Targeted Therapy

New radiolabeled somatostatin analogs to treat gastroenteropancreatic neuroendocrine tumors

Jean E. Boucher, PhD, RN, ANP-BC, AOCNP®, and Robin Sommers, DNP, ANP-BC, ACNP-BC, AOCNP®

About 8,000 adults are diagnosed annually with neuroendocrine tumors (NETs). Most adults diagnosed with NETs are in their early 60s, are African American, and are women (American Cancer Society, 2016; Dasari et al., 2017). Neuroendocrine cancers occur when cells of the gastrointestinal (GI) tract develop into tumors, previously called carcinoids or pancreatic NETs (islet cell tumors) (ACS, 2016). Neuroendocrine cells found in the GI system and in the pancreas are called gastroenteropancreatic NETs, or GEP-NETs, and produce hormone-like substances that help regulate the digestive process through the release of digestive juices. Most NETs are found in the GI tract, such as in the stomach, intestine, appendix, rectum, and pancreas. NETs are grouped into three categories based on their tumor differentiation and grade (National Comprehensive Cancer Network, 2018):

- **G1**: Well differentiated (low grade)
- **G2**: Well differentiated (intermediate grade)
- **G3**: Poorly differentiated (high grade)

Classification of GEP-NETs is based on histopathology, mitotic count, and Ki67 index (antigen counting of tumor hot spots) (Kulke et al., 2010). People who have inherited genetic conditions, such as multiple endocrine neoplasia type 1 (gene MEN1), neurofibromatosis type 1 (gene NF1), tuberous sclerosis (genes TSC1 or TSC2), and Von Hippel-Lindau disease (gene VHL), as well as sporadic mutations (noninherited), are at risk for developing NETs (Kulke et al., 2015).

GEP-NETs are classified by several systems, such as the embryonic origin (foregut, midgut, and hindgut) and hormonal secretion, and further classified as functioning or nonfunctioning. Functioning GEP-NETs often manifest symptoms related to the secretion of high levels of neuropeptides and amines, resulting in symptoms like flushing, abdominal pain, and diarrhea characteristic of carcinoid syndrome. Nonfunctioning GEP-NETs are often asymptomatic but may present with nausea, abdominal pain, weight loss, or symptoms related to tumor mass (ACS, 2016; Kulke et al., 2015).

NETs can occur in the midgut region, where most metastasize to the mesentery, peritoneum, and liver, resulting in a five-year patient survival rate of less than 50% (Strosberg et al., 2013; Yao et al., 2008). Metastatic NETs involving the liver secrete peptide and amine hormones, including serotonin, into the small intestine. These substances enter the circulatory system, which results in carcinoid syndrome, characterized by flushing and diarrhea, or carcinoid crisis (Kulke et al., 2015). NETs are classified as functioning by the hormone secreted, such as somatostatin (somatostatinoma), gastrin (gastrinoma), insulin (insulinoma), glucagon (glucagonoma), and vasoactive intestinal peptide (VIPoma). Most pancreatic neuroendocrine tumors are nonfunctioning.

Staging of NETs involves radiographic imaging using computed tomography or magnetic resonance imaging, somatostatin receptor–based imaging (octreoscan) or gallium-68-dotatate positron-emission...