Neuroendocrine & Carcinoid
Acknowledgment

This slide set was medically reviewed by Dr. Yi-Zarn Wang, DDS, PC, MD, FACS in August 2018.
Workshop Overview

- Introductions
- What Are Neuroendocrine Tumors (NETs) unicoreinvestor?
- Be Part of Your Health Care Team
- Understanding Your Treatment Options
- Clinical Trials
- Managing Side Effects
- Living with NETs and Carcinoid Cancers
- Questions & Answers
Neuroendocrine Tumors

Gastrointestinal and Pancreatic Neuroendocrine (Carcinoid) Cancers
Cancer Doesn’t Have You

You or your loved one may have been diagnosed with cancer, but that doesn’t mean that “cancer has you.”

• Get educated
• You are not alone – have hope and find support
What Are Neuroendocrine Tumors?

• NETs are less common tumors that start in neuroendocrine cells — these cells have traits of nerve cells and hormone-producing cells
• Most of NETs are cancers, but NOT all NETs are cancers — this program is about tumors that are cancers (can spread in the body)
• About 12,000 people in the U.S. are diagnosed with NETs each year
• New cases are increasing by about 5% yearly
• More than 125,000 people in the U.S. are living with NETs
Neuroendocrine Tumors (continued)

- Most common NETs are NETs (carcinoid) of the:
  - Gastrointestinal (GI) tract: Stomach, Duodenum, Small Intestine, Appendix, Colon, Rectum
  - Pancreatic Neuroendocrine Tumors (PNETs)
  - Lung
  - Other endocrine organs: Pituitary, Thyroid, Parathyroid, Thymus & Adrenal
  - Skin

- NETs (Carcinoid tumors) can also develop in other parts of the body
- Some NETs make hormones that cause symptoms (carcinoid and other syndrome)
- NETs are *usually* slow-growing
Classifications of NETs

• Neuroendocrine (carcinoid) tumors are often described by site of origin (e.g., foregut, midgut, hindgut) and vary by:
  - Anatomic locations (Specific part of the body)
  - Size
  - Stage (the extent of your tumor has spread)
  - Grade (how quickly the tumor is likely to grow and spread)
  - Differentiation (How mature the tumor cells are in development)
  - Hormonal production (functional vs nonfunctional)
  - Genetic changes (specific traits or mutations)

• Ask your health care team about your NET so you can participate in treatment decisions.
NET Symptons

NETs can range from causing no symptoms to severe symptoms.

Common symptoms of NETs may include:
- Diarrhea
- Flushing (redness in face)
- Abdominal pain
- Wheezing
- Intestinal ischemia or bowel obstruction
- Racing heartbeat (palpitations)
- Quick changes in blood pressure
- Low or high blood sugar
A pheochromocytoma can be cancer and:
- Usually starts in the adrenal gland but can start in other parts of the body
- Makes excess amounts of “fight-or-flight” hormones and can cause
  - High blood pressure
  - An increased heart rate

May be found during an imaging test for another medical condition

Is often treated with surgery, MIBG-I 131 radiotherapy and alpha-adrenergic blockers (medicines used to lower blood pressure)
NETs tumors can be hard to diagnose. It may take time to get the right diagnosis because:

• Local or small tumors may not cause any symptoms
• Presenting symptoms are often vague
• Symptoms are common to other diseases (mimicking other conditions)
• Imaging studies and tumor markers maybe useful to alert the care providers
• Biopsy of a suspicious mass or more commonly a liver metastasis is usually how the diagnosis is eventually made
Confirming the Diagnosis

Other tests help to:

• Confirm the diagnosis
• Stage your cancer (extent of disease)
• Identify your treatment needs
• Blood and urine tests measure tumor markers and genetic traits of your tumor
• Imaging tests help identify your tumor location and if it has spread
Functional and Nonfunctional NETs

NETs can make a variety of substances (hormones, peptides and proteins)

- Most Mid-gut and Foregut NETs are functional – they cause different syndromes
  - “Functional tumors” release hormones or peptides to cause carcinoid or other syndromes

- PNETs can be functional but more commonly they are non-functional
  - “Non-functional tumors” don’t cause syndrome only mass effect

- Hind gut NETs are almost always nonfunctional
Carcinoid Syndrome

- Carcinoid syndrome occurs because serotonin or other tumor cells released hormones/peptides have bypassed the liver clearance.
- Carcinoid syndrome occurs in only 10% to 20% of patients with NETs; after tumor has metastasized to the liver, retroperitoneal lymph nodes or ovary.
- Most carcinoid tumors have somatostatin receptors for somatostatin analogues to bind thus blocks serotonin and other hormone surges which cause many of the symptoms for which carcinoid tumors are known.
Common Symptoms of Carcinoid Syndrome

- Diarrhea
- Flushing
- Stomach cramps
- Wheezing
- Asthma
- Niacin deficiency

Symptoms of carcinoid syndrome, especially diarrhea, can significantly impact quality of life by limiting ability to work or leave the house.
Be Part of Your Health Care Team
Choosing Your Health Care Team

Your health care team may include:

- Several doctors (a gastroenterologist, oncologist, endocrinologist, surgeon, radiologist, nuclear medicine specialist, pathologist, cardiologist)
- A clinical nurse specialist
- A nurse navigator
- Social worker
- Physical therapist
- Nutritionist
- And others
Choosing Your Health Care Team (continued)

• Communication is important! You need and deserve a health care team you can trust, who can answer your questions, and give you the time to talk about your symptoms, side effects, emotions and treatment options, expected outcomes and costs of care.

• Your health care team should be available, and give you emotional support and excellent care.

• You should feel respected and understood.

• You should feel comfortable with your health care team’s level of expertise.
You’re an important member of your health care team – work with them!

• Ask them to explain your diagnosis, treatment options, test results and costs of care so you can share in making treatment decisions
• Discuss your needs and goals for treatment
• Give your medical history with any medicines (prescribed and over the counter), vitamins and other supplements you take
• Ask for copies of your test results
• Write down questions to bring them to your visits
• Ask for recommended online and print sources of information and support

*Bring a family member or friend with you to visits— they can help ask questions, take notes and provide support.*
Understanding Your Treatment Options
Your treatment is tailored to your:

- Tumor classification
- Size
- Location
- Stage
- Grade of the tumor
- Differentiation of the tumor
- And your overall health, symptoms, your needs and preferences
- Treatment goals are to stop or slow tumor growth and manage your symptoms
- Often, your treatment plan will be a combination of treatments
Treatment Options

• Surgery
• Non-surgical treatment may be combined with or used instead of surgery
• Supportive (palliative) care
  – Eases your symptoms and side effects of treatment
  – Helps with your emotional and social, as well as physical, needs

Getting supportive along with your other treatment may improve your quality of life
Surgery

• Surgery is the most effective & durable 1st line treatment for all well differentiated, low or intermediate grade NETs in low surgical risk patients.

• With surgery, your surgical oncologist removes the tumor along with some surrounding healthy tissue, known as a margin.

• For an early and localized NETs including pheochromocytoma and some other tumors, a less invasive type of surgery (laparoscopic surgery) may be an option

• Surgery can be curative for people whose tumors haven’t spread or caused carcinoid or any other syndrome
<table>
<thead>
<tr>
<th>Tumor Site</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix</td>
<td>Appendectomy is adequate if tumor is &lt; 1.5 cm without any poor prognostic pathologic features. Tumor &gt; 1.5 cm or with poor prognostic features may need a right hemicolecction.</td>
</tr>
<tr>
<td>Intestines</td>
<td>Most common site; extent of surgery depends on tumor size and any spread; helps decrease carcinoid syndrome, pain, prevent further spread, increase survival.</td>
</tr>
<tr>
<td>Liver</td>
<td>Rarely the primary site; a very common site for spread; surgery alone or combined with other treatment can extend life and ease symptoms; liver-directed therapy may be an option.</td>
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<tr>
<td>Lung</td>
<td>Various types of surgery may be used to remove affected parts of the lung.</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>Common site of disease spread; if surgery is an option for the primary (the original tumor), lymph nodes in the affected area shall be removed.</td>
</tr>
<tr>
<td>Rectum</td>
<td>Small rectal tumors (&lt; 1 cm) can usually be removed by an minimally invasive endoscopic excision; tumors ≥1 cm may require a formal oncological resection of the rectum.</td>
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<tr>
<td>Stomach</td>
<td>Gastric carcinoids have 3 different types, each needs to be treated accordingly. Endoscopic excision maybe feasible for smaller tumors; but definitive and extensive surgery may be required.</td>
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</tbody>
</table>
Non-surgical Treatment Options

- Somatostatin analogues
- Mammalian target of rapamycin (mTOR) inhibitors
- Peptide receptor radionuclide therapy (PRRT)
- Systemic Cytotoxic Chemotherapy
- Immune/Targeted therapies
- Vascular endothelia growth factor (VEGF) inhibitors
- Percutaneous ablative therapy
- Stereotactic radiation

These treatments are not cures, but they do:
  - Shrink tumors
  - Stop or slow tumor spread
  - Ease symptoms
• Radiation therapy uses high-energy x-rays or other particles to destroy cancer cells
• Conventional radiation may be used when an NET has spread bone or brain
• Stereotactic radiation for a small localized tumor if surgery is not an option
• The most common conventional radiation is external-beam radiation
• PRRT (Peptide receptor radionuclide therapy) and radioembolization are two other types of radiation therapies which using energy emitted form different radioisotopes to kill tumor cells.
Chemotherapy

• Systemic treatment (travels throughout the body to kill rapidly dividing cells) may be used for patients with a high grade, poorly differentiated NETs or low grade NETs that have spread (metastasized) and progressed while on other therapies.

• Chemotherapies are used in combinations that may include Capectabine/Temozolomide, Carboplatin/etoposide, streptozocin/doxorubicin or others 5-fluorouracil based chemo regiments

• Mostly given intravenously (IV), some chemo is in pill form

• Chemoembolization may be used to treat liver tumors – it cuts off the blood supply to the tumor and may bring high doses of chemo directly to the tumor
Ablative Therapies

• Ablative therapies include:
  – Hepatic artery embolization
  – Radioembolization
  – Radiofrequency ablation
  – Peptide receptor radionuclide therapy

• Length of response varies, but these therapies can be repeated

• The potential short-term benefits are:
  – Decreases tumor size
  – Decreases symptoms
  – Slows and/or halt the tumor progression
## Ablative Therapies (continued)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Description</th>
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<tbody>
<tr>
<td>Hepatic artery embolization</td>
<td>Blocks tumor blood supply by injecting either “embolitic particles” or embolitic particles plus chemotherapy into the hepatic (liver) artery</td>
</tr>
<tr>
<td>Radioembolization</td>
<td>A selective internal radiation therapy (SIRT); minimally invasive, combines embolization and radiation therapy to block liver tumor blood supply and kill tumor cells</td>
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<tr>
<td>Radiofrequency ablation</td>
<td>Minimally invasive, uses high frequency electrical current to generate heat to destroy tumor; can be done laparoscopically, often done with liver resection; may not work for tumors &gt;3 cm and for tumors &gt;5 cm, my need multiple overlapping applications</td>
</tr>
<tr>
<td>Peptide receptor radionuclide therapy</td>
<td>Combines SSAs, ligands and radionuclides to form radiopeptide complexes that are injected into vein to attach to tumor cell receptors thus deliver radiation; 3 different radionuclides can be used, depending on amount radiation needed to kill tumor with limited damage to the surrounding healthy cells; only useful for tumors positive on SSA imagines, inoperable and symptoms not controlled; depending on extent and location of tumors, patients’ kidney and liver health, and prior treatment</td>
</tr>
</tbody>
</table>
Targeted Therapies

• Some people with advanced NETs are treated with targeted therapies
• Tumors are made up of cells that have undergone multiple gene changes that let them grow out of control
• Targeted therapy is directed to tumor cell’s specific genes, proteins, pathways or other factors to block tumor growth with limited harm to healthy cells
• Tumors have different targets so your doctor test your tumor cells to identify your tumor’s traits
• Approved target therapies used for some NETs: avelumab (Bavencio®), everolimus (Afinitor®), sunitinib (Sutent®)
• Many research studies are taking place now to find other targeted therapies
Treatments to Manage Carcinoid Syndrome Symptoms

• You and your health care team will work together on a plan to manage your carcinoid syndrome symptoms that may include:
  – Treating your cancer
  – Using medicines to control your specific signs and symptoms

• Treatment to control your cancer may include:
  – Surgery
  – Hepatic artery embolization with or without chemo
  – Radiofrequency ablation or Electroporation
Treatments to Manage Carcinoid Syndrome Symptoms (continued)

• Somatostatin analogues (SSAs) are medicines that may prevent, control or reduce symptoms of carcinoid syndrome such as skin flushing and diarrhea, but may not relieve all symptoms (due to dose-limiting side effects)

• SSAs (octreotide [Sandostatin®] and lanreotide [Somatuline®]) are given by injection that help to decrease, and prevent symptoms

• Telotristat (Xermelo®) is a prescription pill, can be combined with an SSA for to treat diarrhea that is not controlled by an SSA alone
Carcinoid Heart Disease

• Many people with carcinoid syndrome may develop carcinoid heart disease—it’s often mild or moderate, but can be serious
• The main symptoms are fatigue, shortness of breath and swollen ankles—but some people have no symptoms
• If you have carcinoid syndrome, your health care team will screen you for possible heart problems and monitor your heart health
• Screening and monitoring may include blood and urine tests, electrocardiogram, transesophageal electrocardiogram and cardiac catheterization
Treatment for Carcinoid Heart Disease

• Carcinoid heart disease is monitored and treated by a cardiologist (a heart specialist)
• Treatment is personalized for each patient, based on symptoms, your cancer stage, previous treatments, and other existing medical conditions
• An initial treatment plan may be to monitor your heart with a regularly scheduled echocardiograms and other tests
• For patients with serious carcinoid heart disease treatment may include therapy with somatostatin analogues (such as octreotide) and heart surgery (valve replacement)
Remission and Recurrence

- Remission means no evidence of disease and no symptoms
- Talk with your health care team – know your treatment options, chance for remission and risk of recurrence (return of disease after treatment)
- Talk to your health care team about your concerns for recurrence and ask about support services to help you cope
- Treatment after recurrence may include the same treatments you had – they may be in a different combination or sequence
Questions to Ask About Treatment

Along with any other questions you have, ask your healthcare team:

• Where will tests, procedures or surgery be done?
• What are the side effects of each treatment option?
• Which treatments do you recommend and why?
• How soon will I need to start treatment?
• Are there any over-the-counter medicines, vitamins, herbs, other supplements, foods or beverage that will interfere with my treatment?
Clinical Trials

Ask your health care team whether there are any clinical trials that are right for you.
What Everyone Should Know About Clinical Trials

• Clinical trials are carefully controlled research studies to test new treatments or learn how to use existing treatments better
• Today’s “standard of care” treatment was developed through clinical trials (Tomorrow’s standard of care treatments are developed and proven through today’s clinical trials)
• The U.S. FDA and local review boards oversee all U.S. clinical trials to keep patients safe
• If you join a clinical trial, you can leave at any time and get standard treatment from your doctor
• Every doctor does not have the same trials. In some cases, if another doctor is in charge of the trial, your doctor may still help with your care
• Most often, the trial pays the costs of the drug being studied, and your health insurance only has to pay for “standard” treatment costs. However, your health insurance may not pay for everything. Be sure to ask your health care team
• In “randomized” studies, participants usually receive either a standard of care treatment or the study treatment. Few cancer clinical trials use a placebo or “sugar pill”
What Everyone Should Know About Clinical Trials (continued)

• Study participants are not treated like “guinea pigs.” Clinical trials have oversight to keep patients safe. Many study participants like the extra monitoring they get in a clinical trial.

• All treatment options and known benefits and risks are explained.

• Participating is your choice – you must give informed consent and you may withdraw at any time.

• Your health care team may suggest changing your treatment (leaving the trial) if you are not benefiting, better therapies become available or if your side effects are not manageable.

• All cancer treatments can have serious side effects – study treatment side effects are reported to an internal regulatory board and side effects of all treatments are reported to federal authorities.

• Serious/excessive side effects may result in a trial’s early closure or major changes.
It’s worth asking your health care team about clinical trials before you decide on treatment. Questions to discuss with your health care team include:

- Should I consider a clinical trial?
- How do I find clinical trials that may be right for me?
- How do I find out if I’m eligible for a clinical trial?
- What are my costs if I participate?
- For more information on clinical trials visit: [www.cancer.gov/ClinicalTrials](http://www.cancer.gov/ClinicalTrials). For trials for specific types of tumors search for:
  - Carcinoid
  - Neuroendocrine tumors
  - Pancreatic neuroendocrine tumors
There are many possible new targets for NET therapies, including:

- Vascular endothelial growth factor inhibitors
- CDK4/6 inhibitors
- Heat shock protein HSP90
- Histone deacetylase inhibitors
Is a Clinical Trial Right for Me?

- Be sure to ask your health care team about clinical trials. Clinical trials are research studies to test new treatments or learn how to use existing treatments better.

- A clinical trial may be the only way to get some of the newest, most promising treatments. Talk with your health care team about clinical trial options.

- The U.S. FDA and local review boards oversee all U.S. clinical trials to keep patients safe. Participating in a clinical trial means that you will receive the best available standard of care for your cancer or a new approach that may offer improved outcomes.

- Almost no one receives a placebo or “sugar pill,” and you will be specifically told if this is a possibility.

- If you join a clinical trial, you can leave the trial at any time and continue to get standard treatment by your doctor.

- Every doctor does not have the same trials. Even if another doctor is in charge of the trial, your doctor may still help with your care.

- Most often, the trial pays the costs of the drug being studied, and your health insurance only has to pay for “standard” treatment costs. However, your health insurance may not pay for everything. Be sure to ask your health care team.
Managing Side Effects
• Ask your health care team about the common and less common side effects of your treatment options and how they can be managed

• You play an important part in managing side effects by letting your healthcare team know of any health changes during or after treatment as soon as you notice them

• Remember, your family, friends or caregiver may notice health changes before you do
Common Side Effects*

*Some of these side effects are not common to all treatment types

<table>
<thead>
<tr>
<th>Fatigue</th>
<th>Vomiting</th>
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<tbody>
<tr>
<td>Upset stomach</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Nausea</td>
<td>Loss of appetite</td>
</tr>
<tr>
<td>Low blood cell counts</td>
<td>Hair loss</td>
</tr>
<tr>
<td>Infection</td>
<td>Mild skin reactions</td>
</tr>
<tr>
<td></td>
<td>Thyroid problems</td>
</tr>
</tbody>
</table>

- Side effects may be mild, moderate or severe
- Everyone won’t have all of these
- Many can be well-managed during treatment and usually go away after you finish treatment
Coping with Side Effects

Treatment to ease symptoms and side effects may include:

- Medicines and/or surgery
- Nutrition counseling
- Relaxation techniques
- Emotional support
- Physical therapy
Living with Neuroendocrine or Carcinoid Cancer
Many people feel a loss of hope and control, and are challenged by living with uncertainty and feeling alone. Common concerns include:

- Worry about the future
- Feeling too tired to do what you need/want to do
- Health insurance or money concerns
- Worry about family, children and/or friends
- Sleep problems
- Eating problems
- Changes in work or home life
- Pain or discomfort
Distress has an affect on your energy, how you think, how you feel and how you relate to others.

Your health care team is there to help – talk to them about your feelings, including:

- Fear
- Anger
- Depression
- Anxiety
- Panic
- Sadness
Reach Out for Support

There are many ways to get support:

• Talk openly with trusted friends and family
• Find a support group
• Use a reliable online resource
• Talk with clergy or trained mental health professionals
• Find a comfortable way of expressing yourself through art, music or writing
• Try mind-and-body programs for stress release
Ways to Take Care of Yourself

• Eat well – ask for advice from a nutritionist
• Be active – ask your health care team which activities are right for you during and after treatment
• Spend time with people you enjoy
• Keep up with your hobbies or find new ones
• Seek comfort in your spiritual practice
How to Join?

• Go to www.CancerExperienceRegistry.org
  – Explore the website
  – Register by developing a secure login

• Submit your contact information on the evaluation form for this workshop

• Complete a questionnaire to share your experience

• For additional information, contact: Levi James, Operations Manager, Research & Training Institute (Ljames@cancersupportcommunity.org)
Join Our Grassroots Movement

- Help ensure that people touched by cancer have access to quality, comprehensive cancer care that includes social and emotional support.

- This community will provide you the opportunity to:
  - Get up-to-date information on issues that are important to people affected by cancer
  - Be part of a network that interacts with policymakers on issues important to cancer patients
  - Have your voice heard alongside other voices of patients with cancer and their loved ones
  - To join, visit: [www.cancersupportcommunity.org/become-advocate](http://www.cancersupportcommunity.org/become-advocate)
Resources

• Cancer Support Community - www.CancerSupportCommunity.org
• American Cancer Society - www.cancer.org
• Cancer Legal Resource Center -
  www.disabilityrightslegalcenter.org/cancer-legal-resource-center
• Carcinoid Cancer Foundation - https://www.carcinoid.org/for-patients/
• National Cancer Institute - www.cancer.gov
• Neuroendocrine Cancer Awareness Network - www.netcancerawareness.org
• Neuroendocrine Tumor Research Foundation -
  https://netrf.org/patient-resources/
• North American Neuroendocrine Tumor Society -
  nanets.net/resources/patient-resources
• Patient Advocate Foundation - www.patientadvocate.org
Questions & Answers
This program is provided through an unrestricted educational grant from:

Lexicon Pharmaceuticals