UCLA Health

Peptide receptor radionuclide therapy (PRRT) for gastroenteropancreatic neuroendocrine tumors

Patients with metastatic or inoperable neuroendocrine tumors of the digestive tract or pancreas now have a new treatment option with the first targeted radioactive drug approved in the United States to treat gastroenteropancreatic neuroendocrine tumors (GEP-NETs).

Lutathera (lutetium Lu 177 DOTATATE), a peptide receptor radionuclide therapy (PRRT) drug, was approved in January 2018 by the U.S. Food and Drug Administration (FDA) for adults with GEP-NETs. The treatment has been in use in Europe and Australia for at least a decade.

About one in 27,000 people in the U.S. is diagnosed annually with GEP-NETs, which develop in the hormone-producing cells of the neuroendocrine system. Neuroendocrine cells are found in almost every organ of the body. As a result, neuroendocrine tumors can appear nearly everywhere, including the digestive system, pancreas and lungs.

Center of expertise

UCLA's Ahmanson Theranostics Center has been treating neuroendocrine tumors with PRRT since 2016. Its faculty includes nationally and internationally renowned experts in the diagnosis and treatment of NETs.

Imaging agent improves PRRT patient selection

A new diagnostic agent available at UCLA is helping to identify patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who are most likely to benefit from the recently approved radioactive PRRT drug.

The new FDA-approved imaging agent Netspot (gallium Ga 68 DOTATATE) is an analogue of the hormone somatostatin. Injected into the bloodstream, the radioactive agent binds to the somatostatin receptors on the surface of neuroendocrine tumor cells, and highlights the location of NETs on PET/CT scan images.

Three clinical studies established the safety and effectiveness of Netspot in helping doctors to locate, stage and assess neuroendocrine tumors at a variety of disease stages.

"This imaging agent is a significant improvement over prior agents, and allows us to plan the most appropriate therapy for our patients who have neuroendocrine tumors," said Martin Allen-Auerbach, MD, associate professor in the Ahmanson Theranostics Division, Department of Molecular and Medical Pharmacology at the David Geffen School of Medicine at UCLA

The interdisciplinary program includes experts from nuclear medicine, gastroenterology, oncology, surgery, pathology, endocrinology and interventional radiology. The specialists meet regularly in a NET Tumor Board to review all patient cases.

This comprehensive effort led to UCLA becoming one of the few expanded access investigational sites for PRRT in the U.S. prior to FDA approval. As a result, UCLA NET specialists have significant experience with PRRT, having treated more patients using the new therapy than any U.S. center. UCLA experts have years of clinical and research experience with DOTATATE scans and have consulted at other centers around the country, helping set up PRRT programs.

Other treatment options for GEP-NETs — including chemotherapy, radiation therapy, targeted therapy and surgery — have shown limited effectiveness in treating tumors that have progressed past their earliest stages. The new treatment features a radioactive isotope, Lu 177, attached to DOTATATE, a molecule that binds to somatostatin receptors present on neuroendocrine tumors. Given intravenously, the drug travels to the tumor cells, binds to the receptors and delivers a high dose of targeted radiation.

Clinical trial results

Most patients receiving PRRT at UCLA as part of the expanded access program experienced disease control, with their cancers either getting smaller or being arrested with no further growth. About two-thirds of patients achieved a significant improvement in progression-free survival.

The UCLA results largely resemble those of the pivotal clinical trial that led to FDA approval. The international NETTER-1 trial was a randomized trial of 229 patients with inoperable, somatostatin-receptor-positive NETs. All patients received the standard of care — controlled release octreotide — while one group also received Lutathera. The latter group showed a 79 percent reduction in risk for disease progression compared with patients treated with octreotide alone. Patients receiving Lutathera also appeared to have longer survival, although the data are still being analyzed.

Treatment protocol

Ideal candidates are patients with metastatic or advanced surgically non-curable disease. PRRT is most effective for low- and intermediate-grade GEP-NETs, which have a high expression of somatostatin receptors.

At UCLA, candidates for PRRT begin with an evaluation by a neuroendocrine specialist and a consultation with a specialist in nuclear medicine. Patients receive the drug in four cycles, eight weeks apart, typically spending six to eight hours for each session as an outpatient.

PRRT is usually well tolerated by patients and the most common side effects include a transient decrease in blood counts and nausea during treatment. Patients are exposed to some radiation, but are safe for release by the time they leave the hospital.

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NET Tumor Board

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