89Zr-bevacizumab PET imaging as predictive biomarker for everolimus efficacy in patients with neuroendocrine tumors

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To evaluate the feasibility of 89Zr-bevacizumab-PET imaging as predictive biomarker before and during treatment with everolimus in patients with neuroendocrine tumors.

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

Summary

ID

NL-OMON32849

Source
ToetsingOnline

Brief title
NETPET

Condition

- Endocrine neoplasms malignant and unspecified

Synonym
hormone producing cancer, neuroendocrine tumors

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: grant van farmaceutische industrie voor de

scans en ter beschikking stelling van everolimus,Novartis

Intervention

Keyword: biomarker, mTOR inhibition, neuroendocrine tumors, VEGF imaging

Outcome measures

Primary outcome

The primary endpoint is the change in 89Zr-bevacizumab uptake in tumor lesions between the baseline PET scan and the scans performed after 2 and 12 weeks of everolimus treatment in patients with neuroendocrine tumors.

Secondary outcome

The secondary endpoint is progressive disease according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria on CT after 12 weeks of treatment. Progression is defined as the appearance of new disease or an increase of 20% in the sum of the longest diameters of the target lesions.

Study description

Background summary

Profound angiogenesis is an important characteristic of neuroendocrine tumors. Antiangiogenic drugs including sunitinib, bevacizumab and everolimus have shown antitumor activity in neuroendocrine tumors. We participated in the RAD001 studies for neuroendocrine tumors. From preclinical studies including studies performed in our own lab we know that everolimus downregulates VEGF. Currently it is not possible to predict which individual patient will benefit from treatment with an mTOR inhibitor. A predictive biomarker for efficacy of mTOR inhibitors is urgently needed and would be helpful, as a predictive biomarker may facilitate the development of combination therapies, of individual titration of the dose, and it may facilitate early clinical studies. Furthermore, it may spare the patients unnecessary side effects. mTOR inhibitors may fail in individual patients because angiogenesis is not sufficiently inhibited. Non-invasive imaging of VEGF before and early after start of treatment may have predictive value for treatment efficacy.

Within the UMCG we have eveloped the 89Zr-bevacizumab PET label for non-invasive measurement of VEGF levels in the tumor and its surrounding microenvironment. This tracer can give insight in the tumors* dependency on angiogenesis as we have already proven for a VEGF-receptor tyrosine kinase inhibitor. Currently this tracer is used in clinical trials. We would like to investigate whether all neuroendocrine tumors produce VEGF and whether they differ in their response to inhibition of VEGF by mTOR.

Study objective

To evaluate the feasibility of 89Zr-bevacizumab-PET imaging as predictive biomarker before and during treatment with everolimus in patients with neuroendocrine tumors.

Study design

This is a pilot study for evaluation of 89Zr-bevacizumab PET imaging as predictive biomarker during treatment with everolimus in patients with neuroendocrine tumors.
89Zr-bevacizumab PET imaging will be performed before start of treatment and after 2 and 12 weeks of treatment in the first three patients. If the scan after 2 weeks of treatment is already informative further patients will not undergo a scan at 12 weeks.

Study burden and risks

The first 3 patients will be intravenously injected at 3 times points with 37 MBq, subsequent patients will recieve 2 or 3 injections with 37 MBq 89Zr-becizumab. This results in a cumulative radiation dose of 54 mSv respectively 36 mSv. Some patients will have their scnas with a PET/CT camera, this results in an additional radiation dose of 1.5 mSV pers can (total dose 58.5 mSv for 3 scanas and 39 mSv for 2 scans). According to ICRP 62 this radiation dose falls in category III (moderate risk).
Patients have to pay 2 or 3 extra visits to the hospital for tracer injection. PET scans will be performed on regular visit days. Blood samples for biomarkers will be drawn during routine blood investigations. There is no direct benefit for the patients in this study. If 89Zr-bevcizumab PET imaging however is a predictive biomarker for angiogenesis inhibitors, many patients can be spared unnecessary side effects and society can be spared costs of futile treatment in the future.

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

• adult patients with metastatic neuroendocrine tumors
• radiological documentation of progressive disease over the past year
• measurable disease according to RECIST criteria
• Adequate bone marrow function as shown by: ANC >= 1.5 x 109/L, Platelets >= 100 x 109/L, Hb > 9 g/dL.
• Adequate liver function: serum bilirubin: <= 1.5 x ULN, ALT and AST <= 2.5x ULN. Patients with known liver metastases: AST and ALT <= 5x ULN.
• Adequate renal function: serum creatinine <= 1.5 x ULN.
• Fasting serum cholesterol <=300 mg/dL OR 7.75 mmol/L AND fasting triglycerides <= 2.5 x ULN. NOTE: In cases where one or both of these thresholds are exceeded, the patient can only be included after initiation of appropriate lipid lowering medication,

Exclusion criteria

• uncontrolled medical conditions (eg, unstable angina, symptomatic heart failure, serious

intercurrent infections, uncontrolled diabetes)
• any psychological, familial, sociological condition potentially hampering compliance with the study protocol and follow-up schedule of the study
• Prior therapy with RAD001 (everolimus) or other rapamycins (sirolimus, temsirolimus).

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-07-2010
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	89Zr-becizumab
Generic name:	89Zr-becizumab
Product type:	Medicine
Brand name:	Afinitor
Generic name:	Everolimus
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	08-04-2010
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-05-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2009-017195-24-NL
CCMO	NL30950.042.09