Peptide Receptor
Radionuclide
Therapy (PRRT)

How does PRRT Work?
Peptide Receptor Radionuclide Therapy (PRRT) is a molecular therapy (also called radioisotope therapy) used to treat a specific type of cancer called neuroendocrine tumors or NETs1.

In PRRT, a cell-targeting protein (or peptide), similar to the natural circulating hormone somatostatin, is combined with a small amount of radioactive material, or radionuclide, creating a special type of radiopharmaceutical called a radiopeptide. When injected into the patient’s bloodstream, this radiopeptide travels to and binds to neuroendocrine tumor cells, delivering a targeted high dose of radiation directly to the cancer cells. The mechanism by which this radiopeptide can target the tumor cell is the abundance (called an overexpression) of a specific type of surface receptor—a protein that extends from the cell’s surface—that binds to somatostatin2.

Octreotide (DOTATOC) and Octreotate (DOTATATE) as well as other Somatostatin Analogues (SSA) are laboratory-made versions of the hormone that bind to somatostatin receptors on neuroendocrine tumors. In PRRT, the SSA is combined with a therapeutic dose of the radionuclides. Yttrium 90 (Y-90) and Lutetium 177 (Lu-77) are the most common used radionuclides1.

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 pancreas3, which represent the current U.S. 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 (e.g. ⁶⁸Ga-DOTATATE or NETSPOT PET/CT or OctreoScan).
• Who are not candidates for surgery
• Whose symptoms do not respond to other medical therapies

The main goal of PRRT is to provide symptom relief, to stop or slow tumor progression and to improve overall survival.

How is PRRT performed?
The most common protocol, which is the basis of the FDA and European Medicines Agency approval, includes a series of four PRRT treatments with ¹⁷⁷Lu-DOTATATE spaced approximately two months apart. Local protocols may vary, though, as to the radionuclide (Lu-177 or Y-90), peptide (e.g. DOTATOC, DOTATATE), number of treatments, and dosage per treatment. Depending of the radionuclide being used and local regulations, the procedure may be done as an outpatient procedure or may require a hospital stay of a few days. In the United States, this treatment is done as a full-day outpatient procedure; in rare cases a patient may need to stay overnight as a precaution.

Each PRRT session begins with the appropriate 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 treatment is then injected into the patient (this generally takes about 30 minutes), followed by additional amino acid solution. In total, the treatment session lasts approximately five hours.

Molecular imaging scans (e.g. post-treatment Lu-177 scans) may be taken during and following the treatment process to see where the injected radiopeptide has traveled in the body, although this 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 because radiopeptides can be tailored to the unique biologic characteristics of the patient and the molecular properties of the tumor. PRRT is also considered a targeted therapy because radiopeptides 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 typically is well tolerated⁴.

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 tumor lesions, and slow the progression of the disease⁵. As reported in the *New England Journal of Medicine*, the phase III trial (NETTER-1) provided prolonged progression-free survival and overall survival compared to the control arm of the trial⁶. Numerous phase II retrospective and prospective trials in the United States, Europe and Australia have shown similar results³,⁷-⁹.

**Is PRRT safe?**

All therapies, including PRRT, have side effects and risks. You should discuss with your medical provider the risks and benefits of PRRT and any other therapies you are considering. 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 infusion, especially with some formulations. 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 renal toxicity, or the appearance of second hematologic neoplasms (called myelodysplastic syndrome), are rare. Overall, the treatment is well tolerated by most patients¹⁰.

**Home Care**

Your medical facility will provide you with instructions for special care to be taken following treatment. Because small amounts of radiation 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 following PRRT therapy. As the remaining radionuclide is eliminated from the body through the urine and feces, it is important to maintain good bathroom hygiene during this period. Please refer to the [FDA label](http://example.com/fda-label) and the [manufacturers insert](http://example.com/manufacturers-insert) for a complete list of safety information.
Is PRRT covered by insurance?
Standard therapy with $^{177}$Lu-DOTATATE (or $^{177}$Lu-dotatate or Lutathera) is approved by the FDA in the United States 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 isotopes, other peptides or other routes, 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:
- Radiopeptides in conjunction with other biotherapies or chemotherapies
- Repeated administration of the radionuclide 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

References


**About SNMMI**

The Society of Nuclear Medicine (SNMMI) is an international 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 and optimizing nuclear medicine and molecular imaging since 1954.

The material presented in this pamphlet is for information 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.

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