

Peptide Receptor Radionuclide Therapy (PRRT)

How does PRRT Work?

Peptide Receptor Radionuclide Therapy (PRRT) is a highly targeted and effective form of radiopharmaceutical therapy (RPT) with minimal side effects for treating NETs with an abundance (or overexpression) of somatostatin receptors. In PRRT, the patient receives an intravenous injection of a drug such as Octreotide (DOTATOC) and Octreotate (DOTATATE) that is chemically bound to (or radiolabeled with) a radioactive material mainly lutetium-177. Other radiopharmaceuticals include yttrium-90, or indium-111. The radioactive drug binds octreotide to the somatostatin receptors on the tumor cells with radiation.

PRRT with ¹⁷⁷Lu-DOTATATE was FDA approved in 2018 for the treatment of gastro-entero-pancreatic neuroendocrine tumors. There are ongoing clinical trials featuring other radiopharmaceuticals, isotopes, peptides and combinations with other therapy.

What conditions are treated with PRRT?

PRRT is used to treat NETs, including the gastro-entero-pancreatic NETs, namely NETs arising from the stomach, intestine or pancreas, also known as carcinoids and islet cell carcinomas of the pancreas, which represent the current US Federal Drug Administration (FDA) approved indication. PRRT is an option for patients:

- Who have advanced (metastatic) and/or progressive (e.g. to SSA) neuroendocrine tumors positive on somatostatin receptor imaging. This imaging can be done using ⁶⁸Ga-DOTATATE (NETSPOT) or ⁶⁴Cu Dotatate (Detectnet), which are radioactive tracers used with PET/CT or PET/MR machines
- Who are not candidates for surgery
- Whose symptoms do not respond to other medical therapies

Benefits of PRRT include symptom relief, slowing tumor progression and improving overall survival.

How is PRRT performed?

The most common protocol includes a series of four PRRT treatments with ¹⁷⁷Lu-DOTATATE spaced approximately 8 weeks apart. Local protocols may vary. This therapy may be done as an outpatient procedure or may require a hospital stay of a few days. In the United States, this treatment is performed as a half or full-day outpatient procedure and in rare cases, a patient may need to stay overnight at the hospital.

Each PRRT session begins with anti-nausea pre-medications, followed by an amino acid solution. The amino acid solution is delivered intravenously to protect the patient's kidneys from the effects of the treatment. The radioactive drug is then injected into the patient, which generally takes about 30 minutes, followed by administration of additional amino acid solution. In total, the treatment session lasts approximately four to five hours.

Post-treatment ¹⁷⁷Lu scans may be taken during and following the treatment process to see where the injected radioactive drug has traveled in the body, although this scan is not required as part of the FDA label for treatment.

What are the advantages of PRRT?

PRRT and other molecular therapies offer more personalized cancer treatment. PRRT is targeted therapy because these radioactive drugs are highly selective in their ability to specifically reach and damage neuroendocrine tumor cells, while limiting radiation exposure to healthy tissue. As a result, PRRT is generally well tolerated.

PRRT is a treatment option that is highly effective in controlling advanced, metastatic or inoperable, progressive neuroendocrine tumors. PRRT is rarely curative but has been shown to help relieve symptoms, shrink tumors, and slow the progression of the disease. As reported in the phase III NETTER trial published in the *New England Journal of Medicine*.

Is PRRT safe?

All therapies, including PRRT, have side effects and risks. You should discuss this with your medical provider. Your medical provider will help you determine whether PRRT is right for you, given your medical history. Please make sure you tell your provider about any prior therapies you have received, as this can play a role in determining the correct therapy and dosage.

Side Effects

The administration of the PRRT itself is well tolerated, but patients may experience nausea and vomiting as a result of the amino acid solution given for kidney protection, especially with some types of amino acid solutions. This is managed with anti-nausea medication or slowing down the administration of the amino acids. Long-term side effects can include a suppression of blood cell counts, which is mild to moderate in the majority of cases. Delayed side effects, such as permanent kidney injury, or the appearance of secondary blood disorders (called myelodysplastic syndrome), are rare. Overall, the treatment is well tolerated by most patients.

Home Care

Your medical facility will provide you with instructions for special care to be taken following treatment. Because small amounts of radiation temporarily remain in the body, patients need to follow the radiation safety protocol provided by your facility. This may include staying a safe distance from others for several days and careful hygiene following PRRT therapy. Because the radioactive drug is removed from the body mainly through the urine and feces, it is important to maintain good bathroom hygiene during this period. Please refer to the [FDA label](#) and the [manufacturers insert](#) for a complete list of safety information. For additional information on travel after receiving 177Lu-DOTATATE therapy go to, [Patient Travel Concerns After Treatment with 177Lu-DOTATATE | Journal of Nuclear Medicine \(snmjournals.org\)](#)

Is PRRT covered by insurance?

Standard therapy with 177Lu-DOTATATE (or Lutathera) is approved by the FDA in the US and [by the EMA](#) in the European Union. Insurance coverage is dependent on many factors. Your treating center will work with you to help you understand coverage for your specific indication. Other forms

of PRRT—for example with other radiopharmaceuticals or other procedures, such as intra-hepatic treatments—are currently available through dedicated trials or programs performed at single centers around the world. These may require an out-of-pocket payment for the therapy if the trial is not sponsored by a pharmaceutical partner.

What's new in PRRT research and development?

The current focus of PRRT research includes studying the use of:

- Radiopharmaceuticals in conjunction with other biotherapies or chemotherapies
- Repeated administration of the radiopharmaceutical therapies
- Increasing the number of indications for this therapy, including other disease targets, such as bronchopulmonary NETs, pheochromocytomas and paragangliomas
- Two radiopeptides together
- Different isotopes
- Different peptides
- Specific PRRT predictive imaging and circulating biomarkers
- Intra-arterial administration

Currently, there are several clinical trials that are evaluating the use of different peptides, isotopes and combinations to further enhance the efficacy of PRRT for neuroendocrine tumor patients.

About SNMMI

The Society of Nuclear Medicine (SNMMI) is an international scientific and medical organization dedicated to raising public awareness about nuclear and molecular imaging and therapy and how they can help provide patients with the best health care possible. With more than 18,000 members, SNMMI has been a leader in unifying, advancing and optimizing nuclear medicine and molecular imaging since 1954.

The material presented in this pamphlet is for informational purposes only and is not intended as a substitute for discussions between you and your physician. Be sure to consult with your physician or the nuclear medicine department where the treatment will be performed if you want more information about this or other nuclear medicine procedures.