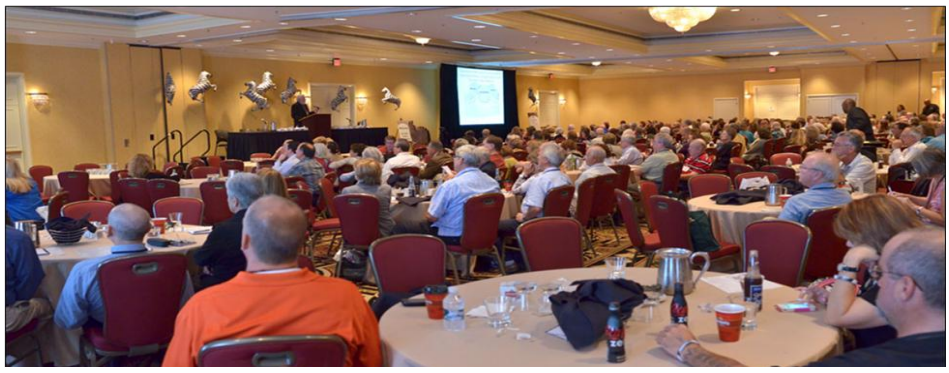
THE JAZZY ZEBRA

Ochsner's Neuroendocrine Tumor Clinic
200 West Esplanade Ave., Suite 200 ▪ Kenner, LA 70065
Phone: 504-464-8500 ▪ 1-866-91-ZEBRA
We're on the Web! Visit us at www.ochsner.org/nets

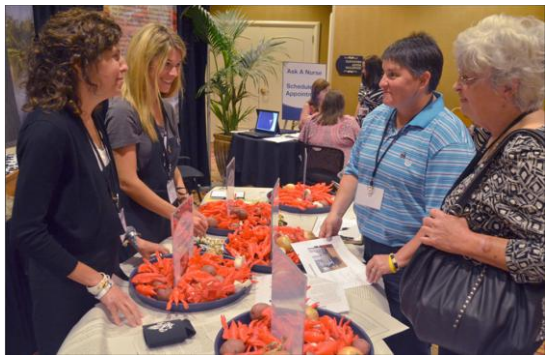
October 2012

Highlights of the 2012 National NET Patient Conference



September 20-22 Ochsner Medical Center-Kenner and The Carcinoid Cancer Awareness Network (CCAN) welcomed 500 patients, caregivers and physicians for the National Patient Conference. Over 20 physicians from all over the world presented on the new, "cutting edge" developments, in the field of NETs.

- Day one kicked off with a welcome reception, starting with some favorite local Creole dishes and ending with a New Orleans second line. The evening gave all the attendees, physicians and patients alike, a great chance to mingle with each other.
- Day two started off with information about the basics of neuroendocrine tumors including radiotherapy, pathology, chemotherapy, and nutrition.
    - Dr. Woltering presented on the new plasma 5-HIAA marker that can now replace the 24-hour urinary 5-HIAA test (no more lugging the jug!). Dr. Joy Ardill from Ireland presented on Neurokinin A, an extremely useful prognostic marker for midgut NETs.
    - Multi-visceral organ transplant (MVOT) patient (and full-time physician), Paul Johnson, MD, presented his personal experience with his transplant for his NET. Dr. Rodrigo Vianna presented the indications and technique for a MVOT.
    - Dr. James Howe presented on rare tumors and rare syndromes and discussed what was new for islet cell tumors, MEN I and MEN II patients.
- The last day of the conference covered endoscopic ultrasound, clinical trials, peptide-receptor radionucleotide therapy (PRRT), and chemo/bland-embolizations.



- Dr. Wang presented on lymphatic mapping (complete with a video from the OR)- a novel technique for detecting tumors intra-operatively. Dr. Boudreaux presented on his surgical experience with the NanoKnife.
- Dr. Thomas O'Dorisio presented exciting information on ^{68}Ga Scans: A new scan that has demonstrated significantly higher detection rates than the conventional OctreoScan, and has recently been approved for a phase 2 clinical trial.

Mark your calendars NOW for the **2014 NET Patient Conference**:
Charlotte, NC; September 18-20, 2014

Recent Research from Our Clinic

Resection of Liver Metastasis in Midgut Neuroendocrine Tumors Affects 10-Year Survival:

By Dr. J. Philip Boudreaux

Midgut neuroendocrine tumors are frequently diagnosed after hepatic metastasis occurs, with a 5-year survival of 50%. We hypothesized that surgical cytoreduction of hepatic metastasis would impact survival rates. Review of 1,362 NET patient charts revealed 319 patients with stage IV, well differentiated, NETs of the jejunum and ileum. Of the 319 patients with distant disease, 117 had liver metastasis only, 37 had extra-hepatic metastasis only, and 165 had both liver and extra-hepatic metastases. The10-year survival rates for patients with only liver metastasis resected (n=80) versus not resected (n=37) were 79% and 39% respectively ($p<0.0001$). The 10-year survival rates for patients with only extra-hepatic metastasis resected (n=31) versus not resected (n=6) were 70% and 67% respectively. Debulking of hepatic metastasis had a positive effect on 10-year survival. However, debulking of extra-hepatic disease had little effect on survival. This study indicates that resection of hepatic metastasis increases survival and is therefore recommended.

Ovarian Metastasis from Midgut Neuroendocrine Tumors: Incidence, Clinical Implications and Management Options

By Dr. Yi-Zarn Wang

Midgut neuroendocrine tumors (NETs) can produce carcinoid syndrome and/or carcinoid heart disease if liver, lymph node or other organ (such as ovary) metastases are present. The incidence of ovarian metastasis, their clinical implications, and the optimal management strategy for these metastases has not been well studied. We hypothesized that patients with ovarian metastases will have a high incidence of carcinoid syndrome and carcinoid induced heart disease. We reviewed the charts of 126 female patients seen in our clinic, with a midgut NET. Twenty-three (23/126, 18%) of our patients were found to have ovarian metastasis. Thirteen of the 23 (57%) patients exhibited carcinoid syndrome and two of the 13 patients with carcinoid syndrome (15%) developed carcinoid-related heart disease. To improve quality of life, routine therapeutic or prophylactic oophorectomy is recommended for female patients undergoing cytoreductive surgery for their midgut NET, especially for those who are peri- or post-menopausal.

Capsule Endoscopy by Case Study

By: Dr. Daniel Raines

In response to a new training requirement that gastroenterology fellows interpret 25 complete capsule endoscopy studies during fellowship (effective July 2012), Dr. Raines created and edited a capsule endoscopy training course consisting of 25 teaching cases accompanied by a textbook of small-bowel disease. To do so, Dr. Raines acquired typical examples of various small-bowel disorders and solicited over 30 nationally recognized experts in small-bowel disease to author individual chapter discussions. Many of the cases included in this publication were obtained through small bowel endoscopy work as part of our Neuroendocrine Tumor Program. Each chapter consists of a case study followed by a discussion including the evaluation, diagnosis, treatment, and prognosis of the specific small bowel disorder being discussed. The chapter on small bowel NETs was authored by Dr. Eugene Woltering. This publication has been adopted by The American College of Gastroenterology for Online dissemination through its educational website (ACG Education Universe) in addition to a printed textbook which will be presented at the American College of Gastroenterology Annual Meeting in Las Vegas, Nevada from October 19-23, 2012.

--Image from: 2012. Capsule Endoscopy by Case Study, Edited by Daniel L. Raines, MD.--

Figures 1 and 2: Capsule endoscopy demonstrating a submucosal tumor with stigmata of hemorrhage. Examination of the ileum by retrograde single balloon enteroscopy reveals multiple submucosal lesions consistent with multifocal carcinoid by biopsy.

The Prevalence of Supplement Use Among Patients with Small Bowel Carcinoid Cancer

By: Dr. Eugene Woltering

Recent increases in the use of over the counter (OTC) medicines partnered with under reporting the use of these medications to physicians has sparked interest in the number and types of “supportive” therapies used by patients with neuroendocrine tumors (NETs). Patients with NETs are of special interest due to the potential interactions/interferences between tumor -associated peptide and amine production and the use of these supplements. Niacin, loperamide and proton pump inhibitors are of special concern due to their actions, which may mask carcinoid symptoms leading to potentially worsened disease at diagnosis or recurrence. A retrospective analysis of 362 patients with small bowel NETs was conducted. 187/362 patients (51.6%) were taking nutritional supplements. Females (n=109) were more likely to take supplements in comparison to males (n=78), $p = 0.037$. Over a third of our patients reported using three or more OTC medicines daily. There is little data on the types and number of supplements being utilized by NET patients, however these interactions may adversely affect the treatment of their disease and therefore, further studies on their significance are warranted.

Clinical Trials

By: Dr. Richard Campeau

^{177}Lu DOTA-TATE: Peptide Receptor Radionucleotide Therapy (PRRT)

Study screening now in progress, enrollment coming soon.

This is a phase III, multicenter, stratified, open, randomized comparator-controlled study. Ochsner Medical Center-Kenner is one of the centers; there are 13 additional centers in the United States and 28 centers in Europe. In this study, treatment with ^{177}Lu-DOTA0-Tyr3-Octreotate plus best supportive care (30 mg Octreotide LAR) (arm 1) will be compared to treatment with high dose (60 mg) Octreotide LAR (arm 2) in patients with inoperable, somatostatin receptor positive, histologically proven midgut carcinoid tumors. The objective tumor response in both groups will be assessed every 12±1 weeks from the first treatment date. The primary objective of the study is to compare progression free survival in arm 1 vs. arm 2.

Inclusion criteria:

1. Presence of inoperable, midgut carcinoid, with progressive disease (as evident on CT/MRI scan within the past three years)
2. Ki67 < 20%; Karnofsky Performance Score (KPS) > 60
3. Must be on Octreotide LAR at a fixed dose of 20-30 mg every 3-4 weeks for at least 12 weeks
4. Confirmed presence of somatostatin receptors, based on positive OctreoScan® imaging (with greater than normal liver uptake)
6. Presence of at least one measurable site of disease
7. Must be at least 18 years of age

Exclusion criteria: All lesions evident on CT/MRI must show uptake on OctreoScan®, and PRRT cannot have been given at any time prior to enrollment in the study.

From the Lab…

By: Dr. Eugene Woltering

Angiogenesis is the growth of new blood vessel and is an important topic in cancer research. In tumors, blood vessels are required for both growth and metastasis. A focus in the lab is studying the "angiogenic switch" which occurs when a resting blood vessel starts to proliferate. A goal in the lab is to identify the genes that are up- and down- regulated when a blood vessel undergoes this "angiogenic switch." Previous research from our lab investigated the changes in gene expression levels between normal tissue and neuroendocrine tumor tissue from the same patient. This study was done using tissue-matched specimens from patients consisting of primary tumor (small bowel) and 2 metastatic sites (lymph node and liver). Out of the 28 genes that were tested, two genes were consistently up regulated in the majority of the tested tissues including both primary and metastatic sites. One of those two genes, Somatostatin Receptor Type 2 (SSTR2), has been well documented by our lab to be involved in neuroendocrine tumor angiogenesis. The other gene, Fibroblast Growth Factor Receptor 3 (FGFR3), has been documented to be involved in breast cancer, bladder cancer and renal cell carcinoma but not yet in neuroendocrine tumors. We performed studies to evaluate the FGFR3 gene expression level in primary neuroendocrine tumors. These studies confirmed that the FGFR3 gene is expressed at a higher level in tumor than tissue-matched normal small bowel from the same patient. Future research needs to be done to determine drugs that may affect this pathway and how this may impact patient care.

Nutrition Corner:

Altering Foods to Help Improve the Intake of Nutrients

By: Leigh-Anne Burns

Consuming a healthy diet can be challenging for patients with NETs however, alterations in food preparation may help. Since many patients are unable to eat large amounts at one time, it is important to consume foods that are high in protein and calorie density. It is also important to get the best possible absorption from these foods. A helpful tip is to eat foods already combined such as casseroles (combination of protein, carbohydrates and fats). Another technique is to use a food processor to chop foods prior to cooking. This will reduce the amount of chewing required which will speed up the digestive process. Good proteins to include are eggs, low fat cheese, peanut butter, yogurts, and lean ground poultry and meats. These foods can be added to many starches and/or vegetables such as sweet potatoes, carrots, peas, quinoa, rice, and noodles. Finely chopped or powdered seasonings such as chives or garlic can add nutrients and flavor.

Interesting Facts

- There are more than 100,000 estimated cases of NETs in the United States alone—Making them more prevalent than other stomach and pancreatic cancers **COMBINED**.
  SEER data (1973-2004). Yao JC et al. J Clin Oncol. 2008;26(18).

- Our program has evaluated patients from all but 4 states!

- Our earliest diagnosed NET patent was in 1969 (that's 43 years ago!), and 20 of our NET patients were diagnosed before 1990 (that's over 20 years ago!)

Mark your calendars…

Carcinoid Cancer Awareness Network 9th Annual Celebration of Life Gala:
The Sterling; Bethpage, NY; November 10, 2012

Louisiana Carcinoid/NET Patient Support Group
Ochsner Medical Center-Kenner; Last Sunday of the month in January and June (1-3pm)
Contact *Louisiana.nets@gmail.com* for meeting dates and times or with any questions.

Don't forget that November is CARCINOID CANCER AWARENESS MONTH and November 10th is Worldwide NET Cancer Awareness Day-- so remember to show your stripes!