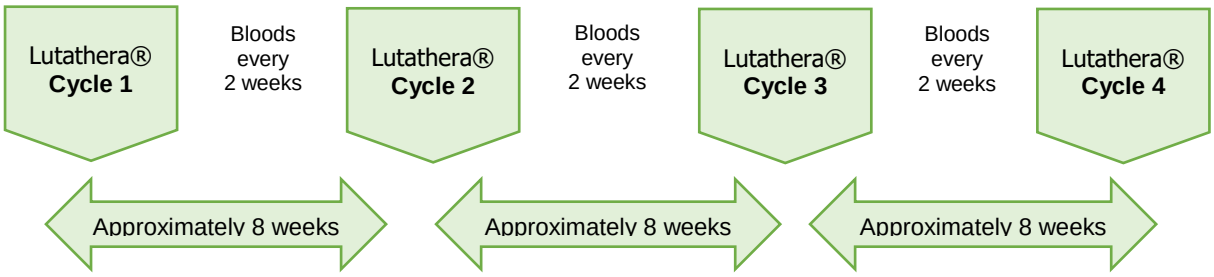
Detailed Information about PRRT

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 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, but duration between infusions may be increased due to response to therapy, availability and potential side-effects. There should not be more than 16 weeks between infusions.
- In general, the infusion will require an overnight stay in the hospital. In some cases the remaining three infusions could be given on a day basis or it will require an overnight stay.
- Between each infusion, you will be assessed at the PRRT clinic 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 treatment.
- You will receive a special scan(s) after each infusion to measure the amount of radioactivity delivered to certain organs.
- 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.



The treatment procedure and the required precautions are discussed in detail in this information leaflet.

Why is this treatment being considered for me?

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

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® effectiveness was assessed in a big international study.

Pre-treatment procedures and advice:

Before starting your course of PRRT, you will have a consultation with a PRRT nurse specialist and a Radiologist /Nuclear Medicine Physician in the Nuclear Medicine department, who will explain the therapy procedure in detail. A medical physicist will also discuss with you the special precautions you will need to take after each infusion. You will be provided with contact details of who to contact should you have any further questions following these initial consultations. On the same day as this consultation, you will also have some blood tests.

Medication:

It is important that any long-acting somatostatin analogue injections are stopped ideally 4 weeks prior to PRRT, and short acting somatostatin analogue injections are stopped ideally 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. **HOWEVER, THE REFERRING NET CONSULTANT WILL DECIDE WHETHER YOU SHOULD STOP THESE INJECTIONS OR NOT BEFORE PRRT TREATMENT.**

Your NET consultant will have already have discussed this with you, and your PRRT appointments should have been timed to coincide with your monthly injections. If not, please get in touch with the Nuclear Medicine Department at the numbers listed below. If necessary, you may be switched to short-acting somatostatin analogues, which need to be discontinued 24 hours before the planned therapy.

Pregnancy / Breastfeeding:
Lutathera® will continue to release radiation for several weeks but the radiation levels will decrease constantly during that time. The radioactivity will have disappeared almost completely after about one month. However, Lutathera® can cause harm to an unborn child so we ask you to not to become pregnant during your entire treatment and for 7 months after your last infusion, or not induce pregnancy for your entire treatment and for 4 months after your last infusion

Breastfeeding must be stopped prior to starting treatment.

PLEASE NOTE THAT THE RADIOPHARMACEUTICAL IS ORDERED SPECIALLY FOR YOUR TREATMENT AND HAS TO BE USED IMMEDIATELY. THEREFORE, IT IS IMPORTANT THAT YOU INFORM US AT LEAST TWO WEEKS IN ADVANCE IF YOU ARE UNABLE TO ATTEND THE TREATMENT.

Procedures on the day of your treatment:

On the day of your infusion you will attend Admissions in St. Vincent's University Hospital (SVUH) and will be directed to St Lucy's ward (Herbert Wing). Before the treatment you will change into a hospital gown. The PRRT nurse will insert a needle into a vein on each arm. Blood tests may be taken if needed at this point. You will also be given some anti-sickness medication to reduce the side-effects of nausea and vomiting during the infusion. You will then be brought to the Nuclear Medicine therapy room.

In the Nuclear Medicine therapy room the Radiologist / Nuclear Medicine Physician will explain the details of the treatment to you and you will be asked to sign a consent form if not already completed to show that you agree to the treatment.

Amino acids will be given to you through one of the needles in your arm; this infusion will last for about four hours in total. The amino acids help protect your kidneys from being damaged by the radiation. Approximately one hour after starting the amino acid infusion, the Lutathera® infusion will start.

Because Lutathera® is radioactive; staff will wear gloves and overshoes, and use special equipment to protect them from the radiation. Once the Lutathera® has been administered you will become a source of radiation to others, so staff will remain at a distance from you whenever possible. This will not affect your care and you will be closely monitored at all times.

The Medical Physics team will also make measurements of the radioactivity in your body after the Lutathera® infusion.

Before and after the Lutathera® is given, your blood pressure and heart rate will be monitored. After you have received the Lutathera®, you must remain in the therapy room for several hours for observation until the amino acid infusion is finished.

Once the observation time is complete, you will be brought to St. Lucy's ward. If it is your first treatment you will remain in St.Lucy's over-night. If it is your second or subsequent treatment you may be able to return home.

Procedures on the day after your treatment

After your first infusion you will return to the Nuclear Medicine department on three separate days ideally, within the first week, for scans. The first scan will be performed the day after your therapy. The timing of the other scans will depend on what day you have your infusion. This will be discussed with you at the time of your initial consultation. On the remaining infusions you will attend the Nuclear Medicine department for a single scan. You will also see the Medical Physicist after each scan, who will make a measurement of the external radiation. These scans will tell the doctor how much radiation is in the tumours and normal organs.

Procedure between each infusion

Between infusions of PRRT, you will have blood tests every two weeks to check your blood, liver and kidney function, This can be done with your GP or at your local hospital and we will give you contact details of how to send on the results to SVUH. The PRRT nurse specialist and the NET team will receive and monitor these blood results. In the event that your blood count falls significantly, we may need to delay the next infusion of PRRT, refer you for additional procedures (such as a blood transfusion) or reassess your treatment plan. You will also have a CT or MRI scan between your second and third infusions to monitor your disease.

Procedure after the last cycle

After you have received four infusions of PRRT, you will continue to have blood tests every two weeks for eight weeks and you will be followed up by your NET consultant, who will refer you for a CT or MRI scan to assess your response to therapy.

Reducing radiation to other people:

For the first few weeks after each Lutathera® treatment a small amount of this radiation will travel outside your body, so people in contact with you will be exposed to this radiation.

Will there be any danger to my family or others?

No, as the radiation levels are very low, however we do ask you to take some simple precautions. These precautions will minimise the radiation exposure to your family and others. The easiest way to minimise radiation exposure to someone is to reduce the time spent in close contact with them, for example, do not sit close to a person if there is a seat available further away. The following precautions and instructions should be followed for the duration stated.

Day of therapy – your stay in the hospital:

During your stay in the hospital you will be asked to drink lots of fluids and use the toilet often (ideally once an hour) to flush any excess radioactivity from your body. We also recommend that you shower in the evening of the first day, and again the following morning.

Your room in St. Lucy's ward is a single occupancy room. The room has its own toilet, shower, and access to the hospital's WiFi. As there will be some radioactive material in your urine, surfaces in the bathroom will be covered with a protective film to prevent radioactive contamination. Once you have been transferred to the ward you will be asked to remain in your room at all times. You will not be permitted to have visitors during your inpatient stay.

Advice for when you leave hospital:

At home 	**For the first week after therapy:** • Shower or bathe every day. • Continue to use the toilet often and sit while urinating. • Flush down the toilet any tissues containing bodily fluids like blood, urine and faeces. • Wash your hands well with soap and water after using the toilet and after any contact with bodily fluids. • Wash your underwear, pyjamas, sheets, and any clothes that contain sweat, blood, or urine separately from the laundry of other members of your household, using a standard washing cycle. You do not need to use bleach and do not need extra rinses.

	• If you have loose stools or urinary incontinence, use protective underwear or incontinence pads. This helps prevent contamination of clothing and your home. Place used underwear / pads in a plastic bag and store outside in an un-occupied area for 70 days before throwing out in the normal bin.
Travelling Home 	• If you need to arrange for assistance in getting home it is preferable that you travel by private transport, and that you sit diagonally opposite the driver i.e. in the back seat, ensuring no other passengers are in the vehicle.
Transport 	• Public transport should be avoided on the day of treatment. Journeys less than one hour are permitted from day 2 onwards. Journeys from 1 – 2 hours are OK from day 3 onwards and journeys of 2 – 3 hours are OK from day 5 onwards.
Contact with your spouse /partner 	• To reduce the radiation dose to your partner it is recommended that you sleep in separate beds for the first 14 days after treatment. • During the day contact should be limited to no more than 2.5 hours at distance of 2m for the first week, and no more than 5 hours per day at 2m for the second week. • For the third week daytime contact should not exceed 6 hours at 1m, contact at distances greater than 1m is OK.
Contact with other adults 	• To reduce the radiation dose to other adults, whom you do not live with, avoid contact within 1 metre for the first 7 days. In the second week you should not spend more than 1 hour per day at a distance of 0.3 m (arm's length distance). Being in their company at distances greater than this is OK.
Pregnant women/ children 	• It is better to have **no** contact with young children (< 11 years old) or pregnant women for the first 7 days after treatment. You should avoid close contact (keep to <1 hour per day at 0.3 m) during the second and third week after therapy. Limited contact at greater distances is OK. • Sleep apart from pregnant women or children for the first three weeks. • Specific advice can be given based on the age of your children.
Contact with over 60's 	• Provided you stay more than an arm's length away from those over 60 years of age in the first 2 weeks, there are no additional restrictions required.
Contact with Family Member caring for you 	• It is possible for an adult family member to look after you before the time periods stated have passed, if you are unwell or disabled for example, provided they are not pregnant. • If your partner or other family member is in this position, he/she may receive a higher radiation dose as a result of looking after you, and must be aware of the small risk involved. **Please ask them to attend your initial consultation with you, and the**

	<u>medical physicist will explain the various risks and precautions involved.</u>
Contact with Pets 	• There is no evidence to suggest that your pet's health will be at risk after your treatment and you do not need to avoid contact with them.
Places of Public Entertainment 	• Such as theatres, cinemas, bars should be avoided in the first 5 days after each treatment.
Returning to Work 	• If working in close contact with adults (within 0.3 metre of the same person for more than 8 hours per day) you should stop working for the first 7 days after each treatment and ensure the distance to your co-workers is greater than 1 metre for the following 2 weeks. • If working with young children or pregnant women you will have to take additional time off work.
Travel 	• If you plan to travel abroad in the 3-month period following treatment, please notify the medical physicist and they will give you a letter indicating that you have had Lutathera® treatment.

What should I bring to hospital with me?

For your inpatient ward stay you are welcome to bring any belongings with you, but please be aware that they must be monitored for radioactivity before you leave. It may be necessary for us to keep any radioactive belongings for a period of time after you have left the hospital. For this reason, we recommend bringing the minimum amount of belongings possible. You will be able to collect any of your belongings we keep from the Nuclear Medicine department after a few weeks.

Items that are useful to bring into hospital include snacks and drinks, pyjamas (very likely to be kept), slippers (may be kept), books/magazines (unlikely to be kept), mobile phone (will not be kept) and toiletries. Please bring a complete change of clothes to wear when you are discharged home.

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®. **<u>Not all patients will experience these side effects.</u>** 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 nurse specialist 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 nurse specialist 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. 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. You might need additional medications or a longer stay in the hospital to treat that. You will be advised to watch for hormonal symptoms after you return home, and what to do in case of emergency.

- ***Tumour lysis syndrome.*** When a lot of bad cells called cancer cells break down really fast in the body following Lutathera infusion, 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 nurse specialist of the NET team.

- ***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 7 months afterwards. Men with partners of child bearing age should also use effective contraception during treatment and for 4 months afterwards.

Other Considerations

In some cases it may be necessary to stay over-night as an in-patient for all four infusions of PRRT. If this is the case you will be informed of this by the NET consultant, radiologist or nuclear medicine physician.

When you are ready to go home, the medical physicist will give you a card with your treatment details on it. You will be required to carry this with you at all times for the time specified on the card.

In the unlikely event of death within the first few weeks after treatment, special precautions are required which may delay burial/cremation for up to a month. In the event of a death it is very important that the hospital is informed (via the contact numbers below), so that appropriate guidance may be given.

More information about this procedure can be obtained by contacting **PRRT@svhg.ie** or:

Medical

Josh Nogales / Anupria Joy
PRRT Nurse Specialist
Dr Nicola Hughes /
Dr Mathilde Colombie /
Department of Radiology
Direct Tel.: 01 - 221 5662
Reception Tel.: 01 - 221 4992

Radiation Protection

Ann McCann / Niamh McArdle
/ Jackie McCavana
Medical Physics Department
St. Vincent's University Hospital
Direct Tel.: 01 - 221 5278 / 4409

NET Team

Dr Hussein Almeamar / Dr Mark Doherty Tel: 012214407

Further Information about PRRT can also be obtained at:

Neuroendocrine Cancer UK
https://www.neuroendocrinecancer.org.uk/
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