

Peptide Receptor Radionuclide Therapy With ^{177}Lu -DOTATATE for Patients With Somatostatin Receptor–Expressing Neuroendocrine Tumors

The First US Phase 2 Experience

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Objectives: Peptide receptor radionuclide therapy with radiolabeled somatostatin analogs is a novel method of treatment in patients with metastatic neuroendocrine tumors (NETs). For the first time in the United States, we present preliminary results of the treatment with Lutetium ^{177}Lu DOTATATE in patients with progressive NETs.

Methods: Thirty-seven patients with grade 1 and grade 2 disseminated and progressive gastroenteropancreatic NET were enrolled in a nonrandomized, phase 2 clinical trial. Repeated cycles of 200 mCi (7.4 GBq; $\pm 10\%$) were administered up to the cumulative dose of 800 mCi (29.6 GBq; $\pm 10\%$).

Results: Among 32 evaluable patients, partial response and minimal response to treatment were seen in 28% and 3%, respectively, and stable disease was seen in 41% of patients. A total of 28% had progressive disease. A response to treatment was significantly associated with lower burden of disease in the liver. No significant acute or delayed hematologic or kidney toxicity was observed. An impressive improvement of performance status and quality of life were seen after ^{177}Lu -DOTATATE therapy.

Conclusions: Treatment with multiple cycles of ^{177}Lu -DOTATATE peptide receptor radionuclide therapy is well tolerated. This treatment results in control of the disease in most patients, whereas systemic toxicities are limited and reversible. Quality of life is also improved.

Key Words: neuroendocrine tumors, ^{177}Lu -DOTATATE, peptide receptor radionuclide therapy

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and the nonspecific signs and symptoms, these tumors are often diagnosed late and present with metastatic disease, making curative surgical resection impossible.³ The currently approved systemic therapies for NET in the United States are streptozocin, everolimus, and sunitinib, the latter 2 for primary pancreatic NET. Multiple European studies have, however, shown that systemic cytotoxic chemotherapy (cisplatin or etoposide) has a rather minimal efficacy in low-grade (grade 1 and grade 2) NET but is more effective in high-grade (grade 3) NETs.^{4,5}

Somatostatin analog therapy seems to prolong the disease-free survival of midgut carcinoid, based on the data from the PROMID (placebo-controlled, randomized study of octreotide long acting release in metastatic neuroendocrine midgut tumors) study.⁶ The CLARINET (clinical trial on nonfunctioning enteropancreatic endocrine tumors) study will assess the effect of lanreotide on progression-free survival (PFS) in patients with nonfunctioning enteropancreatic endocrine tumors. The final data collection for the primary outcome measure is estimated to be released by the end 2013. Scintigraphic study using ^{111}In indium-diethylene triamine pentaacetic acid octreotide (OctreoScan; Covidien, St Louis, Mo) has been widely used as a standard method of imaging for detection of somatostatin receptor–positive NETs.⁷ More recently, somatostatin analogs labeled with Gallium 68—a positron emitter—have been used for positron emission tomography/computed tomography (PET/CT) tumor imaging.⁸

Neuroendocrine tumor treatment with radiolabeled somatostatin analogs has been available since the 1990s for patients with NET.⁹ Peptide receptor radionuclide therapy (PRRT) initially was