Neuroendocrine tumors (NETs), including gastroenteropancreatic NETs, or GEP-NETs, are heterogenous tumors that arise from diffuse neuroendocrine cells and other organs, such as the lung, ovary, and thyroid. Lutetium Lu 177 dotatate (Lutathera®) is a newly approved targeted therapy for patients with advanced GEP-NETs. Patients treated with octreotide long-acting release may be candidates for this second-line therapy. This article discusses lutetium Lu 177 dotatate therapy administration and patient care considerations.

AT A GLANCE

- Lutetium Lu 177 dotatate therapy has been approved as a treatment for GEP-NETs.
- Implications for lutetium Lu 177 dotatate as a second-line therapy for patients with GEP-NETs consist of radiation safety precautions and guidelines for the use of long-acting and short-acting somatostatins.
- Considerations for this therapy include the preadministration of antiemetics and amino acid solution, as well as monitoring for side effects and toxicity.

KEYWORDS
gastroenteropancreatic; neuroendocrine tumors; lutetium Lu 177 dotatate; carcinoid cancer

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Targeted Therapy

New radiolabeled somatostatin analogs to treat gastroenteropancreatic neuroendocrine tumors

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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 [ACS], 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