New OncLive TV Series Focuses on Pancreatic Neuroendocrine Tumors

Pancreatic neuroendocrine tumors, also known as pNETs, form in the hormone-making cells (islet cells) of the pancreas. In this new **OncLive TV** series, moderator Matthew Kulke, MD, Director of the Program in Neuroendocrine and Carcinoid Tumors at Dana-Farber/Brigham and Women's Cancer Center in Massachusetts and Associate Professor of Medicine at Harvard Medical School, leads a panel discussion on the treatment of pancreatic neuroendocrine tumors, with a focus on the effective sequencing of treatment options. The panel of experts consists of:

- **Rodney F. Pommier, MD**, Professor of Surgery, Surgical Oncologist, Oregon Health and Science University, Oregon
- **Jonathan R. Strosberg, MD**, Associate Member, Department of GI Oncology, GI Oncology Research Section Head, Neuroendocrine Oncology, Moffitt Cancer Center, Florida
- **Diane Reidy Lagunes, MD**, Assistant Attending Physician, Memorial Sloan-Kettering Cancer Center, New York

Often confused with the more aggressive form of pancreatic cancer called adenocarcinoma, pancreatic neuroendocrine tumors account for less than 5% of all pancreatic tumors. They are either functional, causing overproduction of hormones, or nonfunctional, producing no hormones. Symptoms vary depending upon the type of neuroendocrine tumor.

The late **Steve Jobs, co-founder, chairman and CEO of Apple, was diagnosed with a pancreatic neuroendocrine tumor in 2003**, underwent a liver transplant in 2009, and passed away on October 5, 2011. Bringing about greater awareness of pancreatic neuroendocrine tumors is critical for patients to be properly diagnosed, treated, and followed.

Episode 1: Pancreatic Neuroendocrine Tumor Diagnosis Challenges

What are the treatment advances and unmet challenges for patients with pancreatic neuroendocrine

tumors? By the time pNET patients are properly diagnosed, about 60% to 80% already have metastatic disease. Dr. Pommier notes that these tumors frequently spread to the liver.

The four classic pNETs, says Dr. Pommier, are gastrinomas, insulinomas, VIPomas, and glucagonomas.

In order to properly diagnose these rare tumors, physicians can begin with several imaging methods including CT scans and MRI. According to Dr. Strosberg, beyond those modalities, octreoscans and EUS (endoscopic ultrasound) can also be used, with EUS detecting tumors as small as half a centimeter in size.

Dr. Reidy also uses CT and MRI scans for identifying pancreatic neuroendocrine tumors and says physicians can find out a lot by talking to patients about their symptoms.

Read more about pNET treatment guidelines in **The North American Neuroendocrine Tumor Society (NANETS) consensus guideline article**, Well-Differentiated Tumors of the Stomach and Pancreas. Click here: http://www.nanets.net/pdfs/pancreas/04.pdf.

Episode 2: Pathologic Classification of Neuroendocrine Tumors

“There is an increasingly important way that we classify neuroendocrine tumors,” says Dr. Kulke, “and that is by grade.” Dr. Pommier stresses that pathology reports must indicate the grade of a tumor as this is critical information regarding a patient’s prognosis. The grade of a tumor can be determined using **mitotic counts** and the **Ki-67 proliferation rate**. For more information about nomenclature, grading and staging of neuroendocrine tumors see the NANETS consensus guidelines, click here http://www.nanets.net/pdfs/pancreas/02.pdf.

Neuroendocrine tumors are divided into well-differentiated and poorly-differentiated tumors. Within well-differentiated tumors there are low, medium and high-grade tumors. Traditionally, a mitotic count of less than 10 has been considered **low grade**, between 10 and 20 is considered **medium grade**, and greater than 20 is a **high-grade tumor**.

The Ki-67 proliferation marker determines how quickly cells are increasing. Dr. Reidy notes that pathologists examine cellular differentiation in addition to markers. She explains that for well-differentiated tumors a Ki-67 marker above 20% traditionally indicated a high-grade tumor. But recent data indicates that a Ki-67 of 55% or higher may now be used to determine high-grade tumors and this can help determine the best therapy for a patient.

Episode 3: Treatment of Neuroendocrine Tumor Liver Metastases

Liver-directed therapies for pancreatic neuroendocrine tumor patients include surgical debulking of the liver, chemoembolization, radioembolization, and ablation. Dr. Pommier notes that by debulking liver metastases it is possible to remove 90% of disease and get very good, long-term survival rates and results. Dr. Pommier says that surgery is the preferred course of treatment and other liver-directed therapies should be considered when patients with extensive disease cannot be treated by surgical debulking.

Episode 4: Alkylating Agents in Pancreatic Neuroendocrine Tumors

Is **chemotherapy** a good treatment option for pancreatic neuroendocrine tumors? Dr. Reidy-Lagunes believes this is a reasonable option, especially for patients who have metastases in more than 75% of their liver when embolization can be especially toxic.

According to Dr. Pommier there is still the need to further investigate whether systemic or targeted therapies are the best treatments for patients with pNETs. An ongoing clinical trial is studying the effectiveness of everolimus in patients with pNETs following the surgical resection of liver metastases.

Dr. Strosberg talks about data from phase II clinical studies of certain alkylating regimens for pNET patients. Recently the oral agent temozolomide has been seen as a promising new option. There are also studies with a combination of capecitabine and temozolomide, demonstrating 70% response rate with a median progression-free survival of 18 months.

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