FIRST LINE TREATMENT WITH 177LU-DOTATATE IN A PATIENT WITH MILIARY LIVER METASTASES AND CARCINOID SYNDROME FROM A MIDGUT NEUROENDOCRINE TUMOR

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Introduction

Neuroendocrine tumors are characterized by limited proliferation. Surgery remains the only curable treatment. However, many patients are diagnosed at an advanced, inoperative stage, aggravating their prognosis. Also, endocrine syndromes may impair both their quality of life and survival. Recently the NETTER-1 study has demonstrated that ^{177}Lu-Dotatate achieved significant progression-free-survival (PFS) on patients with well-differentiated, metastatic midgut neuroendocrine tumors.

Purpose

Evaluate the efficacy of ^{177}Lu-Dotatate in a 21-year-old male patient with inoperable metastatic midgut neuroendocrine tumor.

Methodology

A 21-year male patient was diagnosed with inoperable metastatic midgut neuroendocrine tumor.
At the time of the diagnosis, he had:

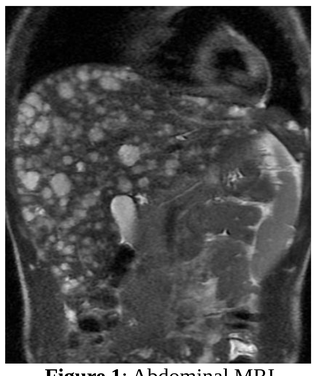


Figure 1: Abdominal MRI

- Multiple liver metastases (>30 lesions, affecting c.75% of the liver) and splenomegaly
- Carcinoid heart disease (affecting both tricuspid and pulmonary valves)
- Carcinoid syndrome (flushing up to 10 times daily and diarrheas)
- Excessively high serotonin (8,1xULN) and 5-HIAA levels (48xULN)

The liver biopsy showed metastasis from well-differentiated neuroendocrine tumor (NET) with serotonine production, Grade-2, ki67%: 8%, 0,6 mitosis per 10HPF, SSTR2a: +++ , Serotonin (+,100%), Chromogranin(+), Synaptophysin(+), CK8.18 (+,100%), NKX2.2(+), CDX-2(+), and the primary tumor has probably origins from midgut.

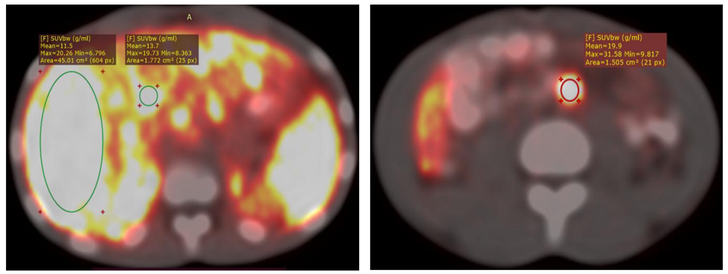


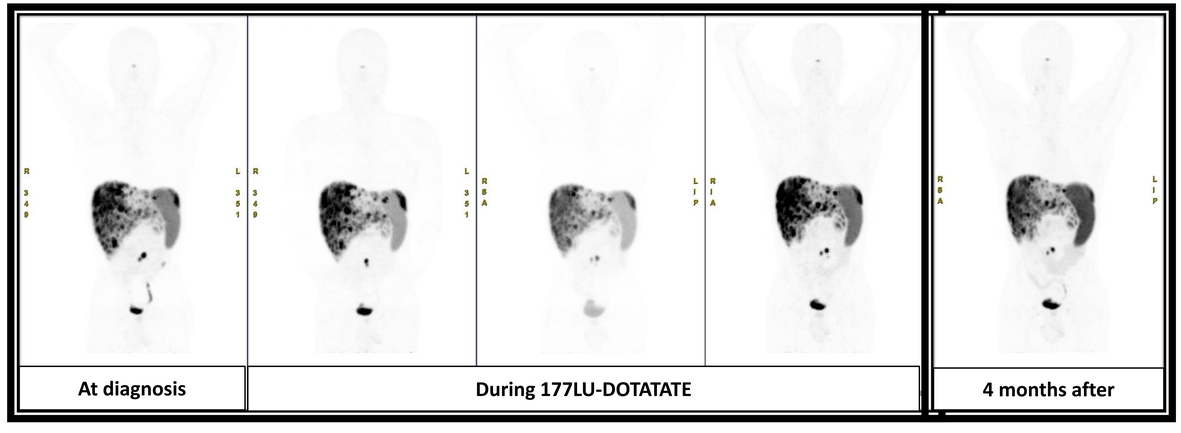
Figure 2: 68Ga-DOTA peptide PET/CT showed uptake from the liver metastases (SUVmax:25) and other abdominal lesions (SUVmax:31)

As for treatment:

A. For symptomatic control, he was started on Lanreotide and Telotristat.
B. Considering the multiple, inoperable metastatic lesions, Peptide Receptor Radionuclide Therapy (PRRT) was decided as first line treatment.

The patient received **Lutetium-177(177Lu)–Dotatate** at a dose of 7355 MBq every 8 weeks.

- Lanreotide was discontinued 4 weeks before each treatment.
- Ondansetron / Metoclopramide was administered intravenously 45' prior to treatment administration
- An amino acid solution for renal radioprotection was administered intravenously, starting the infusion 30' prior to Lutetium infusion and during 4 hours
- Adverse effects (mostly during the infusion of the amino acid solution):
  - Flushing (in every infusion)
  - Nausea and vomit (every time, less incidents during the last infusions)
  - Dyspnea and desaturation in the first time, self- resolved in a few minutes
  - Diarrheas (1st-2nd infusion)
  - Tension and anxiety (3rd infusion)



Post-therapy whole body scans were performed.

Results

Therapy was very well tolerated. No renal or liver dysfunction appeared. After completion of treatment, we noted grade 1-2 myelosuppression. With regards to response, he reports reduced frequency of flushing and recession of diarrheas.
Carcinoid heart disease is stable and normal values of biomarkers have been reported. 4 months after Lutathera completion.:

	At diagnosis	4 months after LUTATHERA completion	Normal Values
CgA - (nmol/L)	625	95,6	*< 4*
5HIAA urine (mg/24h)	394	10	*0,7-8,2*
Serotonin (ng/ml)	2446	288	*70-300*

On imaging, 4 months after the last infusion the disease remains stable according to RECIST criteria (Figure 3) whereas a 20% reduction SUVmax, was noted.

Conclusions

In our case, treatment with 177Lu-Dotatate and somatostatin analogue was well-tolerated and resulted in a 10-month progression-free disease so far, with normalization of serotonin levels, improvement of the patient's symptoms, and stable carcinoid heart disease.

Figure 3: 68Ga-DOTA peptide PET/CT from diagnosis up to 4 months after ^{177}Lu-Dotatate completion
*The first 3 scans were performed in GE DISCOVERY ST and the last 2 in GE DISCOVERY MI DR

References:

-LUTATHERA spc
-NETTER-1 Clinical trial