Increasing the Therapeutic Window in PRRT with Long-acting Somatostatin Analogues: Study Protocol

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Introduction

Treatment for patients with neuro-endocrine tumors (NET) with peptide receptor radionuclide therapy (PRRT) and long-acting somatostatin analogues (LA-SSAs) utilize the somatostatin receptor. To avoid possible competitive binding, current guidelines recommend withdrawing LA-SSAs 4-6 weeks prior to PRRT in order to ensure effective receptor occupation.

We hypothesize that continuous use of LA-SSAs during PRRT does not negatively affect the absorbed dose in tumor lesions due to an absence of competitive binding and could increase the therapeutic window of PRRT.

Aim

To determine the effect of long-acting somatostatin analogues on the absorbed dose in tumor lesions and normal organs during PRRT with [^{177}Lu]Lu-HA-DOTATATE.

Endpoints

The following comparisons will be made:

- Absorbed dose in tumors
- Absorbed dose in normal organs
- Health related quality of life

Previous Results

Retrospectively, long-acting somatostatin analogues lowered the uptake of [^{177}Lu]Lu-HA-DOTATATE in liver and spleen, but did not reduce tumor uptake (Figure 1).[1]

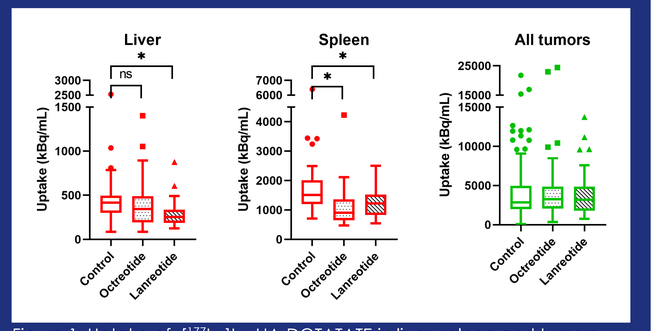

Figure 1: Uptake of [^{177}Lu]Lu-HA-DOTATATE in liver, spleen and tumors after treatment with LA-SSAs.

Prospectively, long-acting somatostatin analogues lowered the uptake of [^{68}Ga]Ga-HA-DOTATATE in tumor tissue, but did not reduce tumor uptake (Figure 2).[2]

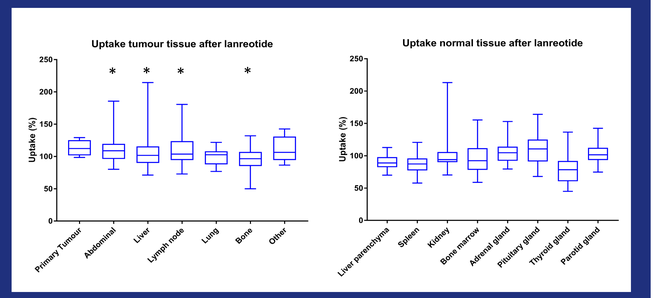

Figure 2: Uptake of [^{68}Ga]Ga-HA-DOTATATE in tumors and normal tissue after treatment with lanreotide as percentage of uptake before treatment with lanreotide.

Trial Design

This prospective trial (Figure 3) is designed to show non-inferiority in absorbed tumor dose of both intervention arms (with LA-SSA) compared to the control arm (without LA-SSA). Patients with LA-SSAs will be randomized to one of the intervention arms whilst patients without LA-SSAs will serve as a control arm. Multiple SPECT/CT scans will be made after PRRT in order to perform dosimetry.

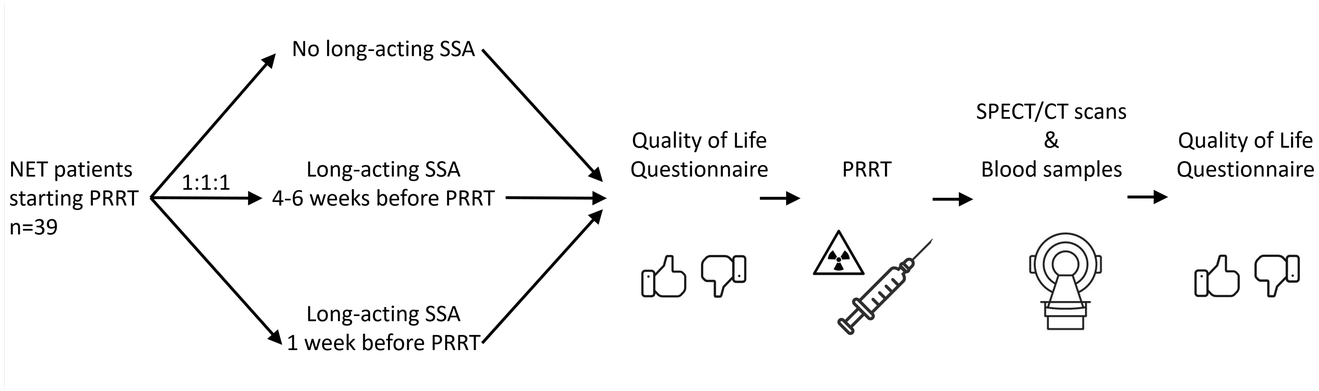

Figure 3: Clinical trial design.

Conclusions/Future Directions

We hypothesize that LA-SSAs do not negatively affect the tumor or healthy tissue absorbed dose when continued during PRRT. If confirmed, this would negate the need for patients to discontinue LA-SSAs multiple times during PRRT and to switch from LA-SSAs to short-acting SSAs. This approach could increase the therapeutic window, i.e. increase the delivered dose in tumor lesions without increasing toxicity.

References

[1] Veerman et al. EJNMMI 2022.

[2] Aalbersberg et al. EJNMMI 2019.

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