCN Foundation, visit NCCNFoundation.org.

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National Comprehensive Cancer Network (NCCN) • 3025 Chemical Road, Suite 100 • Plymouth Meeting, PA 19462 • 215.690.0300

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The Healing NET Foundation

As an organization whose mission is to optimize the care of those with neuroendocrine cancer through the education of and collaboration among physicians, health care providers, patients, and caregivers, the Healing NET Foundation is proud to support the NCCN Guidelines for Patients. www.thehealingnet.org



Neuroendocrine Cancer Awareness Network (NCAN)

The Neuroendocrine Cancer Awareness Network (NCAN) is a non-profit organization dedicated to raising awareness of Neuroendocrine Cancer, providing support for caregivers and people with NETs, and funding for NET cancer research. Since 2003, it has been our mission, or as we like to say, our passion, to educate and support the NET community as a whole. NCAN is proud to support the NCCN Guidelines for Patients: Neuroendocrine Tumors. www.netcancerawareness.org

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The Carcinoid Cancer Foundation, Inc.

Empowering neuroendocrine tumor patients with information about diagnosis, treatment and follow up is critical for achieving the best possible outcomes. The NCCN Guidelines for Patients provide an invaluable tool for every person diagnosed with neuroendocrine tumors and their loved ones. The Carcinoid Cancer Foundation team is proud to endorse these guidelines. www.carcinoid.org

Neuroendocrine Tumor Research Foundation (NETRF)

Neuroendocrine Tumor Research Foundation (NETRF) is pleased to endorse the NCCN patient guideline for NETs. This NCCN guideline, compiled by recognized NET experts, offers patients and families up-to-date, evidence-based information to help increase their involvement in their treatment and survivorship planning, an unmet need identified by patients in an NETRF-funded INCA survey in 2017. www.netrf.org



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Who should read this book?

This book is about treatment for neuroendocrine tumors. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with doctors what care is best.

Are the book chapters in a certain order?

Yes, information in early chapters explains treatment options found in later chapters. Starting with **Part 1** may be helpful for many people. It explains the neuroendocrine system and tumors that grow there. **Part 2** explains the tests doctors use to confirm (diagnose) a neuroendocrine tumor. **Part 3** describes the types of treatments that may be used.

Part 4, Part 5, Part 6, and **Part 7** offer treatment options for certain types of neuroendocrine tumors. **Part 8** is the last chapter of the guideline. It offers some helpful tips for making treatment decisions. You can also get sample questions to ask your doctors. Visit the websites in this section to learn more about neuroendocrine tumors.

Does this book include all options?

This book includes information for many situations. However, it doesn't address treatment for adrenal tumors or Merkel cell skin cancer. If you need more information on these cancer types, visit the NCCN Clinical Practice Guidelines in Oncology

(NCCN Guidelines®) for Merkel Cell Carcinoma or Neuroendocrine and Adrenal Tumors at www.nccn.org.

Your treatment team can help with options. They can point out what sections apply to you. They can also give you more information. As you read this book, you may find it helpful to make a list of questions to ask your doctors.

NCCN experts base the recommendations in this book on science and experience. However, these recommendations may not be right for your situation. Your doctors may suggest other tests and treatments based on your health and other factors. If other recommendations are given, feel free to ask your treatment team questions.

Help! What do the words mean?

In this book, many medical words are included. You will likely hear these words from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don't be discouraged as you read. Keep reading and review the information. Feel free to ask your treatment team to explain a word or phrase that you don't understand.

Words that you may not know are defined in the text or in the *Dictionary*. *Acronyms* are also defined when first used and in the *Glossary*. One example is CT for computed tomography.

1

Neuroendocrine tumors

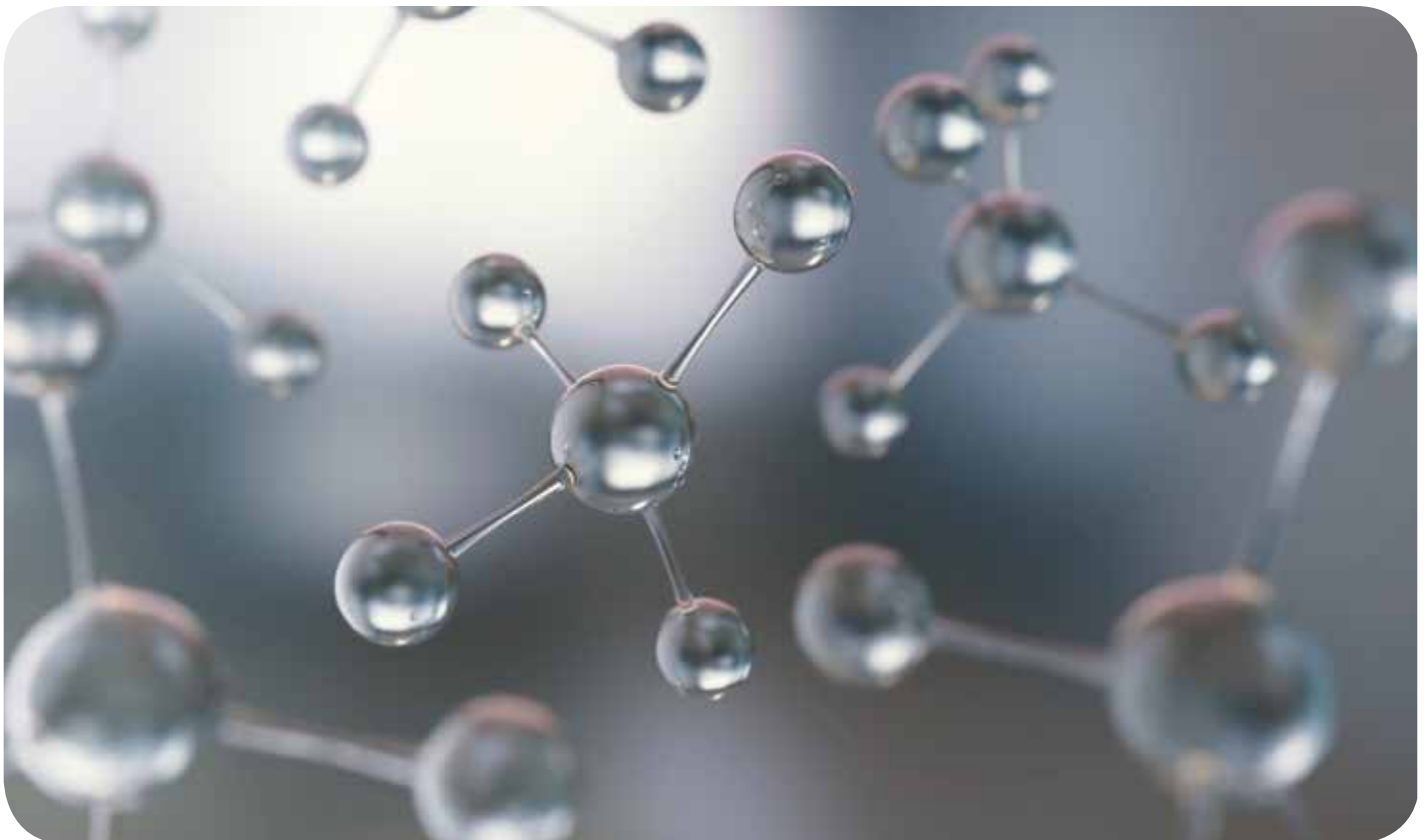
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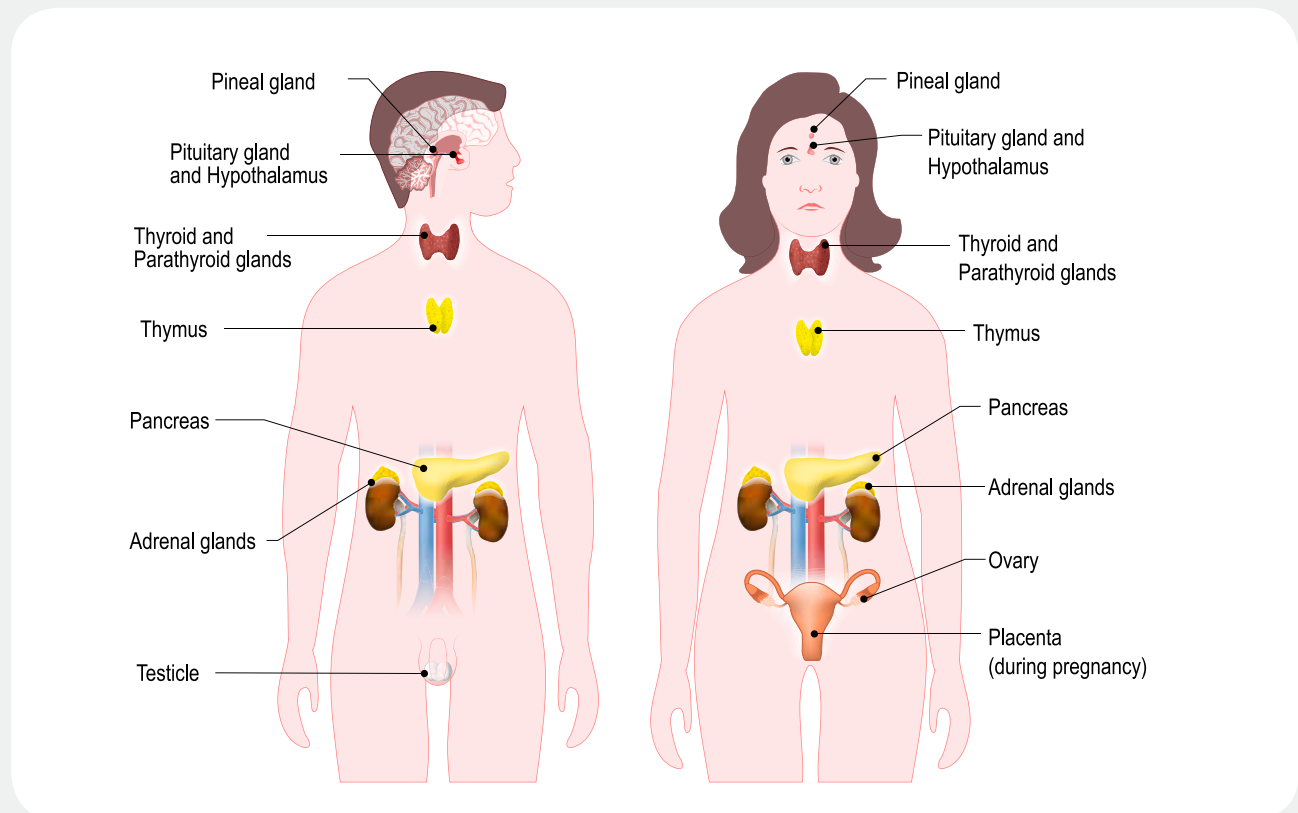


Learning that you or a loved one has neuroendocrine cancer can be overwhelming. It is helpful to find out all you can about this cancer type. It is also a time to talk with your medical team about upcoming tests and treatment options. Part 1 starts with information about the endocrine and neuroendocrine systems. You will also learn about the signs and symptoms of neuroendocrine tumors.

The endocrine and neuroendocrine systems

The endocrine system is made up of glands in the body. These glands help make and release fluids or hormones. Hormones trigger responses from cells and organs. They control many functions in your body. The endocrine system includes major glands such as the hypothalamus, pituitary, pineal, thyroid, parathyroid, pancreas, adrenal, ovaries, testicles, and prostate. Glands make the fluids or chemicals your body needs (**Figure 1**).

Figure 1. The endocrine system



About the neuroendocrine system:

- The neuroendocrine system controls how the brain, spinal cord, and nerves (nervous system) work with the endocrine system.
- The neuroendocrine system contains neuroendocrine cells.
- Neuroendocrine cells are like nerve cells that receive signals from your brain and endocrine cells that make hormones.

Neuroendocrine cells can be found throughout your body. They are mainly in your GI (gastrointestinal) tract, lungs and airways of the lungs (bronchi), thymus, and pancreas. Other less common areas include the thyroid, parathyroid, adrenal, and pituitary glands. [See Guide 1.](#)

Guide 1. Neuroendocrine system

What this system controls in the body
Air flow in the lungs
Heart rate
Blood pressure
Digestion
Metabolism
Blood sugar
Muscle and bone growth
Reproduction



Treating NETs is an art and a science and your medical team should be led by a specialist who understands this complex disease inside and out.

-Stacie

Survivor, neuroendocrine tumor of the pancreas

Cancer basics

Cancer is a disease that starts in the cells of your body. Cells are the building blocks of tissue in the body. The human body contains trillions of cells. DNA (deoxyribonucleic acid) is found within each cell and controls the cells, giving instructions to them on what to do. The coded instructions for your cells found in DNA are called genes. These instructions found in the DNA are the genetic code that tells cells what to become (for example, heart, lung, thyroid) and what to do (pump blood, absorb oxygen, make hormones).

Normal cells and cancer cells

Normal cells grow and then divide to make new cells when needed. They also die when they become old or damaged. Cancer cells make new cells that aren't needed and don't die when old or damaged. As new cells start to form, this growth can get out of control and lead to the growth of a solid mass of cells called a tumor. Some tumors are cancer (malignant), and some are not (benign). Solid tumors can grow anywhere in the body and can affect the way the body works (Figure 2).

Normal cells tend to stay in one location in the body. Cancer cells can escape from where they started and move to other parts of the body—a process called metastasis. Cancer cells can travel to distant parts of the body through the blood or lymphatic system. When cancer cells settle into new places in the body they can replace or damage healthy cells.

Figure 2.
Key differences between normal cells and cancer cells



Normal cells

- ✓ **Make new cells as needed; die if old/damaged**
- ✓ **Stop when they get too close to other cells**
- ✓ **Stay where they belong in the body**



Cancer cells

- ➔ **Grow out of control, forming a tumor over time**
- ➔ **Ignore other cells and invade nearby tissues**
- ➔ **Can spread and make new tumors**

Neuroendocrine tumors

Neuroendocrine tumors are rare. Some people refer to neuroendocrine tumors as “NET.” These tumors can be cancer (malignant) or not cancer (benign). They occur in the endocrine system, which is spread throughout your body. The most common types are carcinoid tumors found in the lung, airways of the lungs (bronchi), small intestine, rectum, appendix, and thymus. Another common type of neuroendocrine tumor is found in the pancreas. Other forms of neuroendocrine tumors can also be found in the body in different organs.

How cancer starts

In general, cancer is named after the place where it started in the body, and it keeps the same name even if it happens to spread. A biopsy can confirm a diagnosis of cancer. A sample of fluid or tissue can be taken during a biopsy and examined under a microscope.

Your doctor can test for the cell type of the neuroendocrine tumor. This is known as histology. Histology is an important piece of a cancer diagnosis and helps doctors determine how to treat a neuroendocrine tumor. A pathologist will classify the cell type based on the size, shape, and structure of the cells. A pathologist is a doctor who is an expert in examining cells and tissue to find disease.

A pathologist will also assess how quickly the cells divide, based on the mitotic rate (proportion of cells that are dividing into two cells) and the presence of the Ki-67 protein (another way of measuring cell division).

Tumor markers are proteins made by tumors that may be found in the blood at normal or higher levels when a tumor is in the body. Generally, higher levels of a particular tumor marker may be associated with larger numbers of tumor cells in the body.



Your treatment team

Doctors with different specialties should help with the diagnosis and treatment of neuroendocrine tumors. This team of doctors will include oncologists, doctors who specialize in the treatment of cancer.

Your team may include:

- ✓ Medical oncologists
- ✓ Radiation oncologists
- ✓ Surgical oncologists
- ✓ Pathologists
- ✓ Endocrinologists
- ✓ Radiologists

Other health care providers may be a part of your treatment team. See page 26 in Part 3 to learn more about your treatment team.

Tumor markers may also be present with other medical conditions. For example, the tumor marker chromogranin A may be measured at higher-than-normal levels when a neuroendocrine tumor is present. However, it may also be higher for other reasons, like taking medications that reduce stomach acid or when there is liver damage. Thus, your doctor will use tumor marker tests along with other tests to confirm (diagnose) a neuroendocrine tumor.

Doctors classify neuroendocrine tumors by the:

- Location of the tumor
- Extent of disease (cancer stage)
- Histology (how the tumor looks under a microscope)

A pathologist will assess the type and shape of cells, and will see how much the cells look like normal cells under a microscope. Your pathology report will have this important information in it. It is helpful to ask your doctor to explain what the results mean.

Risk factors

Anything that increases your chances of having cancer is called a risk factor. Risk factors can be activities that people do, things in the environment, or traits passed from parents to children through genes. Genes are coded instructions for your cells.

An abnormal change in these instructions—called a gene mutation—can cause cells to grow and divide out of control. Risk factors for neuroendocrine tumors are not fully understood. Doctors find that most of these tumors occur randomly in some people. However, others have inherited genetic mutations that put them at risk.

NCCN experts suggest genetic counseling for people with a known or possible personal or family history of inherited genetic syndromes. Your doctor may suggest genetic testing to look for changes in genes that increase the chances of developing a neuroendocrine tumor.

Mutations can be passed on from a parent before you are born (inherited), or they can be caused by genetic damage (acquired) occurring later in life. People with inherited genetic mutations have a higher risk for certain cancers, but that doesn't mean they will definitely develop cancer. Certain inherited genetic syndromes are considered risk factors for neuroendocrine tumors.

These syndromes include:

- MEN (multiple endocrine neoplasia) type 1
- MEN type 2
- Von Hippel-Lindau disease
- Tuberous sclerosis complex
- Neurofibromatosis

These inherited diseases can cause tumors to form in the body. MEN1 involves a mutated gene called *menin* that is associated with multiple tumors of the parathyroid, pituitary gland, and pancreas. MEN2 has mutations in the *RET* proto-oncogenes. It may cause medullary thyroid cancer, pheochromocytoma (adrenal tumor), and too much parathyroid hormone (hyperparathyroidism). Von Hippel-Lindau disease, tuberous sclerosis complex, and neurofibromatosis may also cause abnormal tumor growth to occur in many places in the body.

Guide 2. Symptoms

Symptoms
Diarrhea
Redness of the face and neck (flushing)
High blood pressure (hypertension)
Extreme tiredness (fatigue)
Headache
Nausea
Vomiting

Symptoms

Doctors need to assess your health and learn about your symptoms. Keep in mind, that symptoms of neuroendocrine tumors may be similar to those of other medical conditions. Some people with neuroendocrine tumors may have symptoms, while others may have no symptoms at all. Those with symptoms are said to have functional tumors, and those without symptoms are said to have nonfunctional tumors. Functional tumors can make hormones that cause symptoms.

Large amounts of hormones in the body may be the cause of symptoms for people with neuroendocrine tumors. [See Guide 2](#) for some symptoms that are possible with these tumor types.

Not all of these symptoms are seen with these tumor types or syndromes. People may have other symptoms not listed here. Symptoms occur when certain hormones are made and released (secreted) in the body. You will learn more about the different

neuroendocrine tumors in later chapters. Ask your doctor about the symptoms related to the type of neuroendocrine tumor you have.

Syndromes

Two syndromes that are common with neuroendocrine tumors are carcinoid syndrome and Cushing's syndrome. Your doctor will order certain tests if he or she thinks you may have one of these syndromes. With these syndromes, the tumor is releasing large amounts of hormones into the blood. When your body has too much of a hormone it causes problems.

Carcinoid syndrome may occur with carcinoid tumors. This syndrome occurs because the tumor is releasing too much serotonin and other chemicals into the blood. Serotonin sends messages between nerve cells. It controls things like mood, sleep, and memory. Symptoms of carcinoid syndrome may include your face turning red (flushing) or diarrhea. This syndrome may not always occur with carcinoid tumors of the GI tract unless the cancer has spread to other parts of the body.

Cushing's syndrome may occur with carcinoid tumors of the lung and airways (bronchi). It may also occur with adrenal tumors because this primary tumor also secretes hormones. There may be high levels of cortisol in the body that cause this syndrome. Cortisol controls blood sugar, metabolism, and other functions in the body. If your cortisol level is high, symptoms include weight gain in the abdomen, high blood pressure (hypertension), high blood sugar (hyperglycemia), depression, and extra hair growth.

Sometimes, your doctor will screen for these syndromes if you have a neuroendocrine tumor. Screening is when tests are done to detect a disease

in someone without symptoms. See page 18 for more information on biochemical testing.

It is important to tell the doctor how you are feeling during your visit or call if you have any symptoms. If your doctor suspects a neuroendocrine tumor, he or she will check your blood and order other tests. You will learn more about testing for neuroendocrine tumors in Part 2.

Cancer stage

Cancer staging is a rating by your doctors of the extent of the cancer. It is used to plan which treatments are best for you. The AJCC (**A**merican **J**oint **C**ommittee on **C**ancer) staging system is a common staging system used for the neuroendocrine tumors of the stomach, duodenum and ampulla of Vater, jejunum and ileum, colon and rectum, pancreas, lung, and thymus.

There are four stages—I, II, III, and IV—for each type of neuroendocrine tumor. For some types of neuroendocrine tumors, these stages are further broken down into sub-categories.

In this system, the letters T (**t**umor), N (**n**ode), and M (**m**etastasis) describe different aspects of cancer growth. The T, N, and M scores are combined to assign the cancer a stage.

- T score describes the growth of the primary tumor.
- N score describes spread of cancer cells to lymph nodes.
- M score tells if the cancer has spread to distant sites.

Another factor used to classify the tumor type is the cancer grade. Higher-grade cancers tend to grow and spread faster than lower-grade cancers. The letter G notes the grade. G1 is low grade, G2 is intermediate (middle) grade, and G3 is high grade.

Knowing how different the cells look (well or poorly differentiated; low or high grade) helps your doctors understand how the tumor may grow and behave in the body. Your treatment team will consider your treatment options based on the cancer stage. Well-differentiated cancer cells look almost like normal cells under a microscope. These cancer cells tend to grow slowly. Poorly differentiated means the cancer cells look nothing like normal cells under a microscope. These cancer cells tend to grow quickly.

Most neuroendocrine tumors are placed into 3 histologic groups that include:

- Well-differentiated, G1
- Well-differentiated, G2
- Poorly differentiated, G3

Once your doctors know more about your diagnosis, they can talk to you about what to expect. Talking with your doctor about the type of neuroendocrine tumor and cancer stage will help with treatment planning. Your treatment team will come together and decide on a recommended treatment plan. This treatment plan will be based on the extent of disease in your body and your other health needs, as well as your personal choices. A treatment plan is a written course of action that covers every stage of the treatment process.

Next steps 

To learn more about treatment options, see the *Treatment guides* in Parts 4 to 7. Each chapter is for a specific type of neuroendocrine tumor.

Review

- ▶ Neuroendocrine cells can be found throughout your body. They are mainly in your GI tract, lungs and airways of the lungs (bronchi), thymus, and pancreas.
- ▶ Neuroendocrine tumors are relatively rare. The tumors can be cancer (malignant) or not cancer (benign).
- ▶ Doctors find most neuroendocrine tumors occur randomly in some people. However, some people have inherited genetic syndromes related to neuroendocrine tumors.
- ▶ Large amounts of hormones made in the body may be the cause of symptoms with neuroendocrine tumors.

**What to know about neuroendocrine tumors**

- ✓ Neuroendocrine tumors are rare.
- ✓ Neuroendocrine tumors can be cancer (malignant) or not cancer (benign).
- ✓ Carcinoid tumors are the most common type of neuroendocrine tumors. They grow in the GI tract, lungs, or airways that lead to the lungs (bronchi).



It is critical that you be your own patient advocate and surround yourself with a comprehensive medical team including local doctors and a NET specialist to determine the right course of treatment at the right time especially for you.

-Cindy

Survivor, neuroendocrine tumor of the ileum

2

Testing for neuroendocrine tumors

-
- 17 Medical history & physical exam

 - 18 Blood and urine tests

 - 20 Imaging tests

 - 23 Scopes

 - 23 Biopsy

 - 24 Review



Part 2 includes tests used to confirm (diagnose) a neuroendocrine tumor. Doctors will test your blood and tissue samples to confirm cancer. Some of the tests may continue during and after treatment. The test results will help your doctors and you decide on a treatment plan.

Medical history & physical exam

Two basic tools of diagnosis include a medical history and physical exam. This is when your doctor asks for a full history of your health and does an exam of your body. Your doctor will ask about your medical history, which should include everything that has ever happened to you, related to your health. Doctors often perform a physical exam along with taking a medical history ([Guide 3](#)).

Your medical records:

- ✓ Your doctors will order tests and schedule visits to talk about your care plan.
- ✓ It is helpful to keep track of your test results at all times. Ask your doctors questions about the results.

Guide 3. Medical history and physical exam

Medical history	Physical exam
<p>Your doctor may ask you about:</p> <ul style="list-style-type: none"> • Health events in your life • New symptoms or illness • Medications you are taking now and those you may be allergic to <ul style="list-style-type: none"> ◦ Make a list of your medicine and supplements • Family history of disease such as cancer, heart disease, or diabetes 	<p>Your doctor may:</p> <ul style="list-style-type: none"> • Check your eyes, ears, nose, mouth, and neck • Listen to your lungs, heart, and belly (abdomen) • Feel or use pressure on the body to see if organs are of normal size, soft or hard, or cause pain when touched

Blood and urine tests

Blood tests are not used to confirm (diagnose) a neuroendocrine tumor. Doctors test blood to look for signs of hormone secretion and assess your general health. They may be used to assess the response to drugs that are being used for treatment. Abnormal levels of certain chemicals in the blood may be a sign that the neuroendocrine tumor has spread to distant parts of the body.

Complete blood count

A CBC (complete blood count) measures the number of blood cells in a blood sample. It includes numbers of white blood cells, red blood cells, and platelets. Your blood counts may be low or high because of cancer or another health problem. It is an essential test that gives a picture of your overall health.

Comprehensive metabolic panel

Chemicals in your blood come from your liver, bone, and other organs. A comprehensive metabolic panel often includes tests for up to 14 chemicals. The tests show if the level of chemicals are too low or high. Abnormal levels can be caused by cancer or other health problems.

Biochemical tests

A biomarker is any molecule in your body that can be measured to assess your health. Biochemical testing measures certain substances like hormones that may be present with a neuroendocrine tumor. Certain symptoms are seen when your body makes too much of a certain hormone.

Your doctor may consider biochemical tests if you have symptoms. He or she may also consider these tests if you have no signs or symptoms, if there is concern that you may have a neuroendocrine tumor or syndromes caused by a tumor. [See Guide 4](#) for a list of neuroendocrine tumors, where they are in the body, possible symptoms caused by hormones, and the type of biochemical test needed.

Urine tests

Besides blood, doctors also test urine to look for signs of disease. Urine tests can also assess if your kidneys are working well, and check the results of cancer treatments. Urine may be collected in a one-time sample or a larger sample collected over a 24-hour period. If collected over 24 hours, your doctor or nurse will give you a container with measurements on it to use. You will need to keep it refrigerated until you return it to the doctor's office or hospital. It is helpful to follow the instructions for keeping your sample ready for testing.

5-HIAA test

5-HIAA (5-hydroxyindoleacetic acid) is a biomarker that can be measured in the urine to confirm a carcinoid tumor is present. It may also be used to check a response to treatment. This substance is made by carcinoid tumors that make too much of the hormone serotonin. This urine test usually involves collecting a 24-hour urine sample, since your body may release 5-HIAA at different times throughout the day. 5-HIAA can also be measured in a blood sample.



The biggest question at diagnosis is, 'What now?' Learn as much as you can about your situation and never hesitate to ask questions.

-Mary

Survivor, neuroendocrine tumor of the ileum

Guide 4. Biochemical testing

Tumor or syndrome	Tumor site	Possible symptoms	Testing
Neuroendocrine tumors of GI tract, lung, and thymus (carcinoid tumors)	<ul style="list-style-type: none"> GI tract (ileum, appendix, rectum) 	<ul style="list-style-type: none"> Flushing, diarrhea, heart valve thickening, and airway problems Carcinoid syndrome or Cushing's syndrome related to tumors of the bronchi or thymus (GI tract - symptoms may only occur with metastases) 	<ul style="list-style-type: none"> Chromogranin A 24-hour urine or blood test for 5-HIAA Tests used for Cushing's syndrome
Cushing's syndrome	<ul style="list-style-type: none"> Adrenal, pituitary, or ectopic (often bronchi or thymus) 	<ul style="list-style-type: none"> Weight gain in the belly area, stretch marks, high blood pressure (hypertension), high blood sugar (hyperglycemia), depression, extra hair growth 	<ul style="list-style-type: none"> Screen for high cortisol (hypercortisolemia) and retest if positive If high cortisol, then test serum ACTH (adrenocorticotropic hormone)
Neuroendocrine tumor of the pancreas and *subtypes	Tumor site	Possible symptoms	Testing
Neuroendocrine tumor of the pancreas	<ul style="list-style-type: none"> Pancreas 	<ul style="list-style-type: none"> May be no symptoms (depends on hormone secreted) 	<ul style="list-style-type: none"> Serum pancreatic polypeptide Chromogranin A
*Insulinoma	<ul style="list-style-type: none"> Pancreas 	<ul style="list-style-type: none"> Low blood sugar (hypoglycemia) 	<ul style="list-style-type: none"> Serum insulin Pro-insulin C-peptide See Guide 30
*VIPoma	<ul style="list-style-type: none"> Pancreas or nearby 	<ul style="list-style-type: none"> Diarrhea, low potassium (hypokalemia) 	<ul style="list-style-type: none"> Serum VIP
*Glucagonoma	<ul style="list-style-type: none"> Pancreas 	<ul style="list-style-type: none"> Flushing, diarrhea, high blood sugar (hyperglycemia), skin rash, risk for blood clots 	<ul style="list-style-type: none"> Serum glucagon
*Gastrinoma	<ul style="list-style-type: none"> Pancreas or duodenum 	<ul style="list-style-type: none"> Gastric ulcers, duodenal ulcers, diarrhea 	<ul style="list-style-type: none"> Serum gastrin

Imaging tests

Imaging tests are used to take pictures (images) of the inside of your body. Imaging can be used to see if there is cancer in the body. Your doctor will want to check the primary tumor, or original site of the tumor. CT (computed tomography) and MRI (magnetic resonance imaging) scans are the recommended imaging tests for neuroendocrine tumors.

CT scan

A CT scan uses x-rays to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles (**Figure 3**). All the x-ray pictures are combined to make one detailed picture of the body part. A CT scan of your chest, abdomen, and/or pelvis may be one of the tests to look for cancer.

Before the CT scan, you may be given a contrast dye to make the pictures clearer. You may drink the dye, have it injected into your vein, or both. It may cause you to feel flushed or get hives. Rarely, serious allergic reactions occur. Tell your doctors if you have had bad reactions in the past.

MRI scan

An MRI scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. This type of scan is good at showing the spine and soft tissues like the brain. An MRI scan can also be used to assess the abdomen and pelvis.

An MRI may be used as an initial test, to check treatment results, and to check for the spread of cancer to other parts of the body. Getting an MRI scan is similar to getting a CT scan, but MRI scans take longer to complete.

Figure 3. CT scan

A CT scan machine is large and has a tunnel in the middle. During the test, you will lie on a table that moves slowly through the tunnel.



There has been much progress in the last several years, and we see new surveillance technologies and new treatments being approved all the time. It is an exciting and hopeful forecast for NET patients!

-Mary

Survivor, neuroendocrine tumor of the ileum

For the scan, you will need to lie on a table that moves through a large tunnel in the scanning machine. The scan may cause your body to feel a bit warm. Like a CT scan, a contrast dye may be used to make the pictures clearer.

PET/CT scan

A PET/CT (positron emission tomography/computed tomography) scan shows whether or not your tumor cells are active. To create pictures, a radiotracer first needs to be put into your body by an injection into a vein. After this, you rest for about an hour to allow the radiotracer to reach the cells. The radiotracer emits a small amount of energy that is detected by the machine that takes pictures (PET scanner). Active cancer cells look brighter in the pictures. A CT scan is also done as part of this study to help show where the tumor activity is located. For this part of the study, you may need to drink a dye or a dye may be injected into your vein.

PET/CT is very good at showing small groups of cancer cells. This test may also be useful for showing if cancer has spread. There are two types of PET/CT scans that you could have, depending on the radiotracer that is injected.

FDG PET/CT scan

A PET scan using 18F-fluorodeoxyglucose (FDG-PET scan) shows how fast your tumor cells use up a simple form of sugar called glucose. More active cancer cells use sugar faster than normal cells, and thus look brighter in the pictures. However, many neuroendocrine tumors are not as fast-growing as other cancers, and may not be very bright on FDG-PET scans. Tumor cells also become less active after they are successfully treated.

DOTATATE PET/CT scan

A newer method for taking pictures of neuroendocrine tumors is a DOTATATE PET/CT scan. For this scan a radiotracer known as Gallium-68 dotatate (^{68}Ga -dotatate) is used.



What to know about imaging tests

- ✓ Imaging tests can see if the cancer is in more than one part of the body.
- ✓ The tests continue during treatment to see how the disease is responding.
- ✓ The tests can be used after treatment to check for signs of disease (recurrence).
- ✓ You may not learn of the results of your imaging tests for a few days since a radiologist needs to see the pictures.
- ✓ A radiologist is a doctor who's an expert in reading the pictures from imaging tests.

It is injected into a vein. This radiotracer attaches to the somatostatin receptors that are present on neuroendocrine tumors. These show up very brightly on the PET/CT scan. This can find tumors more easily, and can help distinguish neuroendocrine tumors from other types of tumors. NCCN experts prefer this method when compared to the somatostatin receptor scintigraphy (below).

Somatostatin receptor scintigraphy

Somatostatin receptor scintigraphy is a type of scan that uses a radioactive tracer ^{111}In -octreotide, similar to a drug somatostatin. The radiotracer is injected into a vein. It will show the cells that receive signals (have receptors) for somatostatin. Somatostatin is a growth hormone that helps control the endocrine system. After you are injected, images of your body will be obtained at 4 hours. You will return the following day for additional images (24 hours).

SPECT (single photon emission computed tomography) images will usually be obtained at this time, where the scanner will rotate around your body to generate a three-dimensional image. Tumors with somatostatin receptors will be bright on these images.

Ultrasound

An ultrasound is a test that uses sound waves to form pictures of the inside of the body. Ultrasound is good at showing small areas of cancer that are superficial (on the surface of the body). Ultrasounds are generally painless.

Echocardiogram

An echocardiogram is an imaging test of your heart. It uses sound waves to make pictures. This test is used to check how well your heart is working. It shows your doctor how well your heart is beating and pumping blood.

Figure 4. Upper GI endoscope

This is a procedure to do work in the first parts of the digestive track with a device guided down the throat. It is also called an esophagogastroduodenoscopy.

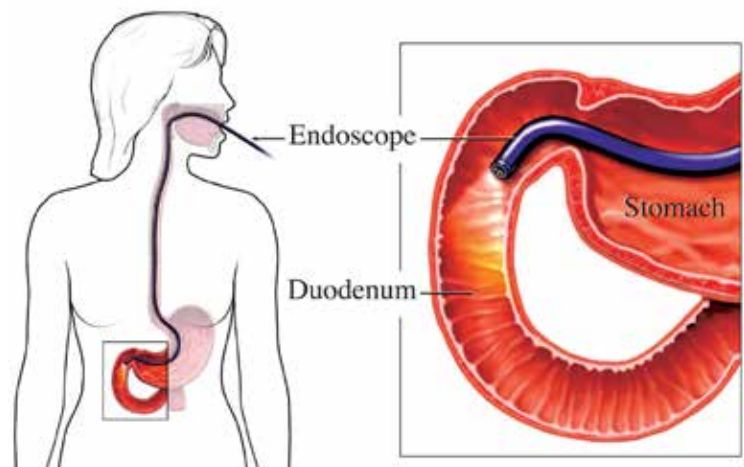


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Scopes

Some imaging tests use a thin, tube-shaped tool called a scope that is inserted into the body to take pictures. One end of the scope has a small light and camera lens to see inside your body. At the other end of the scope is an eyepiece that your doctor looks through to see the images shown by the camera (**Figure 4**). The scope is guided into the body through a natural opening, such as the mouth or nose. It may also be inserted through a small surgical cut. More than one type of scope may be used for imaging tests. You may be sedated during the procedure. This involves the use of sedative drugs to help you relax or go to sleep.

EUS

An EUS (**endoscopic ultrasound**) uses an endoscope that has a small ultrasound probe at the end. The endoscope is inserted through your mouth and guided down your throat and stomach to the first part of the small intestine (duodenum). The ultrasound probe bounces sound waves off your organs to make pictures of the inside of your body. Sometimes an EUS can detect lesions (abnormal areas) that are difficult to see on a CT or MRI. An FNA (**fine-needle aspiration**) or needle biopsy can be performed during an EUS if needed.

Bronchoscopy

A bronchoscope is inserted through the nose or into the mouth, through the throat, to assess the airways that lead to the lungs (bronchi). Your doctor can view the airways for abnormal areas and take images. He or she can also perform a biopsy during this procedure.

EGD

An EGD (**esophagogastroduodenoscopy**) uses an endoscope to assess the upper GI tract. This includes getting a closer look at the esophagus, stomach, and duodenum. The scope is inserted down your throat to view the upper GI tract.

Images may be taken with a camera and a biopsy may be taken of any abnormal areas.

Colonoscopy

A colonoscopy involves the use of an endoscope that is inserted through the anus into the large intestine. The large intestine is also known as the colon. A camera is used to view the colon and check for abnormal areas of concern. A biopsy may be done if needed. A colonoscopy is used to check for disease of the colon or cancer that may start here such as a carcinoid tumor or colon cancer.

Capsule endoscopy

You swallow a capsule with a small camera in it. The capsule travels through your GI tract and allows your doctor to see images of the intestines. The pictures are sent to a small device you wear on the outside of your body.

Biopsy

Tissue or fluid may be removed from your body and tested to diagnose cancer. A biopsy is a procedure that removes samples of fluid or tissue. Sometimes a sample of tissue from the biopsy does not have enough cells to check for cancer. The tissue could also be abnormal but not cancer. If this happens, you may have another biopsy.

For neuroendocrine tumors, a small sample of tissue of a tumor may be removed during an endoscopic test or colonoscopy. The sample is sent to a pathologist to be examined under a microscope.

Test results and next steps

Once your doctors review your test results, they may talk to you about your next steps of care. Talking with your doctor about your diagnosis can help with treatment planning. Shared decision-making is a process in which you and your doctors decide on

the type(s) of treatment together. Shared-decision making is an important part of your treatment plan. Shared decision-making also involves thinking about the things that will change in your daily life. For example, you may think about:

- How treatment will affect your health and ability to do normal activities
- If you might stay in the hospital for a certain period of time
- Whether or not you may need daily help from others, or if you may need in-home care

It may be helpful to talk to your treatment team, family, or friends about your plans. Consider your goals for treatment and discuss any concerns you may have. The list of questions in Part 8 may help you prepare for any talks will you have with your treatment team.

Review

- Tests are used to find cancer, plan treatment, and check how well treatment is working.
- Your health history and a body exam inform your doctor about your health.
- Blood tests check for signs of disease.
- Imaging tests that take pictures of the inside of your body may show cancer.
- A biopsy removes tissue or fluid from your body to confirm (diagnose) cancer.
- Shared decision-making is a process in which you and your doctors decide on the type(s) of treatment together.

List some things that are important to you when it comes to your plan.

Share them with your treatment team.

- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____

3

Overview of cancer treatments

26 Treatment planning

26 Surgery

31 Radiation therapy

31 Hepatic-directed therapies

32 Chemotherapy

32 Targeted therapy

34 Immunotherapy

34 Somatostatin analogs

35 Radiopharmaceutical drugs

36 Clinical trials

38 Review



Part 3 describes the main treatments for neuroendocrine tumors. Knowing what a treatment is will help you understand your treatment options listed in the *Treatment guides* for Parts 4 through 7. There may be more than one treatment for each type of neuroendocrine tumor. Not every person with a neuroendocrine tumor will receive every treatment listed in this chapter.

Treatment planning

Treatment team

Treatment of neuroendocrine tumors takes a team of experts who have experience with these tumors. This includes oncologists and other medical or health care staff.

If you have a neuroendocrine tumor, it is important that the experts meet before your treatment starts. They will meet to create the best treatment plan for you. Your treatment team will also meet while you are going through treatment. After treatment is complete, they will discuss the results and plan your next steps of care. Your team of experts may include a:

In most cases:

- ▶ Pathologist—an expert in testing cells and tissue to find and define the type disease
- ▶ Radiologist—an expert in imaging tests
- ▶ Surgical oncologist—an expert in operations that remove cancer
- ▶ Medical oncologist—an expert in cancer drugs
- ▶ Radiation oncologist—an expert in radiation treatment

- ▶ Endocrinologist—an expert in diseases of the glands (endocrine system)
- ▶ Nurse—an expert trained to directly care for patients

In some cases:

- ▶ Social worker—an expert in meeting social and emotional needs
- ▶ Nutritionist—an expert in healthy foods and drinks
- ▶ Genetic counselor—an expert in explaining and testing for hereditary diseases
- ▶ Nuclear medicine specialist – an expert in radiopharmaceutical treatments

Surgery

Surgery is a primary treatment for neuroendocrine tumors that have not spread or have only spread to a limited extent. Primary treatment is the main treatment used to rid the body of cancer. The goal of surgery is to remove all of the cancer. Surgery may also be used to reduce symptoms caused by the cancer or to extend life. This is called palliative or supportive care.

The method and extent of surgery for a neuroendocrine tumor varies. Both depend on where the tumor is located and the extent of disease. The method of surgery also depends on the organ or tissue in which the neuroendocrine tumor started. Below is a list of some surgery methods to remove neuroendocrine tumors. The method used is based on the tumor site. Your doctor will base the treatment option on whether the tumor can be removed by surgery (resectable) or not (unresectable).



Treatment types

Local treatments are used to treat a focused area of cancer. Surgery and radiation therapy are common local treatments.

Systemic treatments are able to treat cancer cells throughout the body. They come in the form of a drug treatment that includes chemotherapy, targeted therapy, and immunotherapy.

GI tract

Small intestine (jejunum, ileum) and colon

- Bowel resection is surgery to remove a part of the small intestine or large intestine.

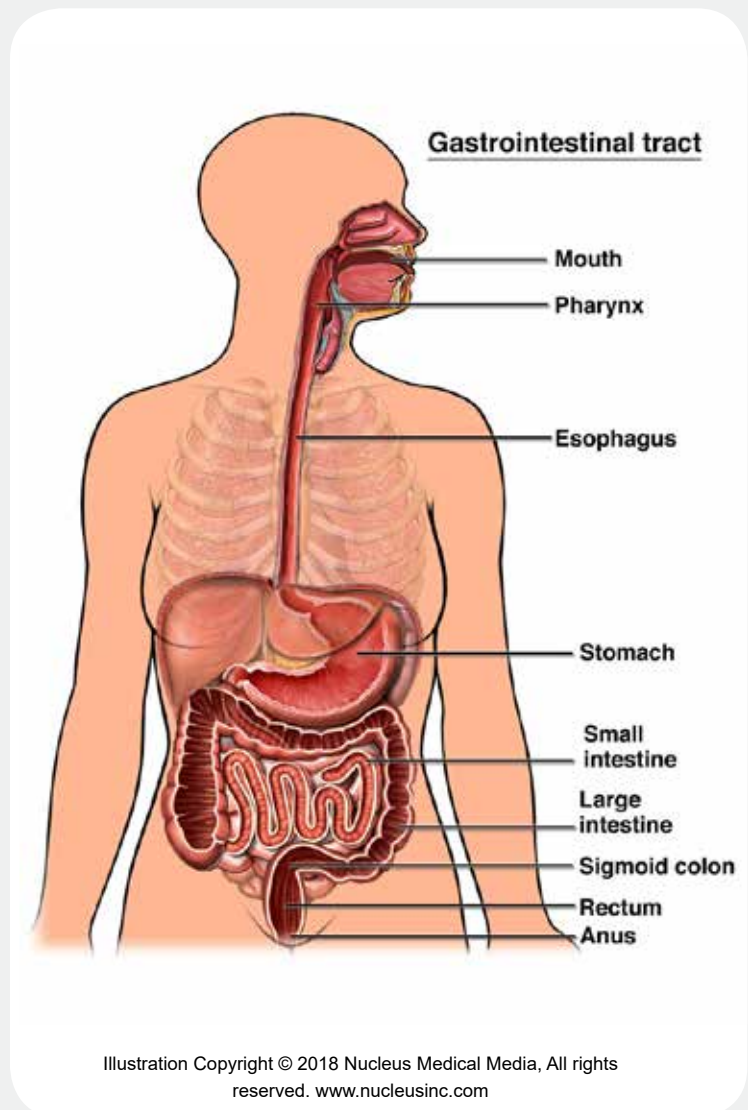
See Figure 5.

Small intestine (duodenum)

- Endoscopic resection involves an endoscope with tools inserted in the tube to remove a smaller-sized tumor from the first part of the small intestine known as the duodenum.
- Duodenotomy is surgery to open up the duodenum and remove a tumor.

Figure 5
GI Tract

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



- Duodenal resection is surgery to remove the first part of the small intestine (duodenum) and connect the intestines.
- Whipple procedure is surgery to remove the head of the pancreas and parts of other nearby organs. Also called pancreaticoduodenectomy.

Appendix

- Appendectomy is surgery to remove the appendix.
- Right hemicolectomy is surgery to remove the right side of the colon and connect the remaining intestines. The appendix is connected to the right colon and is removed during this surgery (if it has not already been removed).

Rectal

- Endoscopic resection involves an endoscope with tools inserted in the tube to remove tissue from the rectum.
- Transanal resection is surgery to remove rectal tumors through the anus.
- Low anterior resection is surgery to remove the upper part of the rectum.
- Abdominoperineal resection is surgery to remove the lower part near the rectum and anus (sigmoid colon), the rectum, and anus.

Stomach (gastric)

- Endoscopic resection involves an endoscope with tools inserted in the tube to remove the tumor in the stomach.
- Surgical wedge resection is surgery to remove the part of the stomach wall with the tumor in it.

- Partial gastrectomy is surgery to remove a segment of the stomach and either reconnect it to the stomach or the small intestine.
- Total gastrectomy or radical resection is surgery to remove the entire stomach and surrounding lymph nodes, and other tissue from the esophagus or small intestine.

Pancreas

- Distal pancreatectomy is surgery to remove the widest part and narrow end of the pancreas as well as other nearby organs. This operation removes the left side of the pancreas.
- Whipple procedure is surgery to remove the head of the pancreas and parts of other nearby organs. Also called pancreatoduodenectomy, it involves removing the right side of the pancreas.
- Primary gastrinoma resection is surgery to remove a gastrinoma that may be in the duodenum or head of the pancreas.
- Enucleation is surgery to remove only the tumor in the pancreas.



It is difficult enough to keep up with appointment scheduling, decision making, insurance issues, etc., but side effects from treatment and recovery from surgery add a whole other dimension. Getting involved in a good support group, whether face-to-face or online, is important to keep balance and sanity in your life.

-Cindy
Survivor, breast cancer and
neuroendocrine tumor of the pancreas



What to know about surgery for the pancreas

- ✓ Tumors of the head of the pancreas are usually treated with the Whipple procedure.
- ✓ Tumors of the body and tail of the pancreas are treated with distal pancreatectomy and either removal of the spleen (splenectomy) or spleen-preserving surgery (considered for benign insulinoma).
- ✓ Before a splenectomy, you may get a few vaccines (pneumococcal, Hib, and meningococcal vaccines). The spleen helps filter bacteria out of the blood, so these vaccines may help prevent a serious infection.

Chest area

Thymus

- Thymus resection is surgery to remove the thymus gland. **See Figure 6.**

Bronchopulmonary (lung and bronchi)

- Lobectomy is surgery to remove a lobe of the lung. **See Figure 7.**
- Other resection is based on the tumor site to remove tumors in the lung or bronchi.

Surgical margin

Your surgeon will try to achieve a cancer-free surgical margin. A surgical margin is a ring of normal-looking tissue around the tumor. Sometimes surgeons can't safely remove the tumor with a cancer-free margin. If this is expected, you may have other treatment after surgery. A surgeon may also remove cancer that has spread, either to stop the growth of cancer or to help relieve symptoms. This surgery is called a metastasectomy.

Possible side effects of surgery

Side effects are unhealthy or unpleasant physical or emotional responses to treatment. You may experience side effects from the anesthesia or surgery. Often, general anesthesia is used for surgery. General anesthesia uses drugs that put you into a deep sleep-like state so you won't feel pain. Ask your treatment team for a full list of possible side effects of the surgery you will have.

Figure 6.
Thymus gland

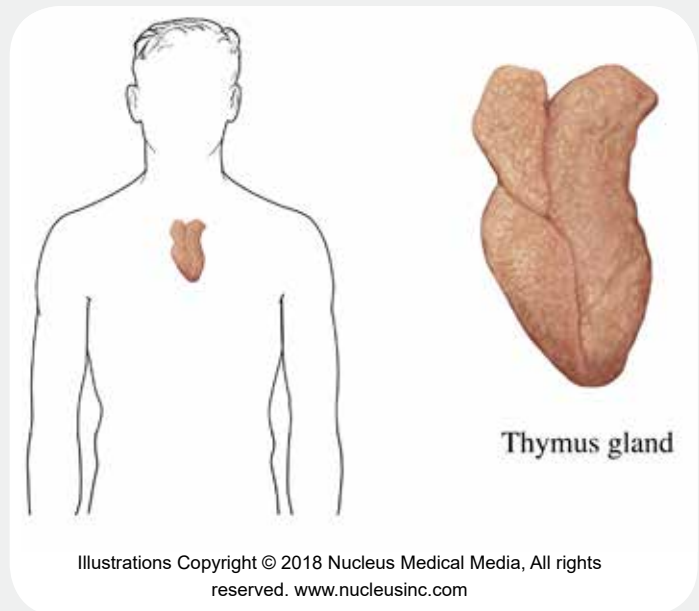
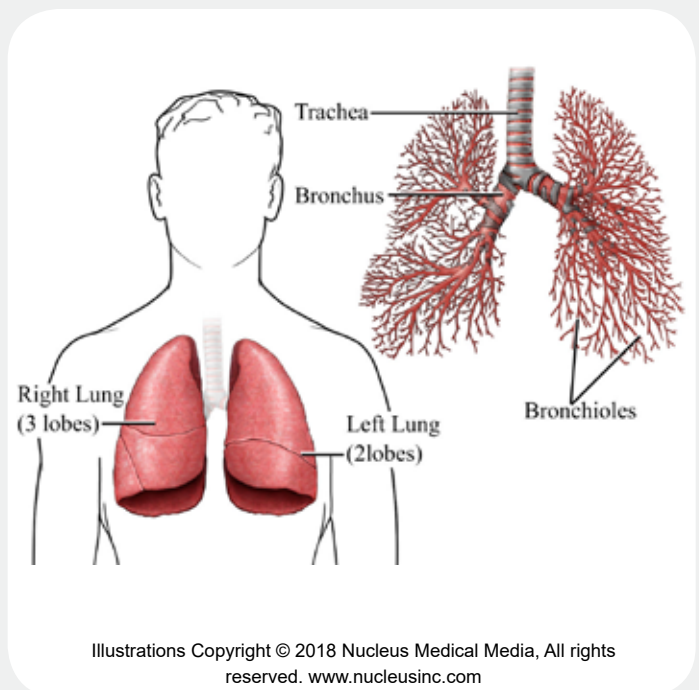


Figure 7.
The lungs and bronchus



Radiation therapy

Radiation therapy uses high-energy rays to treat cancer. The rays damage DNA. DNA is a chain of chemicals in cells that contains genes. Radiation either kills the cancer cells or stops new cancer cells from being made.

There are different ways to give radiation. Which method you get depends on the type of tumor and the purpose of radiation therapy. Some methods are discussed next. You may feel side effects from radiation, although not everyone does. Ask your treatment team for a full list of side effects.

External beam radiation therapy

Radiation is often given using a machine outside the body. This method is called EBRT (**external beam radiation therapy**). To receive EBRT, you first must have a simulation session. For simulation, imaging scans are used to help target the tumor with radiation.

Using the scans, your treatment team will plan the best radiation dose, number and orientation of radiation beams, and number of treatment sessions. Radiation beams will be directed at the tumor with help from images taken prior to each treatment, ink marks on the skin, and/or marker seeds in the tumor. One type of EBRT used for carcinoid tumors is IMRT (**intensity-modulated radiation therapy**). Radiation may be combined with chemotherapy for neuroendocrine tumors of the lungs, bronchi, or thymus. It may also be used to treat poorly differentiated neuroendocrine carcinomas.

During treatment, you will lie on a table in the same position as you did for simulation. Devices may be used to keep you from moving so that the radiation targets the tumor in the same place every day of treatment. You will be alone while the technician

operates the machine from a nearby room. He or she will be able to see, hear, and speak with you at all times. As treatment is given, you may hear noises.

Hepatic-directed therapies

Hepatic-directed therapies are aimed to treat cancer in the liver. This is because carcinoid tumors of the GI tract or pancreatic neuroendocrine tumors tend to spread to the liver. These therapies include different types of embolization, along with cytoreductive surgery, and ablation.

Embolization may be a treatment option for some people with neuroendocrine tumors. It may be performed when surgery is not possible or to relieve symptoms caused by the cancer growing in this area. For this procedure, an object or substance is inserted through a catheter into the main artery that carries blood to the liver (hepatic artery). The goal of this treatment is to stop the blood flow to the tumor.

- ▶ **Bland embolization** involves blocking the blood supply to the tumor by injecting tiny particles into the blood vessels feeding the tumor(s). Stopping the blood flow cuts off the oxygen supply to the tumor and causes cancer cells to die.
- ▶ **Chemoembolization** involves injecting a chemotherapy mixture into the tumor and then blocking the feeding blood vessels to the tumor(s).
- ▶ **Radioembolization** (also known as 90Y) involves injecting glass or resin beads that deliver high-dose radiation directly to the tumor.

Other options such as cytoreductive surgery and ablation may be used to treat metastatic disease. Cytoreductive surgery is done to remove as much tumor as possible. Ablation uses heat (thermal ablation), cold (cryoablation), or radiofrequency waves (radiofrequency ablation or RFA) to kill the cancer cells. These treatments may be an option if the cancer returns after surgery and another operation is not possible. Ask your doctor about hepatic-directed therapies for neuroendocrine tumors in the liver.

Drugs can also be given to treat cancer throughout the body. This is called systemic therapy. Doctors use systemic drugs to treat cancer cells that may have spread beyond the first site of cancer. They are also given when surgery may not be possible. Some drugs are given alone as a single agent, while others are given together as a combination. See Guide 5 for a list of drug treatments.

Chemotherapy

Chemotherapy is the use of drugs to destroy abnormal cells in the body. However, the drugs can also affect normal cells. Many people refer to this treatment as “chemo.”

Different types of chemotherapy drugs work in different ways to kill abnormal cells or stop new ones from being made. Thus, more than one drug may be used. When only one drug is used, it’s called a single agent. A combination regimen is the use of two or more chemotherapy drugs. Other drugs like folic acid or folate analog may be given to support chemotherapy drugs by keeping the healthy tissue safe from the effects of chemotherapy.

Some chemotherapy drugs are liquids that are injected into a vein or under the skin with a needle. Other chemotherapy drugs may be given as a pill that is swallowed.

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

Chemotherapy and radiation given together is called chemoradiation. Sometimes these treatments are given at the same time. Sometimes, the treatments are staggered. For example, chemotherapy is given, then radiation, and then more chemotherapy.

Possible side effects of chemotherapy

The side effects of chemotherapy can differ between people. Some people have many side effects. Others have few. Some side effects can be very serious while others can be unpleasant but not serious. Side effects of chemotherapy depend on the drug type, amount taken, length of treatment, and the person.

Common side effects of chemotherapy may include low blood cell counts, not feeling hungry, nausea, vomiting, diarrhea, hair loss, and mouth sores. Please ask your treatment team for a complete list of side effects.

Targeted therapy

Targeted therapy stops the action of molecules involved in the growth of cancer cells. Some targeted therapy drugs block the chemical signals that tell the cancer cells to grow. Other targeted therapy drugs block signals that cause new blood vessels to form. Other drugs target hormones.

Guide 5. Drug treatment for neuroendocrine tumors

Generic name	Brand name (sold as)	Type of drug
Capecitabine	Xeloda®	Chemotherapy
Carboplatin	–	Chemotherapy
Cisplatin	–	Chemotherapy
Dacarbazine	–	Chemotherapy
Doxorubicin hydrochloride	–	Chemotherapy
Etoposide Etoposide phosphate	– Etopophos®	Chemotherapy
Everolimus	Afinitor®	Targeted therapy
Fluorouracil	–	Chemotherapy
Irinotecan hydrochloride	Camptosar®	Chemotherapy
Interferon alfa-2b, recombinant	Intron® A	Immunotherapy
Lanreotide	Somatuline® Depot	Somatostatin analog
Leucovorin calcium	–	Folinic acid (usually given with chemotherapy “chemoprotectant”)
Levoleucovorin	Fusilev®	Folate analog (usually given with chemotherapy “chemoprotectant”)
Lutetium lu 177-dotatate	Lutathera®	Radiopharmaceutical
Octreotide acetate Octreotide acetate LAR (long-acting release)	Sandostatin® Sandostatin LAR® Depot	Somatostatin analog
Oxaliplatin	Eloxatin®	Chemotherapy
Streptozocin	Zanosar®	Chemotherapy
Sunitinib malate	Sutent®	Targeted therapy
Temozolomide	Temodar®	Chemotherapy

Targeted therapy isn't used for every type of neuroendocrine tumor. Ask your doctor if targeted therapy may help you. It is also helpful to ask about side effects. Targeted therapy harms normal cells less than chemotherapy but still has side effects. Side effects differ between drugs. Most targeted therapies come in pill form but some need to be injected.

Possible side effects of targeted therapy

The side effects of targeted therapy depend on the drug and dose. Some of the side effects listed are caused by only one targeted drug. Others are caused by many targeted drugs but differ in how likely they are to occur.

Some common side effects of targeted therapy drugs are tiredness, joint pain, skin rash, muscle pain, swelling, headache, fever, nausea or vomiting, and diarrhea. These drugs may also cause low blood cell counts.

Not all side effects of targeted therapy drugs are listed here. Be sure to ask your treatment team for a complete list of side effects. If a side effect bothers you, let your treatment team know how you are feeling.

Immunotherapy

The immune system is the body's natural defense against infection and disease. The immune system includes many chemicals and proteins. These chemicals and proteins are made naturally in your body.

Immunotherapy increases the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells.

Possible side effects of immunotherapy

The side effects of immunotherapy depend on the drug and dose. Some common side effects of interferon alfa are flu-like symptoms, nausea, vomiting, not feeling hungry, depression, hair thinning, and liver damage. Ask your doctor about the side effects of immunotherapy.

Somatostatin analogs

Somatostatin analogs are drugs that are similar to the hormone somatostatin. Somatostatin is responsible for controlling the release of certain other hormones in the body. Somatostatin analogs are made to have long-lasting activity in the body when compared to short-acting natural somatostatin. These drugs reduce the amount of hormone secreted from the functional tumors and help stabilize tumor growth.

Possible side effects of somatostatin analogs

The side effects of somatostatin analogs may not be the same for everybody. Some common side effects include not feeling hungry, weight loss, nausea, vomiting, diarrhea, constipation, tiredness, and pain or redness of the injection site. Ask your treatment team for a full list of side effects.

Radiopharmaceutical drugs

Radiopharmaceutical drugs may be used to treat certain types of neuroendocrine tumors that start in the middle of the GI tract, including the small intestine, first part of the colon, and the pancreas. This type of drug includes a radioactive substance that gives off small amounts of radiation. The drug is injected through a vein into the body. The drug targets the somatostatin receptors and sends radiation into the tumor to kill the cancer cells. The radiopharmaceutical drug used is Lu-dotatate (Lutetium lu 177-dotatate [¹⁷⁷Lu-Dotatate]). The procedure used for neuroendocrine tumors is called PRRT (**p**eptide **r**eceptor **r**adionuclide **t**herapy).

Possible side effects of radiopharmaceuticals

Some of the common side effects of radiopharmaceuticals are tiredness, hair loss, nausea and vomiting, and possible damage to the kidney from the radiation. Serious side effects may include blood disorders, leukemia (type of blood cancer), liver or kidney failure, and infertility. You may take supplements or receive an IV protein to prevent the kidney from harm. It is important to talk about the benefits and risks of treatment with your doctor.

After the treatment, your body will release very small amounts of radiation. Your team will give you instructions about after-care. You should avoid becoming pregnant, pregnant women, and small children for a short period of time. Ask your doctor questions about side effects and after-care needed at home.

Order of treatments

Most people with neuroendocrine tumors will receive more than one type of treatment. You may want more information on when and why treatments are given. Talk to your doctor about your treatment plan. The terms that describe the order of treatments are:



Neoadjuvant treatment is given before surgery to shrink the tumor.



Primary treatment is the main treatment given to rid the body of cancer.



Adjuvant treatment is given after surgery to kill any remaining cancer cells.

Clinical trials

Clinical trials are research studies that people choose to take part in. Because of clinical trials, doctors learn how to prevent, diagnose, and treat a disease like cancer. Because of clinical trials, the tests and treatments in this book are now widely used to help people with neuroendocrine tumors.

One of your treatment choices may be to join a clinical trial. NCCN experts strongly support clinical trials as a treatment option. Clinical trials are an important option for people with neuroendocrine tumors.

Phases of a clinical trial

Clinical trials go through levels or phases of testing to find safe and helpful ways to manage a neuroendocrine tumor. These phases help move the research along to find out what works best for people with neuroendocrine tumors.

- **Phase I** looks at how much drug to give, its side effects, and how often to give the treatment.
- **Phase II** tests for side effects and how it works on the cancer type.
- **Phase III** compares the new treatment (or new use of treatment) to what is commonly used.
- **Phase IV** follows late side effects and if the treatment still works after a long period.

Taking part in a clinical trial

All clinical trials have a plan and are carefully led by a medical team. Patients in a clinical trial are often alike with their cancer type and general health. You can join a clinical trial when you meet certain terms (eligibility criteria).

If you decide to join a trial, you will need to review and sign a paper called an informed consent form. This form describes the clinical trial in detail, including the risks and benefits. Even after you sign consent, you can stop taking part in a clinical trial at any time.

Some benefits of a clinical trial:

- You will have access to the most current cancer care.
- You will be closely watched by your medical team.
- You may help other patients with cancer.

Some risks of a clinical trial:

- Like any test or treatment, there may be side effects.
- New tests or treatments may not work.
- You may have to visit the hospital more for treatment and appointments.

Next steps

Ask your doctor or nurse if a clinical trial may be an option for you. There may be clinical trials where you are getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 8.

Complementary and alternative medicine



CAM (complementary and alternative medicine) is a group of treatments sometimes used by people with cancer. Many CAMs are being studied to see if they are truly helpful.

Complementary medicines are meant to be used alongside standard therapies, most often for relaxation, improving your health, or to prevent or reduce side effects.

Alternative medicine is treatment or techniques that are used instead of standard treatments such as chemotherapy or radiation. Some are sold as cures even though they haven't been proven to work in clinical trials.

Many cancer centers or local hospitals have complementary therapy programs that offer acupuncture, yoga, and other types of therapy.

It's important to tell your treatment team if you are using any complementary medicines, especially supplements, vitamins, or herbs. Some of these things can interfere with your cancer treatment. For more information about CAM, ask your doctor and visit the websites listed in Part 8.

Review

- ▶ Local treatments for neuroendocrine tumors include surgery, radiation therapy, and embolization.
- ▶ Systemic treatments are able to treat cancer cells throughout the body.
- ▶ Systemic treatments include drug treatments such as chemotherapy, targeted therapy, immunotherapy, somatostatin analogs, and a radiopharmaceutical drug.
- ▶ Clinical trials help doctors learn how to prevent, diagnose, and treat a disease like cancer.

Your team:

- ✓ Keep a list of contact information of all of your health care providers.
- ✓ Ask a caregiver to help you plan your appointments.
- ✓ Use a calendar or day planner to keep track of your appointments.



Clinical trials are necessary for the development of safe and effective medications to treat many kinds of cancer. Patients should consider entering trials, if the benefits outweigh the risks for them.

-Gary

Survivor, neuroendocrine tumor of the ileum

4

Treatment guide: Neuroendocrine tumors of the gastrointestinal tract (carcinoid tumors)

40 Treatment planning

42 Jejunum, ileum, and colon

43 Duodenum

44 Appendix

45 Rectum

47 Stomach (gastric)

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48 Locally advanced or metastatic
disease

50 Review



Part 4 starts with treatment planning for neuroendocrine tumors of the GI tract. It is followed by a list of treatment options based on the site of the neuroendocrine tumor in the GI tract. This includes options for tumors in the small intestine, which include the jejunum, ileum, and duodenum. Treatment options are also listed for tumors in the colon, appendix, rectum, and stomach.

This information is taken from the treatment guidelines written by NCCN experts of neuroendocrine tumors. These treatment guidelines list options for people with neuroendocrine tumors in general. Thus, your doctors may suggest other treatment for you based on your health and personal wishes.

Treatment planning

A team of experts who treat neuroendocrine tumors of the GI tract should be managing your care. The team will create a plan designed for your needs. After your doctor has confirmed that you have a neuroendocrine tumor, he or she will talk with you about the diagnosis and may order more tests.

Your doctors will take a medical history, including your lifetime medical conditions; do an exam of your body; order imaging tests; and order blood tests to check the fluids in the stomach or your level of vitamin B. [See Guide 6](#) on the next page. Most people will have a CT or MRI of the abdomen and pelvis. Other tests may include other types of imaging tests or scopes to view parts of the GI tract. Ask your doctor about the tests that will be part of your plan.



Helpful tips for reading the treatment guides in the next 4 chapters ➔

- ✓ The treatment guides (the colored charts) are numbered and list possible test or treatment options.
- ✓ It is helpful to read the guides from left to right, using the arrows to follow a path. The titles of the guides are important.
- ✓ The symbol \pm means “with or without.” This is used to show when a test or treatment is given with or without another test or treatment.
- ✓ Acronyms (a group of letters using the first letters of words or phrases) found in the treatment guides are defined on page 93.

Guide 6. Tests for neuroendocrine tumors of the GI tract

Needed for most patients	
<ul style="list-style-type: none"> • CT or MRI of abdomen and pelvis 	
Needed for some patients	
<ul style="list-style-type: none"> • Somatostatin receptor-based imaging 	<ul style="list-style-type: none"> • EGD
<ul style="list-style-type: none"> • Colonoscopy 	<ul style="list-style-type: none"> • EUS
<ul style="list-style-type: none"> • Imaging of small intestine 	<ul style="list-style-type: none"> • Stomach biopsy
<ul style="list-style-type: none"> • MRI of rectum 	<ul style="list-style-type: none"> • Serum gastrin level
<ul style="list-style-type: none"> • Endorectal ultrasound 	<ul style="list-style-type: none"> • Consider gastric pH
<ul style="list-style-type: none"> • CT of chest 	<ul style="list-style-type: none"> • Vitamin B level
<ul style="list-style-type: none"> • Biochemical testing 	

Test results

Once your doctors review your test results, they can talk to you about your options. The options are based on the location of the neuroendocrine tumor and if it spread to areas near the tumor, like lymph nodes, or farther from the tumor to the liver. NCCN experts use the following terms to describe the location of disease:

- **Locoregional disease** is the spread of cancer to places near the first tumor, in a limited area. The disease has not spread far in the body.
- **Metastatic disease** is the spread of cancer from the first tumor to a new site in the body.

Talking with your doctor about treatment and its side effects is important. It is helpful to ask questions and understand what comes next in your treatment plan.

Jejunum, ileum, and colon

Guide 7. Treatment for neuroendocrine tumors of the jejunum, ileum, and colon

Disease status		Primary treatment		Next steps of care
Locoregional disease	→	• Bowel resection with removal of regional lymph nodes	→	• See surveillance in Guide 12
Metastatic disease	→	• See Guide 14		

Guide 7 lists the treatment options for neuroendocrine tumors found in the jejunum, ileum, and colon. Surgery to remove the tumor is usually recommended. Your doctor may remove some lymph nodes and check the blood vessels in the area for cancer. Sometimes surgery may not be an option for disease that has spread to other parts of the body. If the disease has spread, you may be offered a drug treatment instead of surgery.

You will start surveillance soon after surgery. Surveillance consists of testing on a regular basis. Your doctors will watch for tumor growth so that treatment can be started later, if needed, instead of right away. During surveillance, your doctor will plan a schedule of tests for you. See Guide 12 on page 47 for a list of tests.



Nearly all of my treatments have had some side effects, some harder to deal with than others. Patients need to be aware of the risks and the benefits before choosing a treatment.

-Gary

Survivor, neuroendocrine tumor of the ileum

Duodenum

Guide 8. Treatment for neuroendocrine tumors of the duodenum

Disease status	Primary treatment	Next steps of care
Locoregional disease	• Endoscopic resection	• Noninvasive tumors - routine endoscopic surveillance
	• Local excision (transduodenal) ± some lymph nodes	• Invasive tumors - see <i>Surveillance</i> , Guide 12
	• Whipple procedure	• See <i>Surveillance</i> , Guide 12
Metastatic disease	• See Guide 14	

Guide 8 has treatment options for neuroendocrine tumors in the duodenum. If you have locoregional disease, your doctor will consider the type of surgery that is best for you. After surgery, you will begin surveillance to check for the return of cancer. See Guide 12 on page 47 for a list of tests.

For someone with more invasive, advanced disease the tests may occur more often. Regardless of disease status, your doctors will watch you closely for any changes. It is helpful to ask your doctors questions about surveillance tests and the results.

Appendix

Guide 9. Treatment for neuroendocrine tumors of the appendix

Disease status		Primary treatment		Next steps of care
≤2 cm and confined to the appendix	→	<ul style="list-style-type: none"> Appendectomy 	→	<ul style="list-style-type: none"> Surveillance as recommended by your doctor
>2 cm or incomplete resection (lymph nodes, margins)	→	<ul style="list-style-type: none"> Surgery to explore the area again Right hemicolectomy 	→	<ul style="list-style-type: none"> See <i>Surveillance</i>, Guide 12
Metastatic disease	→	See Guide 14		

Guide 9 lists treatment options for neuroendocrine tumors in the appendix. If you have a tumor that is 2 cm or smaller, your doctor will remove the appendix. If the tumor is larger than 2 cm, your doctor may check the area for the extent of disease. He or she may remove the appendix and right side of the colon. This side of the colon is closer to the appendix. For metastatic disease, your doctor will consider a drug treatment (see Guide 14 on page 49).

After surgery, you will begin surveillance to check for the return of cancer. See Guide 12 on page 47 for a list of tests. It is helpful to ask your doctors questions about the tests you may have.

Rectum

Guide 10. Treatment for neuroendocrine tumors of the rectum

Disease status		Next steps of care		Surveillance or other
Small (<1 cm) tumors completely removed	• Negative margins	→	• No other follow-up needed	
	• Unknown margins	→	• Low grade (G1): ◦ Endoscope at 6–12 months to assess for disease	• Negative margin ◦ See <i>Surveillance</i> , Guide 12
			• Intermediate grade (G2)	• Positive margin or intermediate grade ◦ Follow the path below for all other tumors
				• Follow the path below for all other tumors
All other tumors in the rectum	• T1	→	• Transanal resection or endoscopic excision, if possible	• <1 cm: No follow-up required • 1–≤2 cm: Endoscopy with MRI of rectum or endorectal ultrasound at 6 and 12 months, then as needed
	• T2–T4	→	• Options for ≤2 cm tumor: ◦ Transanal resection or endoscopic excision, if possible	• See <i>Surveillance</i> , Guide 12
			• Options for >2 cm tumor: ◦ Low anterior resection ◦ Abdominoperineal resection	• See Guide 14
			• Metastatic disease	

Guide 10 lists treatment options for tumors in the rectum. The options are based on the size of the tumor. Smaller tumors are removed by surgery and the next steps of care depend on whether cancer remains in the margin. If cancer remains in the margin, you may have further treatment.

If the tumor is 2 cm or smaller, you may have surgery to remove the tumor through the anus (transanal resection). If the tumor is larger than 2 cm, you may

have surgery to remove the upper part of the rectum (low anterior resection) or the sigmoid colon, rectum, and anus (abdominoperineal resection).

You will start surveillance soon after surgery. Surveillance consists of testing on a regular basis. Your doctors will watch for tumor growth so that treatment can be started later, if needed, instead of right away. During surveillance, your doctor will plan a testing schedule just for you. See Guide 12 on page 47 for a list of tests.

Guide 11. Treatment for neuroendocrine tumors of the stomach

Disease status		Primary treatment		Next steps of care
Hypergastrinemic/ Type 1 (chronic inflammation of the stomach, or high gastric pH)	→	<ul style="list-style-type: none"> Endoscopic resection of noticeable tumors 	→	<ul style="list-style-type: none"> Yearly endoscopic surveillance and endoscopic resection of prominent tumors, and Consider antrectomy if tumors are increasing in size or number
		<ul style="list-style-type: none"> Metastatic disease 	→	<ul style="list-style-type: none"> See Guide 14
Hypergastrinemic/ Type 2 (Zollinger-Ellison; no chronic inflammation of the stomach, low gastric pH)	→	<ul style="list-style-type: none"> Resect primary gastrinoma 	→	<ul style="list-style-type: none"> See Guide 29
		<ul style="list-style-type: none"> Primary gastrinoma not resected 	→	<ul style="list-style-type: none"> Consider endoscopic surveillance and endoscopic resection of tumors and/or Consider octreotide or lanreotide and Manage gastric hypersecretion with high-dose PPIs (proton pump inhibitors)
		<ul style="list-style-type: none"> Metastatic disease 	→	<ul style="list-style-type: none"> See Guide 14
Normal gastrin/Type 3	→	<ul style="list-style-type: none"> Radical resection with lymph node removal or Consider endoscopic or surgical wedge resection (if no disease is seen in the lymph nodes on EUS) 	→	<ul style="list-style-type: none"> See <i>Surveillance</i>, Guide 12
		<ul style="list-style-type: none"> Metastatic disease 	→	<ul style="list-style-type: none"> See Guide 14

Stomach (gastric)

Guide 11 lists treatment options for neuroendocrine tumors in the stomach. If your doctors find you have higher-than-normal amounts of the hormone gastrin in your stomach (hypergastrinemic) you may have a stomach (gastric) neuroendocrine tumor. Doctors assign the tumor to be Type 1, Type 2, or Type 3. Types 1 and 2 are associated with hypergastrinemia. Type 3 has normal gastrin levels. Other factors for Type 1 and 2 are a high or low level of gastric pH. Gastric pH can cause your stomach acid to be off balance. Stomach acid is responsible for food breakdown (digestion).

Treatment options depend on the gastrin levels and the extent of disease in this area. Your doctor will consider different types of surgery as listed in Guide 11. More details on the types of surgeries for neuroendocrine tumors of the GI tract are defined on pages 27 and 28. If you have disease that has spread (metastatic disease), see Guide 14 on page 49.

After primary treatment, your doctor will base the surveillance tests or further treatment on the results of primary treatment. More surgery may be an option. If surgery is not an option, you may take octreotide or lanreotide to help with symptoms caused by the tumor. High doses of a medication known as a PPI may be given to reduce your stomach acid.

Surveillance

Guide 12. Surveillance for neuroendocrine tumors of the GI tract

Tests

- Medical history and physical exam
- Consider biochemical testing
- CT or MRI of abdomen and pelvis as needed
- CT of chest as needed

See Guide 12 for surveillance after cancer treatment has ended. Surveillance tests are done at certain times to check if the cancer has returned. These tests can help find cancer early and your doctor can start treatment if needed.

Surveillance tests may include a medical history, physical exam, and imaging tests for the first 3 to 12 months after surgery. From 1 year until 10 years after surgery, you may have these tests every 1 to 2 years. If the first imaging tests are negative for disease, the scans may occur less often. Ask your doctor what tests you may have and how often you will see him or her for a doctor's appointment.

Locally advanced or metastatic disease

Guide 13. Tests for locally advanced or metastatic disease of the GI tract

Tests
<ul style="list-style-type: none"> • CT or MRI of abdomen and pelvis
<ul style="list-style-type: none"> • CT of chest as needed
<ul style="list-style-type: none"> • Somatostatin receptor-based imaging <ul style="list-style-type: none"> ◦ Ga-dotatate PET/CT scan preferred or somatostatin receptor scintigraphy
<ul style="list-style-type: none"> • Biochemical testing as needed

Guide 13 and Guide 14 (see Guide 14 on the next page) share the tests and treatments for locally advanced or metastatic disease. This stage of disease has spread to areas near the first tumor or farther in the body. Your doctor will start with measuring the extent of disease on imaging tests. Next, he or she will consider checking the level of biochemicals in your blood. See page 18 for more on biochemical testing.

Treatment options are based on the size of disease, and whether or not surgery is possible. Your doctor will also assess if you have symptoms caused by the tumor. If you have no symptoms or a low amount of disease, your doctor may observe the tumor for growth. He or she may consider octreotide or lanreotide to control symptoms. These drugs can be given with other treatment.

Surveillance will follow primary treatment and include imaging tests every 3 to 12 months. It is helpful to ask your doctor which tests are part of your plan.

Guide 15 (on the next page) lists the treatment options for disease that gets worse (progresses). This is when the cancer continues to grow despite treatment. You may continue taking octreotide or lanreotide if you have a functional tumor that is causing symptoms. These drugs may also be used with the options listed in Guide 15. Your doctor will consider your options and decide if you need local treatment with therapies directed at the liver (hepatic-directed therapies) or if you need systemic treatment. Systemic treatment delivers treatment throughout the body. This includes drugs such as everolimus, interferon alfa-2b, or PRRT with ¹⁷⁷Lu-dotatate. Chemotherapy agents may be recommended if the other treatments do not work. These include 5-fluorouracil (5-FU), capecitabine, dacarbazine, oxaliplatin, streptozocin, and temozolomide. More research is needed to learn how well chemotherapy works in treating carcinoid tumors.

Sometimes surgery is not possible, or you need relief from symptoms the cancer may be causing. Thus, treatments like embolization, cytoreductive surgery, and ablation may be used. These options are directed at cancer that has spread to the liver. (See page 31 for more on locoregional therapies). Embolization may reduce the blood flow to the tumor. Cytoreductive surgery aims to remove as much tumor as possible. Ablation uses things like heat or radiofrequency waves to treat the cancer. Your doctor may also suggest you join a clinical trial to treat disease that has progressed.

Guide 14. Treatment for locally advanced or metastatic disease of the GI tract

Disease status		Treatment	Next steps of care
Complete surgery is possible	→	• Resect primary tumor and metastases	→ • Refer to the guides based on tumor location in GI tract
Low amount of tumors, no symptoms	→	• Observe with tumor marker tests and CT or MRI of abdomen and pelvis every 3–12 months, and CT of chest as needed or • Octreotide or lanreotide	→ • Surveillance with CT or MRI of abdomen and pelvis every 3–12 months, and CT of chest as needed
Local symptoms caused by the primary tumor	→	• Resect primary tumor	
Major amount of tumors	→	• Octreotide or lanreotide	

Guide 15. Treatment for disease progression

If disease progression, consider the following options:

- Everolimus
- PRRT with ¹⁷⁷Lu-dotatate, if somatostatin receptor imaging is positive
- Hepatic-directed therapies for disease in the liver:
 - Arterial embolization
 - Chemoembolization
 - Radioembolization
 - Cytoreductive surgery/ablation
- Interferon alfa-2b
- Chemotherapy

5

Treatment guide:

Neuroendocrine tumors of the thymus, lungs, and bronchi (carcinoid tumors)

52 Neuroendocrine tumors of the thymus

54 Neuroendocrine tumors of the bronchopulmonary

54 Surveillance

56 Locally advanced or metastatic disease

58 Carcinoid syndrome

60 Review



Part 5 starts with treatment planning for neuroendocrine tumors of the thymus, lungs, and airways that lead to the lungs (bronchi). This is followed by a list of treatment options based on where the neuroendocrine tumor is in the chest. The first set of options are for tumors in the thymus. The next set of options is listed for the lungs and bronchi. This is referred to as “bronchopulmonary” in this chapter. Carcinoid syndrome is also discussed.

This information is taken from the treatment guidelines written by NCCN experts of neuroendocrine tumors. These treatment guidelines list options for people with neuroendocrine tumors in general. Thus, your doctors may suggest other treatment for you based on your health and personal wishes.

Your options:

- ✓ Ask questions about your planned tests and the results.
- ✓ Learn more about the treatment options your team recommends.
- ✓ Find out what side effects are possible during and after treatment.

Neuroendocrine tumors of the thymus

Guide 16. Tests for neuroendocrine tumors of the thymus

Needed for most patients

- CT of chest and mediastinum
- CT or MRI of abdomen

Needed for some patients

- Somatostatin receptor-based imaging
- Biochemical testing for Cushing’s syndrome
- Other biochemical tests

Guide 16 shares what tests are needed prior to starting treatment. A team of experts who have experience with a neuroendocrine tumor should assess the extent of disease and make a treatment plan. Your doctors will order imaging tests of the chest, the area in the chest between the lungs (mediastinum), and the abdomen. You may also have other imaging tests or biochemical tests. Your doctor may check for Cushing’s syndrome since it is associated with neuroendocrine tumors of the thymus.

Guide 17. Treatment for neuroendocrine tumors of the thymus

Disease status		Surgery or grade	Treatment or surveillance
Localized disease (Stage I-II)		→ • Surgery	→ • See <i>Surveillance</i> , Guide 20
Locoregional disease (Stage IIIA/IIIB)	• Surgery is an option	→ • Surgery	→ • See <i>Surveillance</i> , Guide 20
		→ • Surgery can't be completed: ◦ Low grade	→ • Consider observation • Consider radiation therapy ± systemic therapy
	• Surgery is not an option	→ • Surgery can't be completed: ◦ Intermediate grade	→ • Consider observation • Consider radiation therapy ± systemic therapy
		→ • Low grade	→ • Consider observation • Consider systemic therapy • Consider radiation therapy ± systemic therapy
	→ • Intermediate grade	→ • Consider radiation therapy ± systemic therapy • Consider systemic therapy	
Metastatic disease (Stage IV)		→ • See Guides 22 and 23	

Guide 17 lists the treatment options for neuroendocrine tumors in the thymus. Treatment options will depend on how quickly the cancer may grow and spread (grade) and the extent of disease (stage). Surgery may be an option for stages I to III. If surgery is not the best first option, your doctor may consider observation, radiation therapy, or systemic therapy. See Guide 5 on page 33 for a full list of systemic therapies. Ask your doctor which systemic therapies may be an option for a neuroendocrine tumor in the thymus.

If the cancer spreads in the area or to distant sites, surgery may not be possible. If you have metastatic disease, see Guides 22 and 23 for treatment options. Your options will depend on the extent of disease, and whether you have symptoms or not. Surveillance will start after treatment is complete.

Neuroendocrine tumors of the bronchopulmonary

Guide 18. Tests for neuroendocrine tumors of the bronchopulmonary

Needed for most patients

- CT of chest and mediastinum
- CT or MRI of abdomen

Needed for some patients

- Somatostatin receptor-based imaging
- Bronchoscopy
- Biochemical testing for Cushing's syndrome
- Other biochemical tests

Guide 18 lists tests your doctor may consider before you start treatment. A team of experts who has experience in treating neuroendocrine tumors in the lungs or bronchi should assess the extent of disease and make a treatment plan. Your doctors will order imaging tests of the chest, the area between the lungs (mediastinum), and the abdomen. You may also have other imaging tests or biochemical tests. Your doctor may also do a bronchoscopy to view and possibly biopsy the abnormal area. He or she may test for Cushing's syndrome since it is associated with neuroendocrine tumors of the bronchopulmonary. MEN1 is also associated with these tumors.

Guide 19 (on the next page) starts with the stage of disease. Knowing the stage will allow your treatment team to assess if surgery is an option. This depends on the extent of cancer. If you have surgery, you will start surveillance soon after. If you have disease that is intermediate grade, not low but not high grade, then your doctor may consider radiation therapy with or without systemic therapy. See Guide 5 on page 33 for a full list of systemic therapies. Ask your doctor which systemic therapies may be an option for a neuroendocrine tumor in the lungs or bronchi. Other treatments are available if surgery is not the best first option, or if you have metastatic disease. See Guides 22 and 23 for the treatment of metastatic disease.

Surveillance

Guide 20. Surveillance for neuroendocrine tumors of the thymus and bronchopulmonary

Tests

- Medical history and physical exam
- Consider biochemical testing
- CT or MRI of abdomen and pelvis as needed
- CT of chest

Guide 20 also shares surveillance tests after cancer treatment has ended. You should have tests to check if the cancer has returned. Surveillance tests may include a medical history and physical exam, biochemical testing, and imaging of your chest, abdomen, and pelvis.

Guide 19. Treatment for neuroendocrine tumors of the bronchopulmonary

Disease status		Surgery and/or grade		Treatment or surveillance
Localized disease (Stage I-II)	→	<ul style="list-style-type: none"> Lobectomy or other surgery (based on tumor location) + mediastinal lymph node removal or sampling 	→	<ul style="list-style-type: none"> See <i>Surveillance</i>, Guide 20
Locoregional disease (Stage IIIA) • Surgery is an option	↷	<ul style="list-style-type: none"> Low grade - lobectomy or other surgery (based on tumor location) + mediastinal lymph node removal or sampling 	→	<ul style="list-style-type: none"> See <i>Surveillance</i>, Guide 20
		<ul style="list-style-type: none"> Intermediate grade - lobectomy or other surgery (based on tumor location) + mediastinal lymph node removal or sampling 	→	<ul style="list-style-type: none"> Consider observation Consider systemic therapy ± radiation therapy
Locoregional disease (Stage IIIA/B) • Surgery is not an option	↷	<ul style="list-style-type: none"> Low grade 	→	<ul style="list-style-type: none"> Consider observation Consider systemic therapy Consider radiation therapy ± systemic therapy
		<ul style="list-style-type: none"> Intermediate grade 	→	<ul style="list-style-type: none"> Consider radiation therapy ± systemic therapy Consider systemic therapy
Metastatic disease (Stage IV)		→		<ul style="list-style-type: none"> See Guides 22 and 23

Certain tests follow a schedule while others are based on any signs or symptoms you have during surveillance. The tests may be done every 3 to 12 months after surgery. From 1 year until 10 years after surgery, the tests will be done every 1 to 2 years unless needed more often.

Locally advanced or metastatic disease

Guide 21. Tests for locally advanced or metastatic disease of the thymus or bronchopulmonary

Tests
<ul style="list-style-type: none"> • CT of chest
<ul style="list-style-type: none"> • CT or MRI of abdomen and pelvis
<ul style="list-style-type: none"> • Consider somatostatin receptor-based imaging <ul style="list-style-type: none"> ◦ Ga-dotatate PET/CT scan preferred or somatostatin receptor scintigraphy
<ul style="list-style-type: none"> • Consider FDG-PET/CT for atypical histology
<ul style="list-style-type: none"> • Consider biochemical testing for Cushing's syndrome (if not done before)

Guide 21 shares the tests for locally advanced or metastatic disease. In this stage, disease has spread to areas near the first tumor or farther in the body. Your doctor will start with measuring the extent of disease with imaging tests. Next, he or she will consider checking the level of biochemicals in your blood. See page 18 for more information on biochemical testing.

Guide 22 (on the next page) has treatment options for locally advanced or metastatic disease. These options are based on the extent of disease and whether or not surgery is possible. Your doctor will also assess if you have symptoms caused by the tumor. If you have no symptoms or a low amount of disease, your doctor may observe the tumor for growth or offer octreotide or lanreotide to control symptoms. These drugs are given if the tumor is

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somatostatin receptor positive on imaging. These drugs can also be given along with other treatment.

If the cancer continues to grow during or after one treatment, you may try another drug. This includes treatment with everolimus. Your doctor may also consider PRRT with ¹⁷⁷Lu-dotatate if somatostatin receptor-positive imaging and disease progresses on octreotide or lanreotide.

Your doctor can guide you on what step is next in line. Joining a clinical trial is also an option and is strongly encouraged. Surveillance will follow treatment and may include imaging tests every 3 to 6 months. It is helpful to ask your doctor which options are best for you. Find out the stage of cancer you have. It is helpful to learn what you can expect during and after treatment is complete.

Guide 23 (on the next page) lists treatment options for locally advanced or metastatic disease. There may be many nodules in the lungs. Imaging may show DIPNECH. This includes abnormal markings in the lungs that may be seen with neuroendocrine tumors in the lungs.

The list of treatment options depends on the stage of disease and how quickly the cancer may grow. With intermediate-grade disease, options include observation or systemic therapy. In certain cases, primary chemotherapy may include cisplatin/etoposide, carboplatin/etoposide, or temozolomide. If the cancer gets worse (progresses) during or after taking systemic therapy, your doctor may offer other treatment. PRRT with ¹⁷⁷Lu-dotatate may also be an option for somatostatin receptor-positive imaging, and if you progress on octreotide or lanreotide.

If there are multiple lung nodules, abnormal areas called tumorlets may receive DIPNECH treatment, which may include observation with or without octreotide or lanreotide. These drugs may be given if you have somatostatin receptor-positive imaging and/or symptoms caused by hormones.

Guide 22. Treatment for locally advanced or metastatic disease of the thymus or bronchopulmonary

Low or major amounts of tumors, or signs of disease progression

Disease status		Treatment		Next steps of care
Low amounts of tumors and low grade, no symptoms	→	<ul style="list-style-type: none"> Observe Octreotide or lanreotide 	→	<ul style="list-style-type: none"> Surveillance with CT of chest and CT or MRI of abdomen and pelvis every 3–6 months
Major amounts of tumors and low grade or Signs of disease progression	→	<ul style="list-style-type: none"> Consider observation if no symptoms Consider octreotide or lanreotide Consider everolimus Consider PRRT with ¹⁷⁷Lu-dotatate 	→	<ul style="list-style-type: none"> Consider changing therapy if progression on first-line therapy

Guide 23. Treatment for locally advanced or metastatic disease of the thymus or bronchopulmonary

Intermediate grade or other disease

Disease status		Treatment		Next steps of care
Intermediate grade	→	<ul style="list-style-type: none"> Consider observation for certain patients Consider octreotide or lanreotide Consider everolimus Consider PRRT with ¹⁷⁷Lu-dotatate Consider chemotherapy 	→	<ul style="list-style-type: none"> Consider changing therapy if progression on first-line therapy
Multiple lung nodules or tumorlets and evidence of DIPNECH (diffuse idiopathic pulmonary neuroendocrine cell hyperplasia)	→	<ul style="list-style-type: none"> Observe ± octreotide or lanreotide 	→	<ul style="list-style-type: none"> Surveillance with CT of chest every 12–24 months or for new symptoms

Surveillance will follow any treatment you have and may include imaging tests of the chest every 12 to 24 months.

Carcinoid syndrome

Carcinoid tumors of the GI tract, lungs, and bronchi may cause carcinoid syndrome. This syndrome usually occurs when the cancer has spread in the body.

Guide 24. Tests for carcinoid syndrome

Tests

- Biochemical testing with 24-hour urine or plasma 5-HIAA
- Echocardiogram
- Imaging tests to assess disease progression

Your doctor will order certain tests to assess your health and rule out other conditions that can also cause flushing, diarrhea, or heart disease. The plan is to treat the carcinoid tumor that is causing the syndrome. He or she may offer treatment to provide relief of your symptoms.

Guide 24 includes tests for carcinoid syndrome. Your doctor may order urine and blood tests to check for chemicals released by the carcinoid tumor. An echocardiogram is an ultrasound of the heart. It will check if your heart is working as it should.

You may also have imaging tests to assess if the cancer has spread. If so, it may be causing the carcinoid syndrome.

Guide 25 (on the next page) lists the treatment options for carcinoid syndrome that is well controlled or poorly controlled. Your doctor may give you octreotide or lanreotide to start. These drugs attach to somatostatin receptors on neuroendocrine cells and reduce the release of the chemicals causing the carcinoid syndrome. Other systemic therapies may be used and are based on the site of the primary tumor.

“Well controlled” means the symptoms are under control and further treatment is not needed at this time. In this case, surveillance tests are done to check the heart, along with imaging tests to check for cancer growth.

“Poorly controlled” means that many symptoms that continue may require further treatment. This treatment may include direct treatment to the liver or systemic therapy (see Guide 5 on page 33). Ask your doctor about your treatment options. After treatment, surveillance may include an echocardiogram and imaging tests. If the disease progresses despite treatment, refer back to Guides 22 and 23 in this chapter. You may also continue taking octreotide or lanreotide if you have a functional tumor that is causing symptoms.

Guide 25. Treatment for carcinoid syndrome

Treatment	Syndrome	Next steps of care
	<p>→</p> <ul style="list-style-type: none"> • Carcinoid syndrome well controlled <p>→</p>	<ul style="list-style-type: none"> • Echocardiogram every 2–3 years or as needed • CT or MRI of abdomen and pelvis every 3–12 months and CT of chest as needed
Octreotide or lanreotide	<p>→</p> <ul style="list-style-type: none"> • Carcinoid syndrome poorly controlled <p>→</p>	<p>For ongoing symptoms (ie, flushing, diarrhea) consider more treatment for disease control:</p> <ul style="list-style-type: none"> • Consider hepatic arterial embolization ± cytoreductive surgery for disease mainly in the liver • Consider telotristat ethyl • Consider other systemic therapy <p>→</p> <ul style="list-style-type: none"> • Echocardiogram every 2–3 years or as needed • CT or MRI of abdomen and pelvis every 3–12 months and CT of chest as needed



What to know about carcinoid syndrome

- ✓ Carcinoid syndrome happens when carcinoid tumors release serotonin and other chemicals into your blood.
- ✓ This syndrome cause symptoms like your face turning red (flushing) and diarrhea. Serious symptoms may include heart and breathing problems.
- ✓ Over half of the patients with carcinoid syndrome may develop heart disease.

Review

- ▶ Treatment planning is an important first step of care and usually includes imaging tests and blood tests.
- ▶ Certain tests follow a schedule while others are based on any signs or symptoms you have during surveillance.
- ▶ Treatment options are based on the extent of disease and whether or not surgery is possible.
- ▶ Observation may be an option if there is little disease and no symptoms.
- ▶ Carcinoid tumors of the GI tract, lungs, and bronchi may cause carcinoid syndrome. This syndrome usually occurs when the cancer has spread in the body.



Friends and family are essential, but many fellow NET patients have decades of experience gracefully navigating the sometimes calm and sometimes stormy waters of this disease.

– Stacie

Survivor, neuroendocrine tumor of the pancreas

6

Treatment guide: Neuroendocrine tumors of the pancreas

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tumors

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Part 6 starts with treatment planning for neuroendocrine tumors of the pancreas. This is followed by a list of treatment options based on the site of the neuroendocrine tumor in the pancreas. The tumors in the pancreas have different names in this chapter.

This information is taken from the treatment guidelines written by NCCN experts of neuroendocrine tumors. These treatment guidelines list options for people with neuroendocrine tumors in general. Thus, your doctors may suggest other treatment for you based on your health and personal wishes.

Nonfunctional pancreatic tumors

Guide 26. Tests for nonfunctioning pancreatic tumors

Needed for most patients

- CT or MRI of abdomen and pelvis

Needed for some patients

- Somatostatin receptor-based imaging
- CT of chest
- EUS
- Biochemical testing
- Consider testing for inherited genetic syndromes



Neuroendocrine tumors of the pancreas

Neuroendocrine tumors of the pancreas start in the islet cells. Islet cells are the cells that make hormones in the pancreas. The different types of neuroendocrine tumors in the pancreas are related to the name of the hormone made by the cells. The tumors are grouped as either functional or nonfunctional. **Functional tumors** release large amounts of hormones that may cause symptoms. **Nonfunctional tumors** do not release the large amounts of hormone and do not cause symptoms.

The types of neuroendocrine tumors of the pancreas in this chapter are described below:

- **Nonfunctional pancreatic neuroendocrine tumors** do not release large amounts of hormones
- **Gastrinomas** start in cells that make gastrin
- **Insulinomas** start in cells that make insulin
- **Glucagonomas** start in cells that make glucagon
- **VIPomas** start in cells that make vasoactive intestinal peptide

Guide 27. Treatment for nonfunctioning pancreatic tumors

Disease status		Tumor	Primary treatment	Next steps
Locoregional disease	→	Small (≤2 cm)	→	→
			<ul style="list-style-type: none"> • Observation • Surgery ± regional lymph node removal • Distal pancreatectomy ± regional lymph node removal/splenectomy • Whipple procedure ± regional lymph node removal 	
	→	Larger (>2 cm) invasive or lymph node-positive tumors	→	
			<ul style="list-style-type: none"> • Head: Whipple procedure + regional lymph node removal • Distal: Distal pancreatectomy + splenectomy + regional lymph node removal 	
Metastatic disease		→		<ul style="list-style-type: none"> • See Guide 38

Guide 26 lists tests for nonfunctional pancreatic tumors that may not cause symptoms. Your doctors will order imaging tests of the abdomen and pelvis. Sometimes the tumor can be small and not easily seen on CT or MRI. If this is the case, you may have somatostatin receptor-based imaging or EUS to assess the tumor further. If you are showing symptoms of releasing excess hormones, then biochemical tests may be considered. See Guide 4 on page 19.

Guide 27 has treatment options for locoregional or metastatic disease. If the nonfunctional tumor is 2 cm or smaller, your doctor may consider observation and different forms of surgery. If the tumor is larger than 2 cm and has spread to nearby lymph nodes, other treatment may be considered. This treatment includes surgery, and the method of surgery is based on where the tumor is growing at the head, the body, or tail of the pancreas. For example, your doctor may remove the body and tail of the pancreas if the tumor is in the distal pancreas.

No matter the size of the tumor, lymph nodes nearby the tumor may be removed if cancer is found or there is risk for metastases. If you have metastatic disease, you would refer to Guide 38 for treatment options. These options include relief of any symptoms you have, or recommended systemic therapy.

Gastrinoma

Guide 28. Tests for gastrinoma

Needed for most patients

- Serum gastrin level
- CT or MRI of abdomen

Needed for some patients

- Somatostatin receptor-based imaging
- CT of chest
- EUS
- Other biochemical testing
- Consider testing for inherited genetic syndromes

Guide 28 lists tests for assessing a gastrinoma. A person may complain of diarrhea, stomach upset, and have a sore (ulcer) on the lining of the stomach or first part of the small intestine (duodenal). If the doctor suspects a gastrinoma, he or she will order a CT or MRI of the abdomen to check the area. Other imaging tests may also be done, including an EUS. Your doctor may check the levels of gastrin. This hormone is released with this tumor type. PPIs can cause the gastrin level to be higher.

Thus, your doctor may ask you to stop taking a PPI more than a week before checking the serum gastrin level. Your doctor can explain what tests you may need to plan treatment for a gastrinoma.

Guide 29 (on the next page) has treatment options for gastrinomas. Your doctor will base the treatment options on where the tumor is located. If it is not seen on imaging (occult), then observation or surgery to explore the area for tumors may be helpful. If the tumor is in the duodenum (small intestine), or the head or distal area of the pancreas, then treatment may be surgery. The method will depend on the location of the gastrinoma. If lymph nodes have cancer in them, they may be removed during the surgery. If there is metastatic disease, your doctor will consider systemic treatment. Gastric hypersecretion can be managed with high-dose PPIs. Octreotide or lanreotide treatment may also be considered. See Guide 38 for treatment options.

After treatment, surveillance will begin. Testing will be done on a regular basis to check for cancer growth or return. See Guide 36 on page 72 for a list of surveillance tests. Ask your doctor about your next steps of care.

Guide 29. Treatment for gastrinoma

Disease status	Tumor location	Primary treatment	Next steps
Locoregional disease • Manage gastric hypersecretion with high-dose PPIs • Consider octreotide or lanreotide	• Occult (not seen on imaging)	<ul style="list-style-type: none"> • Observation • Surgery to explore the area including duodenotomy and ultrasound during surgery; local resection of tumor + periduodenal lymph node removal 	<ul style="list-style-type: none"> • See <i>Surveillance</i>, Guide 36
	• Duodenum	<ul style="list-style-type: none"> • Duodenotomy and ultrasound during surgery; local resection of tumor(s) + periduodenal lymph node removal 	
	• Head	<ul style="list-style-type: none"> • Exophytic or peripheral tumors: removal of the tumor + periduodenal lymph node removal • Deeper or invasive tumors: Whipple procedure 	
	• Distal	<ul style="list-style-type: none"> • Distal pancreatectomy + splenectomy + regional lymph node removal 	
Metastatic disease		<ul style="list-style-type: none"> • See Guide 38 	

Insulinoma

Guide 30. Tests for insulinoma

Needed for most patients
• CT or MRI of abdomen
• Serum insulin, pro-insulin, and C-peptide during low blood sugar (hypoglycemia)
Needed for some patients
• EUS somatostatin receptor-based imaging
• Other biochemical testing
• Somatostatin receptor-based imaging
• CT of chest
• Consider testing for inherited genetic syndromes

Guide 30 lists tests for insulinoma. Your doctors will order imaging tests of the abdomen. He or she will check your insulin and sugar levels, since low blood sugar (hypoglycemia) may occur with these tumors. An EUS or other imaging tests may be done to assess the tumor further. Somatostatin receptor-based imaging may be done if your doctor plans on giving you octreotide or lanreotide.

Guide 31. Treatment for insulinoma

Disease status		Primary treatment		Next steps	
Locoregional disease • Stabilize glucose levels with diet and/or diazoxide	→	• Exophytic or peripheral tumors by imaging tests	→	• Head or distal: removal of tumor (enucleation), consider laparoscopic resection	• See <i>Surveillance</i> , Guide 36
	→	• Deeper or invasive tumors near the main pancreatic duct	→	• Head: Whipple procedure • Distal: Distal pancreatectomy, consider laparoscopic resection	
Metastatic disease	→			• See Guide 38	

Guide 31 shares treatment for insulinomas. Your doctor will assess the extent of disease. If you have disease that is near the site of the primary tumor or in lymph nodes close to where the cancer started (locoregional disease), you may have surgery. Before surgery for locoregional disease, stability of glucose levels with diet and/or diazoxide is recommended. Surveillance will begin soon after treatment is complete. If the disease is metastatic, you will see Guide 38.

Glucagonoma

Guide 32. Tests for glucagonoma

Needed for most patients

- Glucagon and blood sugar (glucose)
- CT or MRI of abdomen

Needed for some patients

- Somatostatin receptor-based imaging
- CT of chest
- EUS
- Other biochemical testing
- Consider testing for inherited genetic syndromes

Guide 32 lists tests that may be used for glucagonomas, usually found in the tail of the pancreas. These tumors may be seen with diabetes, unexplained weight loss, and/or a blistering skin rash. Blood tests will check for the hormone glucagon, which may be higher than normal. Your blood sugar level may be higher with this tumor type, so blood glucose will be measured. A CT or MRI of the abdomen can check for larger tumors or metastatic disease. Other imaging tests may be done if needed. Ask your doctor about the tests you will have for a glucagonoma.

Guide 33. Treatment for glucagonoma

Disease status		Primary treatment		Next steps
Locoregional disease	→	• Octreotide or lanreotide	→	• See <i>Surveillance</i> , Guide 36
		• Treat high blood sugar (hyperglycemia) and diabetes as needed	→	
Metastatic disease	→			• See Guide 38

Guide 33 shares treatment options for a glucagonoma. Locoregional disease may be treated with octreotide or lanreotide before surgery. Your doctor can also manage high blood sugar (hyperglycemia) or diabetes with medicine. Once surgery is complete, surveillance will start to check for the return of cancer. If you have metastatic disease, treatment for symptoms and systemic therapy may be offered in Guide 38 on page 73.

VIPoma

Guide 34. Tests for VIPoma

Needed for most patients

- Electrolytes
- VIP (vasoactive intestinal polypeptide) level
- CT or MRI of abdomen

Needed for some patients

- Somatostatin receptor-based imaging
- CT of chest
- EUS
- Other biochemical testing
- Consider testing for inherited genetic syndromes

Guide 34 includes tests for a VIPoma. This tumor may cause low potassium, watery diarrhea, and dehydration. Dehydration is the loss of water and other fluids from the body. Thus, your doctor may measure your electrolytes that control the amount of water in the body and the VIP level. VIP is a hormone that controls sodium, potassium, and other minerals in the GI tract. This hormone keeps a balance on what is absorbed into the small intestine. Imaging tests may include a CT or MRI of the abdomen. A CT of the chest may be considered. Somatostatin receptor-based imaging and EUS are done as needed. Your doctor may also test for inherited genetic syndromes.

Guide 35. Treatment for VIPoma

Disease status		Primary treatment	Next steps
Locoregional disease	→	<ul style="list-style-type: none"> • Octreotide or lanreotide 	<ul style="list-style-type: none"> • See <i>Surveillance</i>, Guide 36
		→	
		→	<ul style="list-style-type: none"> • Distal- distal pancreatectomy + peripancreatic lymph node removal + splenectomy
Metastatic disease	→	<ul style="list-style-type: none"> • See Guide 38 	

Guide 35 lists treatment options for VIPomas. If you have locoregional disease, your doctor may consider octreotide or lanreotide. He or she may offer treatment for electrolyte imbalance and offer fluids for dehydration. Surgery may occur next. The method of surgery depends on the location of the VIPoma. Surveillance will follow treatment. The tests are listed in the next guide. See Guide 38 on page 73 for treatment options for metastatic disease.



Due to the complexity of neuroendocrine tumors and how they can spread to multiple organs, be symptomatic or silent, be slow-growing or aggressive, it's important to have a multidisciplinary team involved in your care plan.

-Cindy

Survivor, breast cancer and neuroendocrine tumors of the pancreas

Surveillance

Guide 36. Surveillance for neuroendocrine tumors of the pancreas

Tests
<ul style="list-style-type: none"> • Medical history and physical exam
<ul style="list-style-type: none"> • Consider biochemical testing
<ul style="list-style-type: none"> • Consider CT or MRI of abdomen as needed
<ul style="list-style-type: none"> • CT of chest as needed

Guide 36 shares surveillance tests after cancer treatment has ended. You should have tests to check if the cancer has returned. Surveillance tests may include a medical history and physical exam, biochemical testing, and imaging of your abdomen. A CT of the chest may be considered. Certain tests follow a schedule, while others are based on any signs or symptoms you have during surveillance.

Surveillance tests may include a medical history, physical exam, and imaging tests for the first 3 to 12 months after surgery. From 1 year until 10 years after surgery, you may have these tests every 1 to 2 years. Ask your doctor what tests you may have and how often you will see him or her for a doctor's appointment.

Locally advanced or metastatic disease

Guide 37. Tests for locally advanced or metastatic disease of the pancreas

Tests
<ul style="list-style-type: none"> • CT or MRI of abdomen and pelvis as needed
<ul style="list-style-type: none"> • CT of chest as needed
<ul style="list-style-type: none"> • Somatostatin receptor-based imaging <ul style="list-style-type: none"> ◦ Ga-dotatate PET/CT scan preferred or somatostatin receptor scintigraphy
<ul style="list-style-type: none"> • Biochemical testing as needed

Guides 37 and 38 (see Guide 38 on the next page) lists the tests and treatments of locally advanced or metastatic disease. Surgery will be considered. If surgery is not the best option, treatment options will be based on whether there are no symptoms and stable disease, or symptoms with disease that is worsening. Observation may be an option if there is low concern for tumor growth. If the disease is growing and symptoms persist, you may start systemic therapy with octreotide or lanreotide.

Guide 38 also shares treatment options if the cancer keeps growing despite treatment. Doctors refer to this as disease progression. Treatment options after progression may include systemic therapy. These options include everolimus, sunitinib, and PRRT with ¹⁷⁷Lu-dotatate. Chemotherapy may include 5-FU, capecitabine, dacarbazine, oxaliplatin, streptozocin, and temozolomide. Commonly used regimens include temozolomide/capecitabine, 5-FU/doxorubicin/streptozocin, streptozocin/doxorubicin, and streptozocin/5-FU. See Guide 5 on page 33 and ask your doctor what systemic therapies may be an option for disease progression. Your doctor may also consider localized therapy to treat disease that has spread to the liver. It is helpful to learn about your next steps of care.

Guide 38. Treatment for locally advanced or metastatic disease of the pancreas

Disease status		Treatment	Next steps	
Complete surgery is possible	→	<ul style="list-style-type: none"> Resect primary tumor and metastases 	→	<ul style="list-style-type: none"> Refer to <i>Surveillance</i>, Guide 36
No symptoms, low tumor burden, and stable disease	→	<ul style="list-style-type: none"> Observe with tumor marker tests and CT or MRI of abdomen and pelvis every 3–12 months, and CT of chest as needed or <ul style="list-style-type: none"> Consider octreotide or lanreotide 	→	<ul style="list-style-type: none"> For disease progression, follow the path below
Symptoms, major tumor burden, or disease progression	→	<ul style="list-style-type: none"> Manage symptoms as needed If disease progression, consider octreotide or lanreotide (if none before) 	→	If disease progression: <ul style="list-style-type: none"> Everolimus Sunitinib PRRT with ¹⁷⁷Lu-dotatate, if somatostatin receptor-positive imaging Chemotherapy Consider a hepatic-directed therapy for disease in the liver: <ul style="list-style-type: none"> Arterial embolization Chemoembolization Radioembolization Cytoreductive surgery/ablative therapy

Review

- ▶ Treatment planning is an important first step of care.
- ▶ Primary treatment for neuroendocrine tumors of the pancreas is surgery.
- ▶ Other options depend on the type of tumor and if the disease has spread to other areas.
- ▶ Surveillance tests may include a medical history, physical exam, biochemical testing, and imaging of your abdomen and pelvis.
- ▶ If the cancer continues to grow despite treatment, you may switch to another treatment.

7

Treatment guide: Other neuroendocrine tumors

75 Neuroendocrine tumors of an unknown primary

77 Poorly differentiated neuroendocrine carcinomas

78 Review



Part 7 lists tests and treatment options for other, more rare types of neuroendocrine tumors. This includes options for tumors of an unknown primary site, poorly differentiated neuroendocrine carcinoma, and large or small cell neuroendocrine carcinomas.

This information is taken from the treatment guidelines written by NCCN experts of neuroendocrine tumors. These treatment guidelines list options for people with neuroendocrine tumors in general. Thus, your doctors may suggest other treatment for you based on your health and personal wishes.

Neuroendocrine tumors of an unknown primary

A small number of neuroendocrine tumors may not have a clear primary tumor site. The disease could have spread, which will guide your doctor to check for the original location of the tumor. If the original tumor site cannot be found, the neuroendocrine tumor of an unknown primary will be treated based on the histology. Many of these tumors tend to be poorly differentiated and may grow and spread quickly. Some are well-differentiated. In this case, you would refer to treatment options for carcinoid tumors.

Guide 39. Tests for neuroendocrine tumor of an unknown primary

Needed for most patients

- CT of chest
- CT or MRI of abdomen and pelvis
- Somatostatin receptor-based imaging or EUS
- Consider FDG-PET/CT scan, and brain imaging (CT or MRI) for poorly differentiated carcinomas only
- Consider EGD and/or colonoscopy

Guide 39 has tests that may be used to assess a neuroendocrine tumor where the primary site of disease (where the cancer started) is unknown. The cancer may have spread and your doctor will need to examine the disease with imaging tests, along with scopes to see internal areas of the body more closely. Somatostatin receptor-based imaging is not usually done for poorly differentiated disease, so an EUS may be considered. A biopsy may be done to confirm the cell type. These tests will help your treatment team decide on treatment options.

Guide 40. Treatment for neuroendocrine tumor of an unknown primary

Disease status		Next steps	
Primary tumor not found	• Poorly differentiated	→	• See Guides 41 and 42
	• Well-differentiated	→	• See Guides for carcinoid tumors
Primary tumor found	→	• See Guides for the primary tumor type	

Guide 40 shows how the doctor will assess the cell type further when the first site of the tumor is unknown. Examining the cells more closely will allow your treatment team to consider options that fit your needs. Cancer is confirmed by a biopsy. A sample of fluid or tissue is taken during a biopsy and examined under a microscope.

Since there are different cells in the body, there are different cell types of neuroendocrine tumors, which grow and behave differently in the body. The Ki-67 protein is measured to see how quickly the cells are dividing and if they are aggressive. Aggressive, poorly differentiated cells may grow in many organs. If the cells are poorly differentiated, you will see Guide 42. If the cells are well-differentiated, then you will see the guides in Part 4 or Part 5, depending on where the cancer started in the body (primary tumor site).



Do your own research. Ask questions, join a support group, become active on any of the NET Facebook groups... do what you can to understand your treatment and any side effects you may experience.

– Cindy
Survivor, neuroendocrine tumor of the ileum

Poorly differentiated neuroendocrine carcinomas

Guide 41. Tests for poorly differentiated neuroendocrine carcinoma

Needed for most patients

- CT of chest, abdomen, and pelvis

Needed for some patients

- MRI or CT of brain
- FDG-PET/CT scan
- Biochemical testing as needed

Guide 41 lists tests for tumors that are poorly differentiated neuroendocrine carcinomas. Since there are different cells in the body, there are different cell types of neuroendocrine tumors, which grow and behave differently in the body. Your doctor will view the area using imaging tests. Blood tests may be done to measure hormones, including ACTH to see if the adrenal gland is working properly. The adrenal gland controls metabolism and helps the body respond to stress. The results of the tests will guide your treatment team.

Guide 42. Treatment for poorly differentiated neuroendocrine carcinoma

Large or small cell

Disease status		Primary treatment		Surveillance
Surgery is an option	→	Therapy options depend on sites of disease. Options may include: <ul style="list-style-type: none"> • Resection + adjuvant chemotherapy ± radiation therapy • Neoadjuvant chemotherapy ± radiation therapy + resection • Chemotherapy alone • Radiation therapy • Chemoradiation 	→	Every 3 months for 1 year, then every 6 months: <ul style="list-style-type: none"> • Medical history and physical exam • Imaging tests: <ul style="list-style-type: none"> ◦ CT of chest and MRI of abdomen and pelvis or ◦ CT of chest, abdomen, and pelvis
Locoregional, surgery is not an option	→	<ul style="list-style-type: none"> • Radiation therapy and chemotherapy given at the same time or one treatment after the other • Chemotherapy 	→	Every 3 months: <ul style="list-style-type: none"> • Medical history and physical exam • CT of chest and MRI of abdomen and pelvis
Metastatic disease	→	<ul style="list-style-type: none"> • Chemotherapy 	→	or <ul style="list-style-type: none"> • CT of chest, abdomen, and pelvis

Guide 42 (on page 77) lists treatment options for poorly differentiated neuroendocrine carcinomas. The cell types are large and small cell. Poorly differentiated tumors of unknown primary may also be treated as in Guide 42. The tumors can grow and spread quickly, so more than one treatment may be given. Treatments include surgery, chemotherapy, and radiation therapy. Sometimes treatments are given at the same time, while other times they are given one after the other.

Surveillance tests will follow treatment to watch for any cancer growth. These tests include imaging tests every 3 months for at least 1 year or longer. See Guide 42 for more information. Ask your treatment team about the treatment you will receive and any possible side effects you can expect.

Review

- ▶ Treatment planning is an important first step of care to understand more about an unknown primary.
- ▶ Primary treatment for neuroendocrine tumors depends on whether the cells are well-differentiated or poorly differentiated.
- ▶ The Ki-67 protein is measured to see how quickly the cells are dividing and if they are aggressive.
- ▶ Poorly differentiated neuroendocrine carcinomas can grow and spread quickly, so more than one treatment may be given. Treatments may include surgery, chemotherapy, and radiation therapy.
- ▶ Surveillance tests may include a medical history, physical exam, and imaging tests every 3 months for poorly differentiated neuroendocrine carcinomas.



All of your questions and observations are important. No one knows your body better than you. Share your information with your team to come up with the best treatment plan for you.

-Mary

Survivor, neuroendocrine tumor of the ileum

8

Making treatment decisions

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Having cancer can feel very stressful. While absorbing the fact that you have cancer, you must also learn about tests and treatments. And, the time you have to decide on a treatment plan may feel short.

Parts 1 through 7 described the tests and treatment options recommended by NCCN experts. Part 8 aims to help you make decisions and talk with your treatment team about your options. You will also find a list of websites where you can learn more, seek support, or get resources on neuroendocrine tumors.

It's your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. However, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, your treatment team may still ask that you sign a consent form.

On the other hand, you may want to take the lead or share in decision-making. In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you can decide on a plan that works for you when it comes to your personal and health needs.

Questions to ask

You will likely meet with experts from different fields of medicine. It is helpful to talk with each person. Prepare questions before your visit and ask questions if the information isn't clear. You can get copies of your medical records. It may be helpful to have a family member or friend with you at these visits to listen carefully and even take notes. A patient advocate or navigator might also be able to come. They can help you ask questions and remember what was said.

The questions below are suggestions for information you read about in this book. Feel free to use these questions or come up with your own personal questions to ask your doctor and other members of your treatment team.

Questions about testing and the results

1. What tests will I have for this type of neuroendocrine tumor?
2. Where and when will the tests take place?
3. How long will the tests take?
4. How do I prepare for testing?
5. How soon will I know the results and who will explain them to me?
6. Where did the neuroendocrine tumor start? What type of neuroendocrine tumor is it?
7. What is the cancer stage?
8. Have any cancer cells spread to other parts of my body?

Questions about treatment options

1. What treatment options do I have?
2. Can I join a clinical trial?
3. Will my treatment team include specialists who have experience with neuroendocrine tumors?
4. Does this hospital or center offer the best treatment for me?
5. Can you provide me with the research that supports this treatment plan?
6. Will I need more than one treatment?
7. How much time do I have to think about my options?
8. Do I have time to get a 2nd opinion?
9. How do I prepare for treatment?
10. Will I have to go to the hospital or elsewhere? How often will I go?
11. Should I bring someone with me when I get treated?

Questions about clinical trials

1. What clinical trial is right for me?
2. How many people will be in the clinical trial?
3. What are the tests and treatments for this study? How often will they be?
4. How long will I be in the clinical trial?
5. Will I be able to get other treatment if this doesn't work?
6. How will you know if the treatment is working?
7. Who will help me understand the costs of the clinical trial?

Questions about side effects

1. What are the side effects?
2. When can they start?
3. How long will the side effects last?
4. When should I call the doctor about my side effects?
5. How can I prevent or relieve these side effects?
6. Are there any complementary therapies that might help?
7. Are there any long-term effects from this treatment?
8. Is home care after treatment needed? If yes, what type?

Questions about a doctor's experience

1. Are you board certified? If yes, in what area?
2. How many people like me have you treated?
3. How many procedures like the one you're suggesting have you done?
4. Is this treatment a major part of your practice?
5. How many of your patients have had complications?

Deciding between options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another, so science isn't helpful. Some ways to decide on treatment are discussed next.

Getting a 2nd opinion

Even if you like and trust your doctor, it is helpful to get a 2nd opinion. You will want to have another doctor review your test results. He or she can suggest a treatment plan or check the one you already heard about.

Things you can do to prepare:

- ▶ Check with your insurance company about its rules on 2nd opinions. You want to know about out-of-pocket costs for doctors who are not part of your insurance plan.
- ▶ Reach out to patient advocacy organizations (see websites on the next page) for help with 2nd opinions. Some may also give referrals to hospitals or cancer centers who specialize in treating neuroendocrine tumors.
- ▶ Make plans to have copies of all your records sent to the doctor you will see for your 2nd opinion. Do this well before your appointment. If you run into trouble having records sent, pick them up and bring them with you.

If the new doctor offers other advice, make an appointment with your first doctor to talk about the differences. Do whatever you need to feel confident about your diagnosis and treatment plan.

Getting support

Support groups often include people at different stages of treatment. They can be online or meet in person. Some people in a support group may be in the process of deciding while others may be finished with treatment.

At support groups, you can ask questions and hear about the experiences of other people with neuroendocrine tumors. If your hospital or community doesn't have support groups for people with neuroendocrine tumors, check out the websites on the next page. These organizations may give referrals to support groups in your area, have online support groups, or have free hotlines you can call for help.

You can also reach out to a social worker or psychologist. They can help you find ways to cope or refer you to support services. These services may also be available to your family, friends, and to those with children, so they can connect and get support.

Keep in mind:

- ✓ Every treatment option has benefits and risks. Consider these when deciding which option is best for you.
- ✓ Talking to others may help identify benefits and risks you hadn't thought of.

Websites

American Cancer Society

cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging/net-staging.html

cancer.org/cancer/gastrointestinal-carcinoid-tumor/about/what-is-gastrointestinal-carcinoid.html

Los Angeles Carcinoid Neuroendocrine Tumor Society (LACNETS)

NET VITALS - Your New NET Communication Tool

lacnets.org/netvitals

National Cancer Institute

cancer.gov/types

Neuroendocrine Cancer Awareness Network (NCAN)

netcancerawareness.org

Neuroendocrine Tumor Research Foundation (NETRF)

netrf.org

The Carcinoid Cancer Foundation, Inc.

carcinoid.org

The Healing NET Foundation

thehealingnet.org

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your treatment team questions is vital to getting the information you need to make informed decisions.
- Getting a 2nd opinion, attending support groups, and comparing benefits and risks may help you decide which treatment is best for you.



My wife, Maryann, is a neuroendocrine cancer survivor who was diagnosed in 2001. Her journey to diagnosis took 7 years, seeing 6 or 7 doctors with symptoms like rectal bleeding, uncontrollable diarrhea, flushing. They told her to eat more fiber, watch her diet and one asked if she thought marriage counseling would help. NCAN was founded to heighten the awareness of neuroendocrine cancer and make other patients' journeys smoother.

– Robert Wahmann, Board of Directors

The Neuroendocrine Cancer Awareness Network (NCAN)

Glossary

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93 Acronyms

Dictionary

abdomen

The belly area between the chest and pelvis.

adjuvant therapy

Treatment that is given after surgery to lower the chances of the cancer returning.

adrenal gland

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

aggressive cancer

A cancer that grows or spreads fast.

allergic reaction

An abnormal response by the body to an foreign substance that is harmless.

antiestrogen

A cancer drug that stops estrogen from attaching to cells.

anus

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

appendix

A small tubelike organ attached to the first section of the large intestine.

biochemical test

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

biopsy

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

bronchopulmonary

A term used for the airways that lead to the lungs (bronchi) and the lungs (pulmonary).

bronchoscopy

A procedure to work inside the airways with a device that is guided down the throat.

bronchus

One of the airways that extends into the lungs. The plural form is bronchi.

cancer grade

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

cancer stage

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

carcinoid syndrome

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

carcinoid tumor

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

carcinoma

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

chemoradiation

Treatment with a combination of chemotherapy and radiation therapy.

chemotherapy

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

chromogranin A

A protein that may be at a higher level when a neuroendocrine tumor is present.

clinical trial

A type of research that assesses health tests or treatments.

colon

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

coloscopy

A procedure to look inside the colon with a device that is guided through the anus.

computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the insides of the body.

contrast

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

cortisol

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

Cushing's syndrome

A condition caused by the release of excess cortisol in the body.

deoxyribonucleic acid (DNA)

A chain of chemicals in cells that contains coded instructions for making and controlling cells. Also called the "blueprint of life."

duodenum

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

embolization

A treatment that cuts off blood supply to tumors with beads inserted into an artery.

endocrinologist

A doctor who's an expert in glands and hormones.

endoscope

A device that is passed through a natural opening to do work inside the body.

esophagoduodenoscopy (EGD)

A procedure to do work in the first parts of the digestive track with a device guided down the throat. Also called an upper GI endoscopy.

external beam radiation therapy (EBRT)

A cancer treatment with radiation delivered from a machine outside the body.

fine-needle aspiration (FNA)

A procedure that removes tissue samples with a very thin needle.

first-line therapy

The first drug or set of drugs given to treat cancer.

gastrin

A hormone made and released by the stomach.

gastroenterologist

A doctor who's an expert in digestive diseases.

gastrointestinal (GI) tract

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

gene

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

general anesthesia

A drug-induced, deep sleep-like state for pain relief.

genetic assessment

A lab test of abnormal coded instructions in cells that are passed down within a family.

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.

hives

A skin rash caused by the body trying to rid itself of a foreign substance.

hormone

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

hypothalamus

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

ileum

The last section of the small intestine.

imaging

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

immune system

The body's natural defense against infection and disease.

immunotherapy

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

insulin

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

intensity-modulated radiation therapy (IMRT)

Treatment with radiation that uses small beams of different strengths based on the thickness of the tissue.

islet cell

A cell in the pancreas that makes hormones.

jejunum

The middle section of the small intestine.

Ki-67

A protein associated with cell growth.

liver

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

lung

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

lymph node

A small, bean-shaped disease-fighting structure.

magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

medical history

A report of all your health events and medications.

medical oncologist

A doctor who's an expert in cancer drugs.

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 two main types of this syndrome are MEN1 and MEN2.

mutation

An abnormal change.

neoadjuvant treatment

A treatment given before the main treatment to reduce the cancer. Also called preoperative treatment if given before an operation.

neuroendocrine cells

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

neuroendocrine tumor

A tumor that starts in neuroendocrine cells.

nutritionist

A health care worker who completed education in food and diet.

observation

A period of testing for changes in cancer status while not receiving treatment.

ovary

One of a pair of organs in women that produce eggs and hormones.

palliative care

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

pancreas

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

pathologist

A doctor who's an expert in testing cells and tissue to find disease.

pelvis

The body area between the hipbones.

peptide receptor radionuclide therapy (PRRT)

A procedure that uses a radiopharmaceutical drug to target and treat certain neuroendocrine tumors.

physical exam

A study of the body by a health expert for signs of disease.

pineal gland

A small gland in the cerebrum of the brain.

pituitary gland

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

positron emission tomography (PET)

A test that uses radioactive material to see the shape and function of body parts.

primary treatment

The main treatment used to rid the body of cancer.

primary tumor

The first mass of cancer cells.

progression

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

prostate

A male gland that makes fluid, which protects sperm from the acid in the vagina.

proto-oncogene

A gene that has to do with the growth of normal cells. When mutated it is called an oncogene.

radiation oncologist

A doctor who's an expert in treating cancer with radiation.

radiation therapy

A treatment that uses high-energy rays or related approaches to kill cancer cells.

radiologist

A doctor who's an expert in imaging tests.

radiopharmaceutical

A drug that carries a certain amount of radioactive material.

rectum

An organ that holds stool until expelled from the body.

receptor

A cell protein to which substances, such as hormones, can attach.

sedative

A drug that helps a person to relax or go to sleep.

serotonin

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

side effect

An unhealthy or unpleasant physical or emotional response to treatment.

simulation

The steps needed to prepare for treatment with radiation.

social worker

An expert in meeting social and emotional needs.

somatostatin

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

somatostatin receptor scintigraphy

A type of imaging scan used to assess carcinoid tumors that have somatostatin receptors.

stomach

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

supportive care

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

surgery

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

surgical margin

The normal-looking tissue around the edge of a tumor that is removed during surgery.

surgical oncologist

A doctor who's an expert in operations that remove cancer.

symptom

A body sensation that may be caused by a disease.

targeted therapy

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

testicle

One of a pair of egg-shaped glands found inside the sac between the legs of a man.

thymus

A gland that is behind the breastbone.

tumor marker

A substance found in body tissue or fluid that may be a sign of cancer.

ulcer

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

ultrasound

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

vasoactive intestinal polypeptide (VIP)

A hormone that controls the amount of water and minerals absorbed into the small intestine during digestion.

x-ray

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

Acronyms

5-FU

5-fluorouracil

5-HIAA

5-hydroxyindoleacetic acid

ACTH

adrenocorticotrophic hormone

AJCC

American Joint Commission on Cancer

CAM

complementary and alternative medicine

CBC

complete blood count

CT

computed tomography

DIPNECH

diffuse idiopathic pulmonary neuroendocrine cell hyperplasia

DNA

deoxyribonucleic acid

EBRT

external beam radiation therapy

EGD

esophagastroduodenoscopy

EUS

endoscopic ultrasound

FDG

18F-fluorodeoxyglucose

FNA

fine-needle aspiration

GI tract

gastrointestinal tract

IMRT

intensity-modulated radiation therapy

LAR

long-acting release

MEN

multiple endocrine neoplasia

MRI

magnetic resonance imaging

PET

positron emission tomography

PET/CT

positron emission tomography/computed tomography

PPI

proton pump inhibitor

PRRT

peptide receptor radionuclide therapy

RFA

radiofrequency ablation

SPECT

single photon emission computed tomography

VIP

vasoactive intestinal polypeptide

NCCN Panel Members for Neuroendocrine and Adrenal Tumors

Manisha H. Shah, MD/Chair <i>The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute</i>	Daniel Halperin, MD <i>The University of Texas MD Anderson Cancer Center</i>	*Venu G. Pillarisetty, MD <i>Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance</i>
Matthew H. Kulke, MD/Chair <i>Dana-Farber/Brigham and Women's Cancer Center</i>	Jin He, MD, PhD <i>The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins</i>	Leonard Saltz, MD <i>Memorial Sloan Kettering Cancer Center</i>
* Whitney S. Goldner, MD/Vice Chair <i>Fred & Pamela Buffett Cancer Center</i>	Martin J. Heslin, MD <i>University of Alabama at Birmingham Comprehensive Cancer Center</i>	Julie Ann Sosa, MD <i>Duke Cancer Institute</i>
Al B. Benson, III, MD <i>Robert H. Lurie Comprehensive Cancer Center of Northwestern University</i>	Gregory P. Kalemkerian, MD/Liaison <i>University of Michigan Rogel Cancer Center</i>	Jonathan R. Strosberg, MD <i>Moffitt Cancer Center</i>
Emily Bergsland, MD <i>UCSF Helen Diller Family Comprehensive Cancer Center</i>	Fouad Kandeel, MD, PhD <i>City of Hope National Medical Center</i>	Craig A. Sussman, MD <i>Vanderbilt-Ingram Cancer Center</i>
Jordan D. Berlin, MD <i>Vanderbilt-Ingram Cancer Center</i>	Sajid A. Khan, MD <i>Yale Cancer Center/Smilow Cancer Hospital</i>	Nikolaos A. Trikalinos, MD <i>Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine</i>
Lawrence S. Blaszkowsky, MD <i>Massachusetts General Hospital Cancer Center</i>	Wajih Zaheer Kidwai, MD <i>Yale Cancer Center/Smilow Cancer Hospital</i>	Nataliya A. Uboha, MD, PhD <i>University of Wisconsin Carbone Cancer Center</i>
Jennifer Chan, MD <i>Dana-Farber/Brigham and Women's Cancer Center</i>	Pamela L. Kunz, MD <i>Stanford Cancer Institute</i>	Jonathan Whisenant, MD <i>Huntsman Cancer Institute at the University of Utah</i>
Jennifer Eads, MD <i>Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute</i>	Boris W. Kuvshinoff, II, MD, MBA <i>Roswell Park Comprehensive Cancer Center</i>	*Terence Wong, MD <i>Duke Cancer Institute</i>
Paul F. Engstrom, MD <i>Fox Chase Cancer Center</i>	Christopher Lieu, MD <i>University of Colorado Cancer Center</i>	James C. Yao, MD <i>The University of Texas MD Anderson Cancer Center</i>
Paul Fanta, MD <i>UC San Diego Moores Cancer Center</i>	Robert Merritt, MD/Liaison <i>The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute</i>	NCCN Staff
Thomas Giordano, MD, PhD <i>University of Michigan Rogel Cancer Center</i>	Gareth Morris-Stiff, MD, PhD <i>Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute</i>	Jennifer Burns
Thorvardur R. Halfdanarson, MD <i>Mayo Clinic Cancer Center</i>		Ndiya Ogba, PhD
		*Griselda Zuccarino-Catania, PhD

* Reviewed the clinical content of this book.

For disclosures, visit www.nccn.org/about/disclosure.aspx.

NCCN Member Institutions

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
800.999.5465
nebraskamed.com/cancer

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
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Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
877.585.0303
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Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.288.7222 • seattlecca.org
206.667.5000 • fredhutch.org

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
hopkinskimmelcancercenter.org

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Chicago, Illinois
866.587.4322
cancer.northwestern.edu

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
800.446.2279 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
www.mayoclinic.org/cancercenter

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

Moffitt Cancer Center
Tampa, Florida
800.456.3434
moffitt.org

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

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

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

St. Jude Children's Research Hospital
The University of Tennessee
Health Science Center
Memphis, Tennessee
888.226.4343 • stjude.org
901.683.0055 • westclinic.com

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

University of Alabama at Birmingham
Comprehensive Cancer Center
Birmingham, Alabama
800.822.0933
www3.ccc.uab.edu

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La Jolla, California
858.657.7000
cancer.ucsd.edu

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800.689.8273
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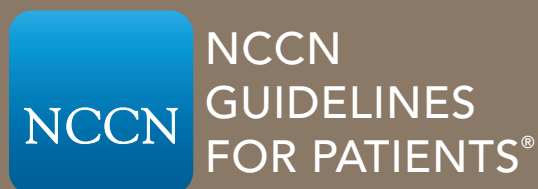
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vicc.org

Yale Cancer Center/
Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW
yalecancercenter.org

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National
Comprehensive
Cancer
Network®

3025 Chemical Road
Suite 100
Plymouth Meeting, PA 19462
215.690.0300

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