Introducing Lutathera Therapy in a Community Practice

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INTRODUCTION

- Lu-177 Dotatate (Lutathera) was approved by the FDA in 2/2019 for the treatment of progressive or non-operable NETs which have progressed on first line Octreotide analogue therapy.
- The FDA approved regimen is 7.4 GBq q8 weeks. Supportive treatment includes
  - Administration of Octreotide analogue 4-24 hours after infusion.
  - Concurrent aminoacid infusion for renal protection 30 minutes before and 3 hours after Lutathera infusion.
  - Appropriate pre-medication
- The challenges in implementing Lutathera in community practice include:
  - Limited parenteral radionuclide therapy experience
  - Low number of patients with progressive metastatic NET
  - Challenging referral pattern with need for collaborative care between authorized users, oncologists and nursing care.

Objectives

- To provide a step by step practical guide on how to implement Lutathera in a community practice.
- MAPMG (Mid-Atlantic Permanente Medical Group) is one of the largest multispecialty private practice in the country including ~1500 physicians caring for ~800,000 patients in the Kaiser-Permanete Plan of the MidAtlantic.
- One of the first private practices to start a Lutathera program in the state of MD.

Radiation Safety and Waste Disposal

Hot Lab Considerations

- Set up Dose calibrator for Lu-177 assay using vendor supplied test dose
- **Prepare waste management plan for Lu-177m (161 day half life) contaminant**.
  - Store all contaminated waste separate from all other isotopes.
  - Assay at regular intervals and dispose with regular trash when at background.
  - If above background at maximal allowable on site decay time limit, dispose at specially licensed waste repository.

Day of administration considerations

- Shielded or non-shielded rooms are acceptable Absorbent chux can be taped to floor and other surfaces to minimize spill contamination.
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- Decide on Gravity pump vs. programmable pump administration.

Patient Instructions

- Private residence after discharge.
- **For 3 days:** dedicated bathroom and bedroom.
- **For 7 days:** avoid sexual activity.
- **3 months:** keep documentation during travel and notify treating team if patient dies to avoid cremation related contamination.
- **6 months:** Avoid pregnancy or fathering children.

Medication Management

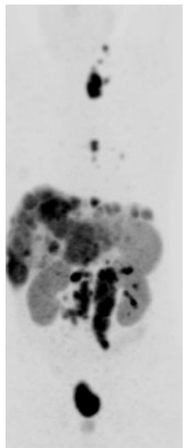
Anti-emetic support

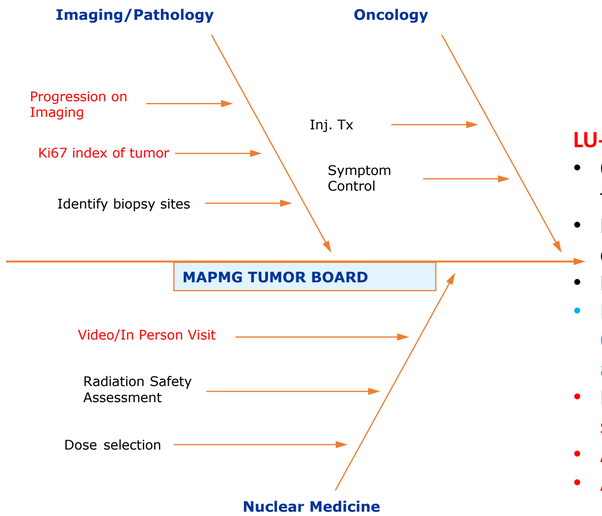
- Patient's getting compounded amino acid solution (25 grams of Lysine and Arginine each in 1 L of saline) require little to no antiemetic support. Our protocol initially used 8 mg of IV Ondasteron 30 minutes before infusion. However, we have since discontinued prophylactic administration.
- Commercial amino acid solutions require aggressive antiemetic support (concurrent use of 5-HT3, NK1 and H2 receptor antagonists).
- **Break through regimen:** 5-10 mg Olanzapine PO once or Prochlorperazine 5-10 mg IV q6-8 hrs for a maximum of 40 mg/day vs. 10 mg PO q6-8 hrs PRN.
- **Special note: Using the least emetogenic amino acid preparation will increase patient satisfaction, support medication cost and limit radioactive contamination from patient emesis.**

Carcinoid Crisis

- **Long term treatment:** Consider addition of Telotristat ethyl 250 mg three times daily in addition to octreotide analogue therapy for patients at high risk.
- **Premedication:** day of treatment PO or IV dexamethasone 4-8 mg, combined H1/H2 blockade – Cimetidine 200 mg PO vs. Ranitidine 150 mg PO plus Loratidine 10 mg PO
- **Crisis management:** aggressive fluid resuscitation, administration of octreotide infusion 500 mcg IV bolus, followed by IV drip at rate of 50-200 mcg/hour, transfer to higher level of care (ensure appropriate notice).

Patient Selection and Overview





GA-68 DOTATATE PET SCAN

- Staging
- Uptake in tumor >/= to liver for eligibility

LU-177 DOTATATE TX DAY

- Offered at a single center in the mid-Atlantic coverage area
- Radiology nurse/CNMT coordinate infusion
- Nuc med MD supervision
- Patient's get post Tx Octreotide analogue 4 hours after infusion
- Major source of patient satisfaction
- Avoid second visit 24 hrs after
- Avoid additional copay

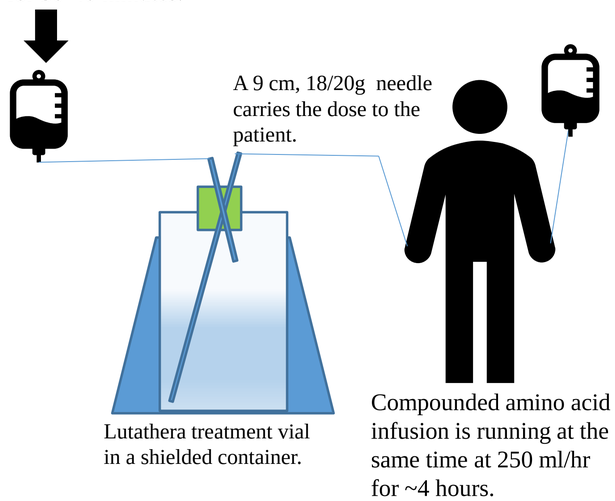
Treatment Room/Infusion Set Up

A. Double channel pump for infusion of amino acid solution and sterile saline.

B. Infusion chair. Chux are placed on the floor chair and infusional apparatus.

C. Portable stand with a shielded Lutathera vial. Gravity pump administration set up is described in detail below.

- 2.5 cm, 20 g needle is connected to 0.9% saline.
- Needle is above fluid level.
- Infusion rates are 100 ml/hr for 5 minutes and 300 ml/hr for 30-40 minutes.



References

1. Hope, T. A. *et al.* NANETS/SNMMI Procedure Standard for Somatostatin Receptor–Based Peptide Receptor Radionuclide Therapy with 177Lu-DOTATATE. *J Nucl Med* **60**, 937–943 (2019).
2. Phan, A. T. *et al.* NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors: Well-Differentiated Neuroendocrine Tumors of the Thorax (Includes Lung and Thymus). *Pancreas* **39**, 784–798 (2010).
3. Strosberg, J. *et al.* Phase 3 Trial of 177Lu-Dotatate for Midgut Neuroendocrine Tumors. *N. Engl. J. Med.* **376**, 125–135 (2017).
4. 3. Brabander, T. *et al.* Long-Term Efficacy, Survival, and Safety of [177Lu-DOTA0,Tyr3]octreotate in Patients with Gastroenteropancreatic and Bronchial Neuroendocrine Tumors. *Clin. Cancer Res.* **23**, 4617–4624 (2017).
5. 4. Tapia Rico, G., Li, M., Pavlakis, N., Cehic, G. & Price, T. J. Prevention and management of carcinoid crises in patients with high-risk neuroendocrine tumours undergoing peptide receptor radionuclide therapy (PRRT): Literature review and case series from two Australian tertiary medical institutions. *Cancer Treat. Rev.* **66**, 1–6 (2018).
6. 5. Pavel, M. *et al.* Telotristat ethyl in carcinoid syndrome: safety and efficacy in the TELECAST phase 3 trial. *Endocr. Relat. Cancer* **25**, 309–322 (2018).
7. 6. Kong, G. *et al.* Efficacy of Peptide Receptor Radionuclide Therapy for Functional Metastatic Paraganglioma and Pheochromocytoma. *J. Clin. Endocrinol. Metab.* **102**, 3278–3287 (2017).
8. 7. Angelousi, A., Kassi, E., Zografos, G. & Kaltsas, G. Metastatic pheochromocytoma and paraganglioma. *Eur. J. Clin. Invest.* **45**, 986–997 (2015).
9. 8. Bergsma, H. *et al.* Persistent Hematologic Dysfunction after Peptide Receptor Radionuclide Therapy with 177Lu-DOTATATE: Incidence, Course, and Predicting Factors in Patients with Gastroenteropancreatic Neuroendocrine Tumors. *J. Nucl. Med.* **59**, 452–458 (2018).
10. 9. Mittra, E. S. Neuroendocrine Tumor Therapy: 177Lu-DOTATATE. *Am. J. Roentgenol.* **211**, 278–285 (2018).
11. 10. Strosberg, J. R. *et al.* First update on overall survival, progression-free survival, and health-related time-to-deterioration quality of life from the NETTER-1 study: 177Lu-Dotatate vs. high dose octreotide in progressive midgut neuroendocrine tumors. *J. Clin. Oncol.* **36**, 4099–4099 (2018).