zebra talk

navigating the world of neuroendocrine tumors

a handbook for the newly diagnosed & their primary care physicians
What Are Neuroendocrine Tumors? (NETs)

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This booklet is intended as a reference for those newly diagnosed with NETs, in the process, or hoping to explore this bewildering world. It is also a guide to resources that can empower patients through knowledge and the mentorship of others to make informed decisions for medical care. It is not intended as medical advice, but as a collection of useful facts and pursuable options. Opinions expressed are based on the experiences of NET patients and the Editor, Suzi Garber, of Bucks County, PA. As a Stage IV carcinoid patient for the past eight years, founder/support group leader, ‘hospital to community liaison’ and patient advocate, she wears many hats. She has been misdiagnosed, tardily diagnosed, treated for the wrong disease, and turned down for surgery five times until she heard a yes. All information has been reviewed by the professionals recognized on the back cover. It would be remiss not to also acknowledge Melissa Stevens, MPH, (NOLA NETs), Michael Hasker, DMD, and Jack Martin, MBA, friend, fellow patient, and self-proclaimed “pesty-proofer” for their generous help.

In the medical community, the term “zebra” is a universal reference to an orphan (rare) disease. Physicians learn the core tenet of diagnosis—to assume that the simplest explanation is usually the best answer, so, it is generally more productive to look for common, rather than exotic causes for diseases—hence the phrase “If you hear hoof beats, think horses, not zebras.” (Based on Occam’s Razor principle—i.e., the simplest answer is often the correct one). To encourage disease recognition and awareness, the worldwide NET community adopted the zebra to symbolize our uniqueness and create awareness through the zebra’s eye-catching appeal of its flamboyant camouflage (oxymoron).
What are Neuroendocrine Tumors? (NETs)

NETs can be indolent (slow growing), non-aggressive, low-grade tumors that are well-differentiated. These low grade tumors such as carcinoid & islet cell (5% of all pancreatic tumors) are the most common types of NETs. They can metastasize to anywhere in the body (the liver being the most frequent site). The other end of the spectrum, fast-growing, i.e., high grade tumors, are poorly differentiated and highly aggressive.

NETs are a group of solid tumors (tissues growing or dividing abnormally) that arise from cells that release hormones in response to a signal from the central nervous system. These tumors secrete large amounts of hormones which in turn can cause a range of symptoms. The most common site of origin is in the gastrointestinal tract, but they can occur in the lungs, reproductive organs, kidneys, and thymus (actually anywhere). There are many types of NETs and each requires a different approach in terms of diagnosis and subsequent treatment. NETs can be functional or nonfunctional depending on if they produce hormones (functional). Each functional syndrome (see p.4) has a predilection for certain sites. At the early stages of the disease there may be no symptoms. Some people remain asymptomatic indefinitely; nonfunctional NETs may produce symptoms due to increased tumor size over time.

Types of NETs.

Carcinoid. [German] karzinoide: meaning “carcinoma (cancer)-like”

These types of tumors originate from the diffuse (primitive) neuroendocrine system nerve cells and the hormone-producing endocrine cells. They are found throughout the body, mostly in the gastrointestinal tract, but can occur most anywhere. If the tumor is functional, it secretes excessive levels of serotonin and other hormones that can affect the functioning of other bodily systems which can produce a group of symptoms called carcinoid syndrome (see next page).

Gastrointestinal (G.I.) carcinoids are the most prevalent NETs. They arise from the neuroendocrine hormone-making cells in the G.I. tract and compose over 60% of diagnosed carcinoid tumors. They are classified as foregut, midgut, or hindgut (see p.5). These cells help control digestive juices and affect muscle activity in the G.I. tract; if these tumors produce large amounts of hormones they can cause carcinoid syndrome (see next page). Gastrointestinal carcinoid is often misdiagnosed as irritable bowel syndrome, Crohn’s disease, asthma, menopause, rosacea, and acid reflex because of the presenting symptoms of carcinoid. The average time for a correct diagnosis is usually 5-7 years.

Bronchial (lung) carcinoids (typical or atypical) The typical tumors (considered low grade) tend to grow slower than other lung cancers and occur in 90% of NET lung patients. They tend to recur locally but can metastasize to other areas, the liver being the most common site. They account for about 1-2% of all lung malignancies in adults and 20-30% of all carcinoid tumors. They are many times more common than atypical (considered high grade) carcinoids which have a higher proliferation rate (more cells dividing at any given time). Low grade tumors are treated with surgery and usually a regimen of octreotide (a protein with 8 amino acids, and a somatostatin analog (see pp.16-17 for definitions). High grade tumors are usually initially treated with chemotherapy.
**Types of NETs. (cont’d)**

Having a diagnosis of carcinoid sometimes presents the additional challenge of controlling “**carcinoid syndrome**”, which is caused by high levels of vasoactive (affecting blood vessels) substances, such as serotonin, histamines, bradykinins, tachykinins, and prostaglandins, produced by the tumors, generally after the tumors have metastasized (spread) to the liver.

The symptoms vary according to the amount of hormone produced, the tumor site, and if the cancer has spread to other organs (see also pp.9 and 18). **This syndrome most commonly presents with small bowel carcinoid (midgut) and can include:**

- Wheezing
- Swelling (ankles or feet)
- Shortness of breath
- Abdominal pain
- Fatigue
- Diarrhea or cramping
- Heart disease (valvular)
- Flushing, redness, warmth in face/neck
- Feeling of fullness in abdomen (bloating)
- Rapid heart rate (palpitations)

**Pancreatic Neuroendocrine Tumors. (p NETs)**

These tumors typically develop in the pancreas or duodenum. They’re a type of low-grade, rare NET that occur in the pancreas’ islet cells. They comprise 5% of all pancreatic tumors and are diagnosed with the same types of scans that find carcinoid tumors and have similar treatment protocols. The most important hormone these cells produce is **insulin**. Most are nonfunctioning; those that are **functioning** (see below) produce hormones that can cause symptoms. They can be benign or malignant and functional or nonfunctional. If they are functional, they are classified by the type of hormone they secrete. Symptoms vary accordingly:

- **Gastrinoma**—*Gastrin. Zollinger-Ellison Syndrome*  
  Symptoms: abdominal pain, diarrhea, stomach and small bowel ulcers, occasionally vomiting blood.

- **Insulinomas**—*Insulin. Hypoglycemia* resulting from hyperinsulinism.  
  Symptoms: tired, weak, shaking or sweating, headache, hunger, nervousness, anxiety, hazy thinking, uneasiness, double or blurry vision, fast/pounding heart.

- **Glucagonomas**—*Glucagon. 4-D Syndrome*  
  Dermatosis, Diabetes, Deep Vein Thrombosis, and Depression.  
  Symptoms: **diabetes** (most patients), inflamed mouth and tongue, crusty or scaly skin rash on face, abdomen, buttocks or feet.

- **VIPomas**—*Vasoactive Intestinal Polypeptide. VIPoma Syndrome*  
  Symptoms: abdominal pain, cramping, diarrhea, nausea, weight loss.

- **Somatostatinomas**—*Somatostatin*. Found in the pancreas & duodenum.  
  Symptoms: gallstones, diarrhea, diabetes, weight loss.

- **PPomas**—*Pancreatic Polypeptidesomas (PP)*. A polypeptide secreted by PP cells in the endocrine pancreas. PP inhibits gastric emptying rate, exocrine pancreatic secretion, and gallbladder motility.  
  Symptoms: abdominal pain, enlarged liver, and diarrhea.

**Paragangliomas & Pheochromocytomas.**

“Pheos” are chromaffin cell tumors that form in the adrenal glands and are called **pheochromocytomas**; tumors that form outside the adrenal glands are called **(extra-adrenal) paragangliomas**. Pheochromocytomas and paragangliomas may be benign or malignant. If tumors make excess catecholamines (epinephrine & norepinephrine), patients can present with symptoms such as high blood pressure...
How Are NETs Diagnosed & Classified?

Types of NETs. (cont’d)

(most common), fast pulse and heart rate, hyperglycemia, palpitations, anxiety, fever, headaches, nausea, and clammy skin. Tumors are mostly found in the abdomen and pelvis, but can be in the head, neck and spread to bone, liver and other organs. These tumors can be caused by genetic disorders including: von-Hippel Lindau; SDH mutations; multiple endocrine neoplasia type 2 (MEN-2); and, neurofibromatosis type 1.

Merkel Cell Carcinoma. (Skin) A very rare tumor which originates in the cells just beneath the skin and in hair follicles. Sun exposure and a weakened immune system are risk factors. Diagnosis is made by tumor biopsy.

Diagnostic Studies. These tests (called assays or biomarkers) include blood and urine tests.

- Carcinoid Labs
  (For all carcinoid primary tumor sites)
  - Neurokinin A (midgut only)
  - Chromogranin A (CgA) - See p. 15
  - Pancreastatin (all carcinoids)
  - Serotonin
  - Substance P
  - 24 Hour 5-HIAA Urine
  or
  - Plasma 5-HIAA (Blood) *
* Available thru ISI Lab: www.intersciencieinstitute.com (For test preparations/info)

- Islet Cell Labs
  (Pancreas)
  - Pancreatic Neuroendocrine Tumors
  - Growth Hormone
  - Glucagon
  - Vasoactive Intestinal Polypeptide
  - Ghrelin
  - PTH
  - Insulin-like Growth Factor IGF-1 also known as Somatomedin C
  - Pancreatic Polypeptide
  - Gastrin
  - Motilin
  - Calcitonin
  - Fasting glucose

- “Pheo” Labs
  (Adrenal)
  - Plasma-free metanephrines
  There are two subsets of combinations of diseases that include pheochromocytomas:
  Carney-Stratakis dyad: paraganglioma and gastrointestinal stromal tumor (GIST).
  Carney triad includes paraganglioma, GIST and pulmonary chondroma.

ALL NET PATIENTS: Knowledge of stage, classification, primary site, and rate of proliferation are necessary to plan your treatment. A proper and thorough diagnosis combines your labs, diagnostic scan results (see p.6) and a biopsy of the tumor.

Tumor Classifications. (All Types of Cancer)

SEER (a cancer data program of the National Cancer Institute) uses the terms Localized, Regional, and Distant. This is the most basic way of categorizing how far a cancer has spread from its point of origin. The SEER database shows a 5-fold increase in the incidence of NETs from 1973 to 2004, and it is predicted the rate will continue to rise faster than other malignancies. The SEER database doesn’t necessarily include completely accurate demographic information, so “take the data with a grain of salt.”

The TNM Classification of malignant tumors classifies the extent of cancer in a patient’s body. Each type of NET can have different characteristics.

T describes the size of the tumor and whether it has invaded nearby tissue.
N describes regional lymph nodes that are involved.
M describes distant metastases (spread of cancer from one body part to another).

The classifications below are used by the World Health Organization (WHO).

NET Grade 1
Well-differentiated, low rate of cells actively dividing.

NET Grade 2
Well-differentiated, higher rate of cells actively dividing.

NET Grade 3
Poorly differentiated, most aggressive of NETs.

Tumor Classifications by Site. (Carcinoid Only)

Foregut: Lung, esophageal, stomach, pancreas, liver, gallbladder, thymus, duodenum (1st/2nd parts), ovaries.

Midgut: Jejunum, ileum, appendix, cecum, ascending colon, duodenum, appendix, 2/3 proximal colon (descending), transverse colon. Midgut has the highest predisposition for carcinoid syndrome.

Hindgut: Distal 1/3 of transverse colon, rectum, descending colon, and sigmoid colon.
If NETs are suspected, one of the first diagnostic studies recommended is the octreoscan™ (a full body nuclear scan). It uses the radioactive isotope $^{111}$indium, that is ‘tagged’ to a somatostatin analog and binds to certain tumor receptors. It can be a 1, 2 or 3-day study; the scan can reveal elusive primaries and metastases. A positive octreoscan™ usually predicts a good response to octreotide treatment; and you must have this to receive certain systemic radioisotope treatments such as $^{177}$Lu and $^{90}$Yttrium (not FDA approved as of this printing, June 2014).

Other imaging techniques used are chest, lung, and small bowel x-rays, nuclear bone scans, CT scans, MRIs, upper GI series, $^{18}$F DOPA PET scans, $^{123}$I-MIBG scans, $^{18}$F FDG-PET, $^{68}$Gallium PET scan (not FDA approved as of this printing June 2014, but is in clinical trials). See p.19 for $^{68}$gallium clinical trials information.

Biopsy—Surgical removal of a tumor tissue sample; a pathologist will interpret tests to determine your tumor characteristics. Considered mandatory for all NET patients.

Blood (Serum) Tumor Biomarkers (assays)—Gives values of hormone levels excreted by tumors or circulating in the body. Certain substances are linked to specific cancers.

Bone Scan—A radioactive injection is given before a whole body x-ray. Useful for detecting bone metastases.

CT Scan—(Computerized tomography) Using a rotating scanner which resembles a large vanilla Dunkin’ Donut®, each complete rotation shows a separate slice of your organs. It can be done with and without contrast. Some studies require you drink dye beforehand. Do double-check your Doc’s prescription to be certain you know what the procedures are. A ‘routine’ CT scan for a NET Patient could include the chest area and/or abdomen/pelvis.

Echocardiogram—A test that uses sound waves to create a moving picture of the heart. The picture is much more detailed than a plain x-ray image and has no radiation exposure. Initially this is noninvasive, but if the view of the heart is obstructed, the technician may inject a dye for a better view. Patients with carcinoid should have this test performed routinely to detect any early valvular damage (carcinoid heart disease) which can lead to heart failure.

Endoscopic diagnostic studies—These are frequently used in addition to other scans to look inside your body, mostly the digestive tract and the colon (colonoscopy), through a long flexible tube with a camera on the end.

$^{123}$I-MIBG—A scintiscan is an imaging test that uses a radioactive substance to find/or confirm carcinoids and pheochromocytomas.

Laparotomy—The wall of the abdomen is cut to check your organs for disease.

MRI—(Magnetic resonance imaging) Combines strong magnetic fields and radio waves to form images of the body using a computer to produce detailed pictures. This is preferred over the CT scan for liver studies and patients who are allergic to iodine.

PET Scan—Positron emission tomography (PET) is a nuclear medicine imaging technique producing a three-dimensional image or picture of functional body processes.

PillCam® SB (capsule endoscopy)—The patient swallows a camera the size of a multi vitamin pill and all the images are transmitted to a recorder you wear. It is widely used for directly visualizing the small bowel.

Ultrasound—Ultrasound uses high-frequency sound waves to look at organs and structures inside the body. Unlike x-rays, ultrasound does not involve exposure to radiation. Most frequent NET diagnostic ultrasound procedures are endoscopic, abdominal, and intraoperative (during surgery). A transducer sends sound waves that bounce off tissues; these sounds are captured to create images.

Each facility has its own pre-test protocols for scans and medical procedures (blood draws, urine samples, biopsies). Most patients call beforehand, or research online to learn of any special requirements, for example fasting or eliminating certain food and medications.
Aggressive Surgery. Some patients are candidates for surgery that removes or destroys as much tumor as feasible for a cure or debulking the tumor. This is now considered the first line of defense by the NET specialists.

Staged Procedures. Sometimes a patient undergoes staged procedures (any operation done in two or more separate parts) with a rest period in between to limit surgical trauma.

Invasive. PRRT—(peptide receptor radionuclide therapy) is a targeted therapy that uses $^{90}$Yttrium and $^{177}$Lutetium with a somatostatin analog similar to octreotide and is coupled with a radionuclide-emitting beta radiation. This therapy is in clinical trials as of June 2014 at numerous sites throughout the U.S. The following link has a detailed explanation of the procedure and provides recommendations for the best way to travel to Europe (should you prefer) for this treatment. http://tinyurl.com/9l969q5

Minimally Invasive. Procedures, such as laparoscopic which is an abdominal operation performed through small incisions; not suitable for every patient.

Open Procedures.
Cryosurgery — A surgical modality; the process freezes & kills abnormal cells.
Liver transplantation — can be an option for select patients. Steve Jobs of Apple, Inc. had pancreatic NET cancer and opted for this surgery.
Neoprobe-guided surgery — Uses a gamma probe; the patient receives a radioactive substance (e.g., MIBG) that assists the surgeon in finding tumors.
Radiofrequency ablation (RFA) — This procedure uses a probe needle electrode placed inside the tumor and the heat from high-frequency radio waves, destroys or vaporizes the tumor.
Resection (debulking/cytoreduction) — See aggressive surgery above. The liver, pancreas, diaphragm, bowels, ovaries, (typical) bronchial carcinoid, lymph nodes or other involved organs can be treated with surgery. Sometimes the blood supply to certain organs is encased in tumors. It is common practice for knowledgeable surgeons to peel the tumors away from the blood vessel thus improving blood flow and making the patient eligible for a second stage aggressive approach.

Liver-directed.
Chemoeembolization — involves a catheter (thin tube) placed into the liver through an artery. The tumor site is then injected with one or more chemo-therapeutic agents along with an occluding agent (embolic) to block the blood supply to the tumor and starve it. Bland embolization is a similar process but without the chemotherapy drugs.
Cyberknife — Combines a linear accelerator with sophisticated image-guided technology. The resulting high-dose radiation beams destroys tumors with extreme accuracy.
Radioembolization — involves microscopic, radioactive beads that are delivered to the tumor area (usually within the liver) through a catheter inserted into an artery.
Targeted radiolabelled somatostatin analog — involves an intravenous injection of radioactive octreotide, or MIBG, usually in high doses.

Medical Therapies. (agents made from living organisms to treat disease). These include somatostatin analogs such as Sandostatin® (Novartis) and Somatuline Depot ® (Ipsen Pharma S.A.S.), and interferons (proteins released by host cells). The data suggest that these agents may stabilize NETs and delay their progression; research is being done to discover whether these biotherapies can keep new blood vessels from forming to provide nutrients to...
Medical Therapies.

cancer cells. Both somatostatin analogs are used as therapies for carcinoid syndrome and are thought to slow tumor growth; they may be used to treat bronchial carcinoids and p NETs.

**Chemotherapy** In the general sense “chemo” is the systemic treatment of disease by chemicals which kill cancerous cells but can also damage healthy tissue. Chemotherapy is used for aggressive NETs, e.g., atypical bronchial carcinoid and others that are poorly differentiated and have a high rate of mitosis (cell division).

**Investigative Agents** are drugs that are under study, but not yet approved by the FDA for sale in the United States. Patients may receive them by taking part in NIH (National Health Institute) clinical trials or by travelling to Europe for treatment.

**Targeted Therapies** block the growth and spread of cancer by interfering with specific molecules involved in the tumor’s growth and progression.

**Anti-tumor & Anti-angiogenic agents** Angiogenesis is the process of making new blood vessels. In a cancer patient, this same process creates blood vessels that give a tumor its own blood supply for its growth. These two agents are systemic, but do not harm normal cells. One well-known expert has been researching the use of black raspberry powder (extract) for these purposes. The number of treatments for carcinoid and other NETs has increased greatly during the last 15 years; however, *surgery is still considered the first line treatment*, if at all possible. Sometimes other treatments are used as a prelude to surgery to shrink tumors so that they become operable (see p.7).

Since almost all NET patients have their own “unique” form of disease, treatments are specific to each case and devised by a multi-disciplinary team (MDT) or by the NET specialist working with your team. **No two zebras have the same ‘stripe pattern’ just as no two NET patients have the same disease manifestations.** This list is by no means all-inclusive; not all of the treatments are optimal for all types of NETs. **Discuss any concerns with your doctor and/or your team.**

**Unknown primary** A significant percentage of carcinoid cases that present with metastatic disease of “cancer of unknown primary site” (CUPs). They are similar to midgut carcinoid patients presenting with metastatic disease with regard to hormone production, survival, and treatment. “CUP” can be an indolent disease process with slow progression over decades. These patients receive treatments similar to carcinoid patients. **Bio Theranostics** (in California) has developed genomic testing using patients’ tissue samples to help determine the tumor site of origin. For more information, visit their website, [www.biotheranostics.com](http://www.biotheranostics.com).

Most of the NET community feels “he who hesitates could be lost.” Don’t hesitate to find someone who has had any of the procedures or therapies suggested here, and dig deep to find any caveats you might have missed. There are a number of ways to do this: give a shout out on the ACOR listserv; ask Dr. Woltering directly on the ACOR listserv; contact a group leader from the list on [www.carcinoid.org](http://www.carcinoid.org); research the archives at [http://listserv.acor.org/archives/](http://listserv.acor.org/archives/); research government sites, for starters, [www.pubmed.gov](http://www.pubmed.gov) (part of National Institute of Health).
Possible Complications of Carcinoid Syndrome

Carcinoid heart disease. Some patients with carcinoid syndrome, and some without it, develop carcinoid heart disease. Carcinoid syndrome causes a thickening of heart valves, making it difficult for them to function properly. As a result, they may leak. Symptoms of carcinoid heart disease include fatigue and shortness of breath during physical activity. Your physician may recommend certain medications. Carcinoid heart disease may eventually lead to heart failure. **Doctors will detect carcinoid heart disease in 20% of patients with carcinoid syndrome (Medscape).** Surgical repair of damaged heart valves may be an option in advanced carcinoid heart disease. **Regular echocardiograms will keep you ahead of the game.**

Bowel obstruction. Signs and symptoms of a bowel obstruction may include severe cramping, abdominal pain, and vomiting. Surgery may be necessary to relieve the obstruction. A desmoplastic reaction (the growth of fibrous or connective tissue) in the bowel wall and surrounding tissue, secondary to a biological insult, such as an abnormal growth or scar tissue from abdominal surgery, can lead to a narrowing and kinking of the bowels. This can in turn lead to **obstipation (stoppage of bowel movements).**

Carcinoid crisis. This is a severe episode of flushing, low blood pressure, confusion and difficulty breathing (the same symptoms of carcinoid syndrome but all at once) Carcinoid crisis can occur in patients with carcinoid tumors when they are exposed to certain triggers, including anesthesia during surgery, and it can be fatal. Your surgical team should be aware that **today’s protocol mandates the continuous infusion of octreotide throughout surgery is best to reduce the risk of carcinoid crisis (see p.18).**

Statistics*,

- 2 out of 3 cases of NETs occur in the digestive system (G.I.). Carcinoid is the most common NET of the G.I. tract and makes up 50% of all small intestine cancers. The 5 year survival rate of those with G.I. carcinoid (no metastases) ranges from 65%-90%.
- 66% of all NETs diagnosed are carcinoids.
- Up to 44% of those reported with NETs/carcinoid have either regional or distant metastases at diagnosis as a result of delayed, correct diagnoses.
- 25%-30% of carcinoid tumors are found in the lungs (4% of all lung cancers). Most often these types of tumors are slow-growing. Estimated 5-year survival rate for typical lung carcinoid is 85%-90%.
- Estimated time to diagnosis for gastroenteropancreatic (GEP) NETs from the beginning of symptoms is 5-7 years. The probability of metastatic disease is increased the later the diagnosis occurs. Late diagnoses may be the result of misdiagnoses, lack of awareness or lack of knowledge of how to treat the disease, and a ‘wait and see attitude’ from a surprising number of physicians. The inflexibility of health insurance companies to pay for a specialist who is out of their contract network is also a factor.
- NETS are more prevalent than other stomach and pancreatic cancers—combined. (SEER database).

Between 11,000 and 12,000 carcinoid neuroendocrine tumor (NETs) cases are diagnosed each year in the United States. The number of cases has been increasing, partly because of technological advances in scans and new diagnostic tools and a growing awareness of NETs. There are at least 115,000 people in the United States living with carcinoid/NETs. Recent statistics show an incidence at autopsy of 650 cases per 100,000.

*Statistical Sources: Carcinoid Cancer Foundation, NOLA NETs, SEER database, Novartis Pharmaceutical, Elsevier Corp., Dr. Richard Warner.
Use These E’S Frequently.  
(Editor’s viewpoint as a carcinoid patient)

Don’t look back,  
You are about to become an EMPOWERED PATIENT.

Energy — Maintain your equilibrium and balance to channel your energy to understanding and learning to live with your disease. Welcome your family and friends into your “support circle”. It is vital to stay ahead of your disease to the greatest extent possible.

Educate Yourself— Use the resources on p.14 for a jump start; follow where the links lead you. Adopt the mantra “copious notes”; record your thoughts and activities, daily if you can. In today’s vernacular, own it!

Engage — Become engaged and involved in the community by interacting with your fellow patients. This community, like so many other similar groups, passes on trust-worthy, valuable information from its elders (senior “noids”) to those new to the group. “Noids” began as slang for a carcinoid patient but is now used globally for all NET patients.

Equip Yourself — Make intelligent choices in scheduling procedures, treatments, medical professionals, financial issues and your lifestyle issues. Equip yourself for appointments, emergencies, surgical and medical procedures, blood draws, and travelling. Some patients keep a travel kit in their car. With your new sense of empowerment, you will become “the driver of the car,” not the passenger, and have confidence in your knowledge to make wise health care and life decisions. The PhillyNETs support group has an information packet (free) available for those newly diagnosed which includes a silicone awareness bracelet—zebra style. Please email info@phillynets.org or call 267.288.5642.

Helpful Hints.

- Keep a current health history: date; disease; event; test; doctor and interventions. Retain support documents and/or reports.
- If you use nitroglycerin for heart issues, have hypoglycemia and use glucose, or have allergies, bring what you might need to all of your appointments for scans and blood work—just in case something unexpected occurs. If you’re claustrophobic and having a scan, tell the technicians. They’ve heard it all before. This editor wears a blindfold.
- If you are a difficult stick for blood draws, make certain to give your phlebotomist (vampire) a heads-up on any issues you have.
- It’s a good idea to wear a medical ID and keep a back-up list of your health issues with you at all times. A medical ID is an excellent way to tell those treating you that “EPI” (epinephrine) is contraindicated for NET patients; if you have allergies; or you are on certain medications.
- If you have prediabetes/diabetes or another life-threatening disease, it is important that those treating you are aware of this.
- Try and keep all your medical records in one place; a spreadsheet is ideal for a chart of dates, procedures, and test results. The NET community watches for bellweathers of its biomarkers, or any other symptom that could be a trend. If there is a rise in certain markers, be wary; a decline in these markers — is a good thing. Stability is our goal.
- Keep copies of preparation protocols for blood work, urine analysis, scans, surgery, or any chemo treatments.
- Every operation is unique—even if only by a hair breadth. Many of us keep our operating room (OR) reports with our current information. Should you need them, they are handy and not stored in the attic with old crayon drawings.
Top Internet Resource Links.

www.oncolin.uk.pen.edu—University of Pennsylvania’s cancer site (the web’s first cancer site).
http://www.ochsner.org/programs/neuroendocrine_tumor_program/ —
The neuroendocrine program at Ochsner Medical Center in association with Louisiana State University Health Center. (Dr. Eugene Woltering, Clinic Director).
www.interscienceinstitute.com—Supports NETs conferences, publishes peer-reviewed papers and Neuroendocrine Tumors: A comprehensive Guide to Diagnosis & Management which has detailed descriptions of blood tests/biomarkers.
http://www.radiologyinfo.org/ — Excellent site for info on scans & studies.
clinicaltrials.gov/search/open/condition=%22Carcinoid+Tumor%22 — current clinical trials.
www.carcinoid.org—Carcinoid Cancer Foundation. Educating patients and medical professionals about carcinoid & other (NETs); supports research.
http://www.carcinoid.org/content/videos — Videos of lectures.
www.health.gov — Portal to government health agencies (includes Affordable Care Act (Obamacare) and Medicare.
www.rarediseases.info.nih.gov — NETs are listed here.
http://www.biotheranostics.com/—State-of-the-art molecular profiling which can find an unknown primary with a degree of certainty.
http://netcancerday.org — Website raising NET awareness worldwide.
www.scholar.google.com — Search for (research) clinical/medical papers.

Caring for Carcinoid Foundation—U.S. non-profit (all-around resource)
http://www.caringforcarcinoid.org/videos?page=1
http://www.caringforcarcinoid.org/clinical_trials
http://www.caringforcarcinoid.org/doctor-database

Carcinoid Cancer Awareness Network—U.S. non-profit (events & referrals)
http://www.carcinoidawareness.org — Informational site. This group organizes many fundraising events & conferences and archives relevant videos on this site.

Carcinoid Cancer Foundation—U.S. non-profit (best for newly diagnosed)
http://www.carcinoid.org/patient/living-with-carcinoid/nutrition
Comprehensive discussion of nutrition for NETs.
http://www.carcinoid.org/patient/treatment/find-a-doctor
Experts are in a blue-shaded box.
http://www.carcinoid.org/support/support-groups/directory
USA and International listings for support groups.

http://www.youtube.com/watch?feature=player_embedded&v=9U6q78a1xaQ
Three of the world’s leading experts on Carcinoid and NETs cancers introduce the ABC’s of these diseases: Dr. Richard Warner, Dr. Edward Wolin, and Dr. Eugene Woltering.

Net-pedia.org — a project of The Patients’ Project — U.S. non-profit
Coming soon...
Getting Started.

Since most primary care physicians do not know a great deal about the diagnosis or treatment of NETs, this not only deprives you of medical support at its most personal level, but, you may find that your physician who has always been a comfort to you, can’t adequately support and advise you in the way you’d like. The responsibility of educating your doctor is yours, if you choose to do so. Most patients find that their local physician and a specialist (regional or distant) insures their multi-disciplinary care runs smoothly.

You are far from being alone. The nationwide NET community is close-knit with a robust and fiercely loyal attitude; it rallies around patients or caregivers who need support or information, especially those who are new to the community. The affectionate term “zebra hugs” demonstrates our concern and caring for fellow “Noids” (diminutive of carcinoid and nickname for a patient with NETs). Like most communities, we pass the torch of knowledge so that you can share information and resources with those who come after you.

- **Before you do anything else, join ACOR.org** (Association of Cancer Online Resources—carcinoid list—see p.14). It is moderated by Dr. Eugene Woltering, one of the top NET doctors in the USA. Yahoo hosts a carcinoid, carcinoid lung group, islet cell and a doctor’s group. They are all informational, not support groups. Thanks to Charles Hamilton for creating and managing these valuable groups:
  - https://groups.yahoo.com/group/lungnoids
  - NET_IsletCell-subscribe@yahoogroups.com (email address)
  - https://groups.yahoo.com/neo/search?query=carcinoid
- You’ll find numerous peer-reviewed clinical papers of interest on the Internet. Below are a few links where you can begin a search. Each has extensive information about neuroendocrine tumors as well as listings of additional resources (see p.11).
  - www.caringforcarcinoid.org/peer-reviewed-publications
  - www.carcinoid.org
  - www.ncbi.nlm.nih.gov/pubmed

**Get a second expert opinion:** www.carcinoid.org has an excellent list of experts. If necessary, get a third or fourth opinion. Have your doctor(s) join the e-group at www.carcinoid.org where doctors can ask questions of carcinoid specialists. By the time you’re on the way to understanding and living with your disease, you will probably have the support of a multidisciplinary team for your care. However, if your doctor is in a “huff” and dismisses your request to work within the parameters of a NET expert or team, it’s time to move on. It’s not easy. Ask someone about the “yellow corvette” parable, or read it on PhillyNETs’ website, www.phillynets.org.

**For Doctors:** www.nanets.net The purpose of this professional organization is to improve NET disease management through increased research and educational opportunities. www.enets.org is a group of 1000 European physicians from different specialties.

**Ask Inter Science Institute** to send you two free copies of their latest book on the diagnosis and management of NETs. Give one to your doctor. 1.800.255.2873. Mia Tepper is our contact there and volunteered to help edit this handbook.

- If you are on Sandostatin® LAR or daily shots of octreotide (sub-q), keep a copy of the prescribing information and give one to your doctor. Novartis Pharmaceutical, the manufacturer of Sandostatin® LAR, has a large web presence, http://tinyurl.com/9y48luc
- If you’re using Somatuline Depot® (lanreotide long-acting) Ipsen’s NET drug, click on http://somatulinedepot.com
**Exercise** — Of course you should exercise, but don’t "over-exercise" which could bring on excessive flushing and other symptoms. This editor’s cardiologist has approved swimming, walking, and leaving my desk chair ever so often. Some patients run in marathons, bike, practice yoga, golf, dance. Most everyone has different levels of tolerance and physical limitations for exercise. Check with your primary Doc and/or specialists before starting or changing your exercise plan after being diagnosed.

**Emotion** — Temper your moods. Anger can provoke symptoms. Fear is also a provocateur for some; *scanophobia* (fear of scans+claustrophobia+scan outcomes) is a primary stressor for many NET patients.

**Ethanol** — Alcohol. Some patients can still drink, some can’t. Red wine can provoke your symptoms, so most Docs recommend white wine or beer instead.

**Eating** — This is a very individual thing. Many avoid spicy food; aged foods like salami, certain cheeses, or any foods containing tyramine, can trigger an unwanted response. A number of patients can’t eat cooked tomatoes; they eat pizza and spaghetti at their own risk. You’ll find your way. Citrus fruits can also affect NET patients. On p.11 you’ll notice a link to the Carcinoid Cancer Foundation’s nutrition page. It’s a must read. Be aware that certain bio-marker tests might require some temporary dietary changes.

**Epinephrine** ("epi") — This is the first intervention EMTs (*emergency medical technicians*) want to use if you’re in the middle of a heart issue or allergic reaction. This editor’s medical ID bracelet reads “carcinoid, no epi”. EMTs need to be aware of its possible effect on carcinoid patients. Your dentist should also be told; he can give you a local anesthetic without epi. These numbing agents are shorter-acting without epi, and you may require additional injections. **One of the things to be wary about are chemicals/medicines that end in "ine". Morphine is an exception.** The other drugs that end in “ine”— like caffeine, theobromine, and norepinephrine can trigger a carcinoid crisis. Any other drugs— talk to your pharmacist; if they end in “ine” ask him if the drug has amine-like effects. *(Thanks to Dr. Eugene Woltering for this advice).*

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**Worldwide N.E.T. Cancer Awareness Day • November 10**

“We constantly need to raise awareness of NET cancers among decision-makers, health professionals and the general public ... information is key to improving quality of life and prognosis for NETs cancer patients; raising awareness is therefore one of our primary goals”. This quote is from the website of the World NETs Community. To learn more: [http://netcancerday.org/](http://netcancerday.org/).
What's in Your Toolbox?

**THE Internet**

- Close to 50 U.S. Support Groups. Some groups cover an entire region.
- The Carcinoid Cancer Foundation website: [http://www.carcinoid.org/patient/treatment/find-a-doctor](http://www.carcinoid.org/patient/treatment/find-a-doctor) Click for a list of specialists worldwide. Those experts meeting certain criteria are shaded in light blue. Most every doctor listed will consult with your local doctor if appropriate. See p.11 for more links.
- Caring for Carcinoid Foundation website. [www.caringforcarcinoid.org](http://www.caringforcarcinoid.org) (See p.11)
- Inter Science Institute’s publications and services. [www.interscienceinstitute.com](http://www.interscienceinstitute.com)
- ACOR (Listserv moderated by Dr. Eugene Woltering and other volunteers). Association of Cancer Online Resources. [www.acor.org](http://www.acor.org)—carcinoid cancer and other NETs has over 1300 members. “Provides information, support, and encouragement for patients, their caregivers, family members, and other supporters”. It also welcomes healthcare professionals who want to learn about these diseases.

NET cancers, which are among the rarest worldwide, in this editor’s opinion, head up the list of “do-it-yourself” diseases. It is ultimately up to the patient to find resources for his medical care. We encourage you to use your wherewithal and ingenuity to **R.A.C.E.** (research, assess, choose and employ) and expeditiously begin your medical care. A quick start is emotionally satisfying in the long run and these lists are a good starting place.

**Resources & Support**

- Hospital-based NET clinics and multidisciplinary programs.
- Others who are already living as NET patients can be your mentors.
- Your team of doctors. Your primary care physician as traffic director. Provide him/her with the resources and he/she will probably join your team.
- Novartis Pharmaceuticals (or the manufacturer of your medications).
- Ipsen Pharmaceuticals (or the manufacturer of your medications).
- Social workers, family therapists, psychologists and psychiatrists.
- Groups that will help patients financially in need including, but not limited to Internet resources such as crowd-funding and non-profit foundations.
- Your family friends, neighbors, and acquaintances.
- Integrative medical practitioners.
- ISI (Inter Science Institute) handbook of NETs and research papers for biomarkers.
- Experts and specialists are scattered geographically throughout the US. Visit [www.carcinoid.org](http://www.carcinoid.org) to review their listings (use the top menu “Patients”).
- Clinical trials (National Institute of Health, Bethesda MD)
- Regional conferences; the national conference is currently held every other year in different locations across the U.S.

**Paraprofessionals**

- Phlebotomist
- Dental hygienist
- X-Ray and scan technicians
- Pharmacist
- Ultrasound technicians (cardiac, etc.)
- Physical Therapists

**Genetics and NET factors** that may increase the risk for G.I. carcinoid include a family history of **MEN1** (multiple endocrine neoplasia, type 1) and having certain conditions that affect the stomach’s acid production. **MEN2** is also a genetic condition presenting in three subtypes. Sex, race and age factors have been studied; you’ll find many multi-disciplinary teams recommend genetic counseling and testing when appropriate.

**Internet**

- Genetics and NET factors that may increase the risk for G.I. carcinoid include a family history of **MEN1** (multiple endocrine neoplasia, type 1) and having certain conditions that affect the stomach’s acid production. **MEN2** is also a genetic condition presenting in three subtypes. Sex, race and age factors have been studied; you’ll find many multi-disciplinary teams recommend genetic counseling and testing when appropriate.
Useful Facts to Know about Testing.

Chromogranin A (CgA) & PPIs (NOLA NETs Protocol)

Many NET patients are on PPIs (proton pump inhibitors, e.g., Nexium®, Prilosec®, Prilosec OTC® and Previcid®) which can cause artificially high “CgA” readings. CgA is currently the gold standard of tests to diagnose and show NET disease progression. Experts recommend that you not take the medication for one month before being tested. Check with your own physician.

Proton pump inhibitor (PPI) use increases circulating gastrin, which in turn increases the amount of stomach acid produced. Increased gastrin stimulates the enterochromaffin-like cells of the stomach to produce chromogranin A. Since pancreastatin is not increased with PPI use, a number of patients have chosen to substitute this assay for the CgA so they can continue using PPIs. The consensus of NET experts is that there are two choices: 1. stop the PPIs for a short time, or, 2. your doctor can substitute the pancreastatin assay.

What can you do? In order to obtain baseline test values you will need to stop using PPIs. However, you should not stop taking PPIs suddenly; but rather taper off usage by replacing your PPI with a H2-blocker such as Pepcid (famotidine) or Zantac (ranitidine) which can be purchased over the counter. This booklet was designed as a constructive aid for NET patients to grow a relationship with their physicians through dialogue and information. Risks and benefits of all treatments mentioned throughout this handbook should be discussed with your physician and/or multidisciplinary team. Therefore patients should consult their physicians prior to changing their medication protocol and not just switch from PPI’s because of the implications of CgA levels. Every patient is different, just as no two zebras have the same stripes.

✔ The 5-HIAA 24-hour urine test shows levels of a metabolite of serotonin (hormone secreted by functioning carcinoid tumors). Some medicines and foods can increase the 5-HIAA found in your urine, so it’s recommended that you eliminate certain foods. Each diagnostic lab, e.g., Quest or Labcorps, has its own protocols so it’s a good idea to check with your lab beforehand. The list can include bananas, plantains, avocados, kiwis, plums, eggplants, tomatoes, pineapples, walnuts; acetaminophen, salicylates, and L-dopa.

✔ There is a new assay, 5-HIAA plasma (blood). Contact ISI for the details. This assay requires special tubes called “Z” tubes (also required for ISI’s pancreastatin and neurokinin A assays). They are proprietary to Inter Science Institute; ISI will ship them to you for free. There is no special preparatory diet, no “lugging the jug” and the test has the same degree of accuracy as the more traditional 5-HIAA 24-hour urine.

✔ Most facilities (hospitals, clinics, cancer centers, diagnostic labs) now have online programs (patient portals) that allow patients to view and print test results, prescriptions, appointments, and other useful information for managing their care. All programs are HIPAA-compliant and electronically secure.

✔ According to Dr. Eugene Woltering “Progression-free” means:
  ✔ No new tumors  ✔ No tumor growth  ✔ No increasing symptoms

Woltering’s Adage “Normal is normal”.

✔ Caveat (carcinoid patients only): In 1/3 of carcinoid patients the 24-hour urine 5-HIAA test is negative, therefore the 5-HIAA and chromogranin A (CgA) should be done together, possibly along with a serotonin blood level. Additionally, these two tests could show a positive result, even with a negative 5–HIAA.
Ablation
Surgical removal of tumor (see p.7).

Radiofrequency Ablation

Acronyms
- CBC Complete blood count
- GI Gastrointestinal
- SUV Standard Uptake value
- CNS Central nervous system
- EUS Endoscopic ultrasound
- CAP Chest, Abdomen, Pelvis
- SSA Somatostatin analog (see next page)

VEGF Vascular endothelial growth factor is a signal protein that restores oxygen to tissues when blood circulation is inadequate.

Adenoma
A benign epithelial tumor; the cells form recognizable glandular structures. Epithelium is one of the four basic types of tissue. It lines cavities and surfaces of structures throughout the body.

Analog
A chemical compound having a structure similar to another except that one component will be different. It may be similar or opposite metabolically. Octreotide is an analog of somatostatin.

Angiogenesis
The physiological process through which new blood vessels form from pre-existing vessels. Affected by drugs, diet, lifestyle.

Anti-angiogenic
An anti-cancer strategy that prevents new blood vessels from growing and providing nutrients for actively proliferating tumor cells. Most of today’s anti-cancer drugs indiscriminately target all rapidly dividing cells.

Assay
An investigative lab procedure to assess/measure the presence, amount, or functional activity of a drug, biochemical substance or hormone.

Biomarker
Provides a measurable characteristic that shows the severity or presence of some disease or physiological state.

Cancer
A malignant tumor of potentially unlimited growth that expands locally by invasion and systemically by metastasis.

CAP-TEM (NEW)
Combination capecitabine and temozolomide (CAPTEM) offers long-lasting neuroendocrine tumor control for patients whose tumors have not responded to standard high-dose octreotide therapy.

Chemotherapy (Systemic)

Chromogranin A
In the granin family of neuroendocrine secretory proteins and an indicator for carcinoid syndrome. Chromogranin A produces several peptide fragments, including pancreastatin. It identifies a range of neuroendocrine tumors and is highly specific for benign or malignant NET cells.

Embolization
Bland embolization (targeted) is an injection of small particles, sometimes mixed with liquid agents, to block the blood supply to liver metastases (see p.7 for additional embolization procedures).

Enterochromaffin
Also known as "Kulchitsky cells". A type of enteroendocrine and neuroendocrine cells occurring in the epithelia lining, the lumen (interior) of the digestive tract and the respiratory tract. About 90% of the body's serotonin (5-HT) is contained in these cells.

Epinephrine
(Adrenaline/Adrenalin) A hormone & neurotransmitter.

Everolimus
Also known as Afinitor. Class of drug: protein kinase inhibitor (along with Sunitinib). Used to treat pNETs.

5-HIAA
Main metabolite (any substance produced during digestion or other bodily chemical processes) of serotonin. Used in analyzing urine or plasma samples to determine serotonin levels in the body.

Hormone
A class of regulatory biochemicals produced by glands and transported by the circulatory system to a distant target organ to coordinate its physiology and behavior. Simply, they are chemical messengers.

The definitions on pp. 16-17 were sourced from the following: Wikipedia, Medline Plus, Cancer.gov, MedicineNet.com, CancerCenter.com, Merriam-Webster Medical Dictionary, Pfizer Oncology.
### Incidence
The number of new cases of a condition, symptom, death, or injury that develop during a specific time period. **Prevalence** is a measure of disease that allows determination of a person's likelihood of having a disease. The number of prevalent cases is the number of cases existing in a population divided by the total population.

### Intervventional Radiologist and/or Oncologist
“**Surgical radiology**” is a sub-specialty of radiology utilizing minimally-invasive image-guided scans and procedures to diagnose/treat diseases in almost every bodily system using the least invasive techniques available.

### Idiopathic
Of unknown cause or arises spontaneously.

### Ischemia
Is a restriction in blood supply to tissues, causing a shortage of oxygen and glucose needed for cellular metabolism.

### Isotope
A radioactive form of an element.

### Ki-67
A marker to determine the growth fraction of a given cell population or how fast your cancer cells are actively dividing.

### Metabolic Profile
A basic metabolic panel is a group of blood tests that provide information about your body's kidney function, blood acid/base balance, and blood sugar levels, that is, the processes that convert and use energy. **Metabolites** are usually small molecules that are products of metabolism.

### Mitotic Index
The mitotic index is a prognostic factor predicting both overall survival and response to chemotherapy in most types of cancer.

### Neurotransmitter
These are chemicals our bodies that are the core components of the nervous system. They transmit signals (electrical or chemical) across a **synapse** (structures signals travel over) from one neuron (nerve cell) to another.

### Primary Tumor
A tumor growing at the anatomical site where tumor progression began and proceeded to yield a cancerous mass.

### Resection
The surgical removal of part of an organ or structure.

### Debulking or Cytoreduction
The surgical removal of part of a malignant tumor which cannot be completely excised; this enhances the effectiveness of radiation, chemotherapy, or allows for future surgery.

### Sequential Multi-Modality Treatment
Treating cancer by optimizing and integrating surgery, radiotherapy (RT), and systemic therapy.

### Serotonin
A neurotransmitter/hormone (see above) primarily found in the G.I. tract, platelets, and the central nervous system.

### Well, Moderately or Poorly Differentiated Cancer Cells
Well-differentiated cancer cells look more like normal cells and tend to grow and spread slower than moderately, poorly differentiated or undifferentiated cancer cells.

### Somastastatin
GHIH (growth hormone inhibiting hormone) inhibits the activity of certain pancreatic and gastrointestinal hormones.

### Syndrome
Group of symptoms that collectively characterize a disease.

### Tumor or Neoplasm
An abnormal mass of tissue. Can be solid or fluid-filled. Tumors can be **benign, pre-malignant, or malignant.**

### Tumor Marker
Substances that can be found in the body (usually in the blood or urine) when cancer is present. Along with other tests, tumor markers can be used to help show if cancer is present.
**Use Of Octreotide During Surgery: Prophylaxis Against Carcinoid Crisis**

Dr. Eugene Woltering, our medical advisor and our conscience, felt very strongly that the following protocol for octreotide during surgery be disseminated by patients to the anesthesiologists and surgeons who treat them since this protocol is not as well-known as it should be. You’ve read on p.9 that carcinoid crisis can be very serious, and since more and more medical teams are choosing surgery as the first intervention, a knowledge of precautions used to minimize the risk of triggering a crisis during surgery is extremely important. “Our NOLA NETS group uses the following protocol, others use less; I can’t speak to their results, but even with these “higher than others” type dosing, we have had a 3% incidence of carcinoid crisis out of about 500 operating room (OR) visits versus 24% when only a 500 microgram bolus was given prior to surgery”.

**[ALERT] Doctor-speak:** Two hours before surgery give 500 micrograms of octreotide acetate IV push. Then start a 500 microgram per hour IV infusion - start this immediately after the IV push and continue infusion during and after surgery. Depending on the severity and duration of surgery, taper the infusion over 1-24 hours, say for colonoscopy, taper over 1 hour; after huge liver cases, taper over 12-24 hours.

**Several warnings are in order.** If the patient becomes hypotensive do not use pressors such as epinephrine, norepinephrine or dopamine except as a last resort. To treat the hypotension, use fluids and 1-5 mg bolus of octreotide (can repeat). We have also seen two cases of malignant hyperthermia that occurred as part of the carcinoid crisis. We used dantrolene in normal doses along with rapid fluid administration and octreotide bolus administration (bolus: a medication, drug or other compound given to raise its concentration in blood to an effective level) and the hyperthermia responded to this treatment. “If all else fails, print this out and hand it to your anesthesiologist along with my cell phone number, 504.884.3555, if they get into trouble have them call me day or night”.

**Patient Experience:** This editor experimented during several recent operations to document what a carcinoid patient can do to help assure a successful outcome. Giving a nicely typed sheet of paper with the above critical information to someone “in charge” who speaks “medical” is like handing out a car wash flyer to passersby during NYC rush hour.

- Communicate with the surgeon/staff weeks (2 maybe) before surgery about the octreotide prophylactic for carcinoid crisis; continue until the anesthesiologist takes pity on the OR (operating room) staff and anesthetizes you.
- The anesthesiologist is your friend. He’s the man (or woman). I have used the words “death” and “coma” to get their attention. I always asked to see the bottle of octreotide. They did forget the octreotide for one of the operations; this held up surgery for two hours while they located some. After an ah-hah moment, we were good to go.
- Beware of any “Doc” who tells you that he knows the protocol from his textbook in medical school. Begin your mission to speak to this Doc about 1 week before your scheduled operation. The hospital will tell you they never know the staff schedule beforehand. Work around that. Ask to speak to head of anesthesiology if need be. When you receive your insurance documents, make certain the charge for octreotide appears.
Used in Europe and Australia, the $^{68}$Gallium DOTATATE PET/CT scan is a high resolution scan that is able to detect tumors not seen by traditional MRIs, PET scans, CT scans or Octreoscans™. $^{68}$Gallium DOTATATE has a very high affinity and attaches tightly to the somatostatin receptors making this scan more effective at diagnosing smaller tumors and metastases. Currently, the average time to proper diagnosis (from onset of symptoms—(see p. 4) exceeds 5 years. NETs often grow and metastasize prior to proper diagnosis. Therefore, early detection of smaller NETs, lymph node involvement and metastases is critical for appropriate treatment and long-term survival.*

* Courtesy The Carcinoid Cancer Foundation and Dr. Campeau, NOLA

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<tr>
<th>Trial Site</th>
<th>Principal/Contact</th>
<th>Phone and Status</th>
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<tbody>
<tr>
<td>Indiana University Health University Hospital Indianapolis IN ** IND = Investigational New Drug</td>
<td>Dr. James Fletcher Chief, Nuclear Medicine Director, Cancer Imaging Cnt. (as of June 2014)</td>
<td>P 317.944.1800 Under an Expanded Access IND** from the FDA. (Not a clinical trial)</td>
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<td>UCLA Nuclear Medicine &amp; Radiology, Ahmanson Biological Imaging Center Los Angeles CA</td>
<td>Dr. Johannes Czernin Principal Investigator (as of June 2014)</td>
<td>P 310.794.1005 Expected to end soon</td>
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<tr>
<td>Excel Diagnostics Houston TX (Only non-university site)</td>
<td>Dr. Ebrahim Delpassand Principal Investigator (as of June 2014) Ms. Susan Cork-Contact</td>
<td>P 713.341.3203 Ongoing</td>
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<tr>
<td>Stanford University Stanford CA</td>
<td>Dr. Andrei Iagaru Principal Investigator (as of June 2014) Euodia Jonathan-Contact</td>
<td>P 650.723.7419 Ongoing</td>
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<tr>
<td>University of California (SF) Helen Diller Cancer Center San Francisco, CA</td>
<td>Dr. Emily Bergsland Clinical Trials Dept. (as of June 2014)</td>
<td>P 877.827.3222 Recruiting</td>
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<td>National Institutes of Health, (NCI) Bethesda, MD</td>
<td>Dr. Electron Kebebew Principal Investigator (as of June 2014)</td>
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<tr>
<td>University of Iowa, Iowa City, IA</td>
<td>Dr. Sue O’Dorisio Principal Investigator (as of June 2014)</td>
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<tr>
<td>Vanderbilt –Ingram Cancer Center, Nashville, TN</td>
<td>Dr. Eric Liu Principal Investigator</td>
<td>P 615.322.2391 Closed</td>
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<td><strong>Summer 2014, Louisiana State University Health Science Center, Affiliate: Ochsner Medical Center, Kenner, LA NOLANETS</strong></td>
<td>Dr. Richard Campeau Principal Investigator Dr. Eugene Woltering, Clinic Director (Louisiana Neuroendocrine Tumor Specialists Clinic)</td>
<td>P 504.464.8500 Beginning Summer 2014</td>
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This handbook was made possible by a grant from the Caring for Carcinoid Foundation (CFCF). CFCF is happy to support neuroendocrine patient and advocate groups in their efforts to provide information through projects like these. Any views or opinions expressed in this piece are solely those of the author and do not necessarily represent those of the Caring for Carcinoid Foundation. CFCF is the most focused nonprofit funder of carcinoid and pancreatic neuroendocrine cancer research.

We hope this handbook will inspire conversation between NET patients and the medical professionals who treat them. Since we are not medical professionals, we recommend you consult with your physician team for all medical issues.

Our mission is to create awareness of neuroendocrine tumors (NETs) and a bridge to medical resources, support, education and the professional community for all NET patients.