IDENTIFICATION OF NEUROENDOCRINE NEOPLASMS AND ASSESSMENT OF RESPONSE TO PEPTIDE RECEPTOR RADIONUCLIDE THERAPY (PRRT) WITH 177Lu-OCTREOTATE UTILIZING A MULTIGENE PCR-BASED BLOOD ANALYSIS

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Ethical review	Approved WMO
Status	Pending
Health condition type	Endocrine neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON41217

Source
ToetsingOnline

Brief title
The LuGenIum PRRT tumor response study

Condition

- Endocrine neoplasms malignant and unspecified

Synonym
Carcinoid Tumor, Neuroendocrine Tumor

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: LuGenIum consortium

Intervention

Keyword: multi gene analysis, Neuroendocrine Tumor, PRRT, Response evaluation

Outcome measures

Primary outcome

- Significant changes in levels of circulating NEN transcripts during and after

treatment with PRRT utilizing 177Lu-octreotate

- Significant relation between final tumor response to PRRT and changes in

levels of circulating NEN transcripts

- To identify if variations in levels of circulating NEN transcripts may

constitute as an early predictive marker for response to PRRT

Secondary outcome

Not applicable

Study description

Background summary

Treatment of Neuroendocrine Tumors (NETs) using PRRT is valuable and takes about 6 months to complete the intended 4 cycles with 177Lu-Octreotate. There is a lack of an adequate blood marker which can be used as indicator for tumor response between the different cycles of PRRT. Currently Chromogranine A (CgA) is used as marker, however, there is no 1:1 correlation with tumor response and it is not uncommon to see an elevation of the CgA levels after the start with PRRT. Normally, the response evaluation via CT-/MRI-scan takes place after finishing all the intended cycles with PRRT. Especially for patients who are not responding to treatment with PRRT it is important that they can switch to

another form of therapy in an early stage to prevent any delay in further treatment.

Transcriptome analysis with the PCR technique in the treatment of NETs with biotherapy or surgery demonstrated that this test can differentiate between treated and untreated GEP-NETs (sensitivity and specificity 85-96%), determine whether a patient has residual disease (100%), determine if a patients can be categorized as clinically stable following surgery or LAR therapy (90-95% correct), exhibits progressive or non-responsive disease (75% correct). Preliminary results demonstrated a clear superiority of this test compared to conventional CgA assay.
We expect to find a comparable sensitivity, specificity, PPV and NPV also in the assessment of patients treated with PRRT.

Study objective

The purpose of this study is to evaluate the effect of PRRT with 177Lu-octreotate on circulating NET transcriptomes. In particular, the variation of circulating NEN transcripts will be correlated to the response to PRRT to test whether this analysis may constitute an early predictive marker.

Study design

International multi-centre observational study.

A consortium was formed named *LuGenIum Consortium* with the following participating medical centers:
- Erasmus Medical Centre Rotterdam, the Netherlands
- European Institute of Oncology Milan, Italy
- Zentralklinik Bad Berka, German

Study burden and risks

A vena puncture has been considered as diagnostic tool with minimal side effects. Participation in this study is associated with a minimal risk and burden for patients, because;

- New for the patient is that according the protocol extra 10ml blood will be collected at three time points around the infusion of PRRT. The patient will be hospitalized for 24 hours for administration of the PRRT, during this hospitalization the blood samples will be collected.

- During regular follow-up after completion of treatment with PRRT blood is collected as a procedure of standard care and an extra amount of 10ml will be drawn. No extra moment of blood collection will be introduced during the follow-up.

- Patient is not required to invest extra time during, like visiting the outpatient clinic, when participating in the study.

- Possible risks associated with a venipuncture are minimal

Because of the observational design of the study no negative side effects can be expected.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patient is affected by an inoperable Neuroendocrine Tumor and eligible for treatment with PRRT based on the following criteria:;- The capacity to understand and willingness to sign an informed consent form, obtained prior to enrolment into the study;And meets the standard

conditions for treatment with PRRT:
- Presence of histology proven GEP tumor(s), including bronchial carcinoids
- Presence of somatostatin-receptors on the known tumor lesions demonstrated by OctreoScan® within 6 months of the first dose of radiolabelled octreotate/octreotide. The uptake on the OctreoScan® should be at least as high as normal liver uptake on planar imaging
- Life expectancy greater than 12 weeks
- Serum creatinine <=150 µmol/liter or 1.7 mg/dL, and a measured creatinine clearance (or measured GFR using plasma clearance methods, not gamma-camera based) of >=50 mL/min
- Hemoglobin (HgB) concentration >=5.5 mmol/L (>=8.9 g/dL); WBC >=2.0*109/L (2000/mm3); platelets >=75*109/L (75*103/mm3)
- Total bilirubin <=3 x ULN
- Serum albumin >30 g/L, or serum albumin <=30 g/L but normal prothrombin time
- Karnofsky Performance Status >=60
- Presence of at least 1 measurable site of disease

Exclusion criteria

Patient is not eligible for PRRT or an alternative treatment is available:;A potential subject who meets any of the standard contraindications for treatment with PRRT will not be able to participate in this study:
- Possible surgery with curative intent
- Surgery, radiotherapy, chemotherapy or other investigational therapy within 3 months of the start of therapy
- Patients with known brain metastases unless these metastases have been treated and stabilized for at least six months prior to study start. Patients with a history of brain metastases must have a head CT with contrast to document stable disease prior to study start
- Uncontrolled congestive heart failure
- Any subject who is taking concomitant medications which decrease renal function
- Any subject receiving therapy with somatostatin analogues in whom these analogues cannot be interrupted for 12 hours before and 12 hours after the administration of the radiolabelled somatostatin analogues, or any subject receiving therapy with long-acting somatostatin analogues in whom these analogues cannot be interrupted for at least 6 weeks before the administration of the radiolabelled somatostatin analogues, unless the uptake on the OctreoScan® during continued somatostatin analogue medication is at least as high as normal liver uptake on planar imaging
- In patients with unusual haematological parameters, including an increased MCV (>105fL), and especially in those who had previous chemotherapy, the advice of a hematologist should be seeked, for adequate further work up
- Subjects with another significant medical, psychiatric, or surgical condition, currently uncontrolled by treatment, which may interfere with completion of the study.
- Pregnancy
- Prior radiation therapy to more than 25% of the bone marrow

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2014
Enrollment:	45
Type:	Anticipated

Ethics review

Approved WMO

Date:	24-07-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL48623.078.14