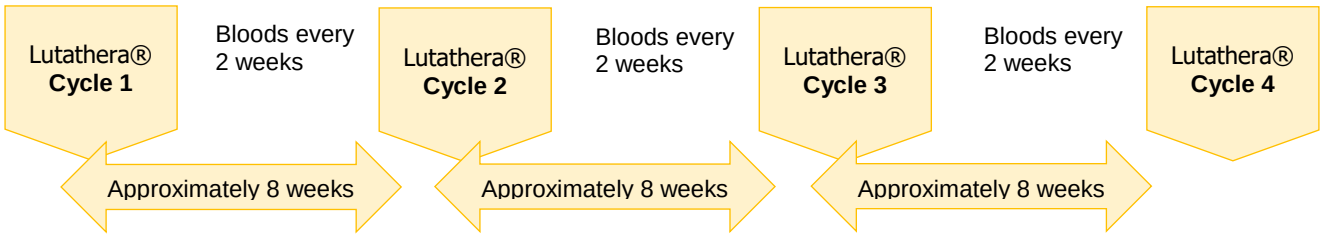
Introductory Information for Patients receiving PRRT (lutetium (^{177}Lu) oxodotreotide (Lutathera®)) to treat neuroendocrine cancer.

Introduction:

Peptide Receptor Radionuclide Therapy (PRRT) is a treatment for neuroendocrine cancer. This leaflet explains why PRRT is being considered for you, what is involved and the benefits and risks of the treatment.

What is PRRT (Lutathera®)?

- **P**eptide **R**eceptor **R**adionuclide **T**herapy or **PRRT** is an approved treatment for neuroendocrine tumours. **PRRT** delivers radiation therapy directly to any tumours in your body that are visible on your DOTATOC PET/CT Scan.
- The type of PRRT that has been recommended for you is called Lutathera®.
- The procedure consists of four treatments (infusions) ideally given about eight weeks apart and may be increased to up to 16 weeks if you have certain side effects. In general the first infusion will require an overnight stay in hospital and the remaining three infusions may be given on an out-patient basis.
- Between each infusion, you will be contacted by the nurse specialist/ doctor to review how the treatment is working for you. You will also have regular blood tests to ensure it is safe for you to proceed to the next infusion.
- To protect other people from the radiation you have been given, you will be asked to take some precautions for 2-3 weeks after each treatment.



Why is this treatment being considered for me?

You may have already had other treatments, including chemotherapy or surgery. These treatments may no longer be effective on your cancer. PRRT is an internationally well recognised and used treatment for neuroendocrine cancer. A team of specialist doctors have decided to offer you this treatment as they feel it is the best option for you.

In making their decision, the doctors will have considered your general health and a range of diagnostic tests, including special imaging investigations.

How does it work?

Some neuroendocrine cancer cells have proteins (receptors) on the outside of them called somatostatin receptors. Lutathera® works by specifically targeting these receptors with a drug containing somatostatin (a hormone) and lutetium-^{177} (a radioactive substance). When injected into the bloodstream, the hormone somatostatin attaches to these receptors and the lutetium-^{177} then enters the cancer cells and releases radiation that destroys the cells from the inside. By delivering a high, radiation dose directly to cancer cells, PRRT minimises the damage to surrounding healthy cells.

Before being considered for PRRT you will have had a Gallium PET-CT scan to check whether the neuroendocrine cancer cells in your body have these somatostatin receptors. If these scans show that they do, they can be targeted with Lutathera®.

How can I benefit from this treatment?

Since every patient is different, it is difficult to predict exactly how much you may benefit from this treatment. Lutathera® is one of the only effective treatments for inoperable neuroendocrine cancer that has spread in the body. It cannot cure the cancer, but it can cause it to shrink, delay it spreading, and prolong life.

Lutathera® was assessed in a clinical trial called the NETTER-1 study. In this study, PRRT was compared with a high dose of a standard therapy (long-acting octreotide 60 mg) in patients with advanced-stage neuroendocrine tumours (NETs) of the small bowel or ascending colon. Results showed that Lutathera® was 82% more effective in preventing tumour growth and spread. Lutathera® was also shown to significantly improve patients' quality of life, reducing pain, fatigue and diarrhoea. Further information about the Netter-1 trial results can be found in the academic paper listed at the end of this leaflet.

Are there any side-effects from this treatment?

There are several possible side effects from the treatment procedure, some arising from the amino acids and some from the Lutathera®. Not all patients will experience these side effects. Detailed information about the side effects can be found on-line in the Summary of Lutathera® Product Characteristics (on-line address listed at the end of this document). The most common side effects are listed below. A side effect is considered "very common" if they affect at least 1 in 10 patients, "common" if they affect at least 1 in 100 patients and "uncommon" if they affect at least 1 in 1,000 patients.

Short-term side effects:

- ***Tiredness.*** This is a very common but usually mild and may last for a few weeks after treatment.

- ***Nausea / vomiting / decreased appetite.*** Nausea and vomiting are very common during the treatment. You will be given anti-sickness medication before your treatment to help with this.

- ***Fall in blood count.*** This is very common and usually temporary, but could cause a delay in your next cycle of PRRT. A fall in blood count can leave you more prone to infection, bleeding and bruising or leave you feeling tired and short of breath. Your blood count will be checked before you start treatment and every 2 weeks while you are undergoing treatment. If you notice any bruising or bleeding it is important to contact the PRRT specialist nurse or the NET team. Some drops in blood count may require treatment with a blood transfusion.

- ***Diarrhoea.*** This is common but is usually mild and usually should not need any specific treatment.

- ***Abdominal Pain:*** Stomach pain is common and may last for a few days after treatment. If you have persistent or severe pain you should contact the PRRT specialist nurse or the NET team.

- ***Mild hair loss.*** This is common but usually minimal (much less than chemotherapy), and re-grows after the treatment has finished.

- ***Hormonal syndromes.*** The treatment can cause a sudden release of hormones, resulting in so-called *"functional syndromes"* or *"neuro-hormonal syndrome"*, such as carcinoid syndrome, which vary depending on the type of hormone. Symptoms may include flushing, wheezing, increased heart rate and breathlessness. This is uncommon but if left untreated can result in a hormonal crisis. This is most likely to occur in the first 48 hours after your treatment. We will be monitoring you closely throughout your stay for any signs of this. If it occurs, we will give you additional medication to treat the syndrome, and we may need to keep you in hospital for longer than planned. If you develop any of these symptoms after you return home you should attend your closest emergency department and contact the PRRT specialist nurse or the NET team.

- ***Tumour lysis syndrome.*** Tumour cells can be destroyed quickly following Lutathera® infusion and uncommonly this results in tumour lysis syndrome which can cause an irregular heartbeat, kidney problems or seizures. If you develop any muscle cramps or weakness, confusion, or shortness of breath it is important to contact the PRRT specialist nurse or the NET team and attend your nearest emergency department.

- ***Allergic reaction.*** Allergy is uncommon and you will be monitored for this during and after your infusion.

Long-term side effects

- ***Impaired kidney function.*** This is common and in some cases patients have experienced kidney failure. The risk of this is minimised by giving you amino acids during the therapy. However, your kidney function will be checked before treatment and every two weeks during treatment, as well as routine monitoring after treatment.

- ***Impaired liver function.*** Patients with liver metastases may be more prone to impaired liver function. Your liver function will be checked before treatment and every two weeks during treatment, as well as routine monitoring after treatment.

- ***Blood cancer.*** Bone marrow disease also known as myelodysplastic syndrome of the bone marrow (usually a forerunner of leukaemia) and acute leukaemia has been noted in about 2% of patients. Your blood counts will be checked before treatment and every two weeks during treatment, as well as routine monitoring after treatment.

- ***Infertility.*** Treatment may cause infertility which can be temporary or permanent.

- ***Risk from radiation exposure.*** Lutathera® contributes to overall long-term radiation exposure. Cumulative radiation exposure is associated with increased risk of cancer. Every effort is made to minimise your radiation exposure and special precautions are provided below which will minimise your risk and your household contacts risk of exposure.

Harm to an unborn child. Lutathera® can cause harm to an unborn child if given to a pregnant woman. It is advisable that women of child bearing age use effective contraception during the treatment and for 6 months afterwards and that men with partners of child bearing age use effective contraception during treatment and for 6 months afterwards. Breastfeeding must be stopped prior to commencement of therapy.

Preparing for your PRRT treatment:

It is important that any long-acting somatostatin analogue injections (such as lanreotide (Somatuline® LAR), ocreotide (Sandostatin® LAR), or pasireotide (Signifor LAR), are stopped 4 weeks prior to PRRT and short acting somatostatin analogue injections are stopped 24 hours prior to PRRT. This is because these drugs may block the receptors that the therapy is designed to target and therefore potentially reduce the success of the treatment.

Prior to starting your course of PRRT, you will have a consultation with a Radiologist in the Nuclear Medicine department and the PRRT nurse, who will explain the therapy procedure in detail and address any concerns you may have.

You will also meet with a Medical Physicist who will give you written and verbal instructions about the precautions you will need to take after each therapy cycle to minimise the radiation exposure to others. For example, it will be necessary for you to

- Limit contact with young children and pregnant women for three weeks after each treatment cycle.

It may be also necessary for you to avoid places of work where you are in close contact with other people for up to two weeks after therapy. A sick note will be provided if required.
More information about this procedure can be obtained by contacting prrt@svuh.ie or:

Radiology
Josh Nogales PRRT nurse specialist
Dr. Nicola Hughes/
Dr. Mathilde Colombie
Department of Radiology
Reception Tel.: 01 - 221 4992

Radiation Protection
Ann McCann
Niamh McArdle
Jackie McCavana
Medical Physics Department
Direct Tel.: 01 - 221 5278 / 4409

Further Information about PRRT can also be obtained at:

NET Patient Foundation website:
http://www.netpatientfoundation.org/
Includes information, leaflets, news and a patient forum.

Summary of Lutathera® Product Characteristics: Available on-line at:
https://www.ema.europa.eu/en/documents/product-information/lutathera-epar-product-information_en.pdf

Academic paper about the NETTER-1 Clinical Trial:
Strosberg J, et al. Final overall survival in the phase 3 NETTER-1 study of lutetium-^{177}-DOTATATE inpatients with midgut neuroendocrine tumors 2021; 332-311. Available on-line at: https://pubmed.ncbi.nlm.nih.gov/34793718/