89Zr-bevacizumab labelled PET imaging in patients with Renal Cell Carcinoma treated with sunitinib or bevacizumab plus interferon; a pilot study

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The primary objective of the study is to evaluate the feasibility of 89Zr-bevacizumab PET imaging as a biomarker before and during treatment with sunitinib or bevacizumab plus interferon in patients with RCC.

Ethical review	-
Status	Recruitment stopped
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON33835

Source
ToetsingOnline

Brief title
VEGF imaging in Renal Cell Carcinoma

Condition

- Renal and urinary tract neoplasms malignant and unspecified
- Renal disorders (excl nephropathies)

Synonym
kidney cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: een grant van een farmaceutisch bedrijf,Roche

Intervention

Keyword: angiogenesis inhibitor, biomarker, renal cell carcinoma, VEGF imaging

Outcome measures

Primary outcome

The primary endpoint is the change in SUVmax between baseline 89Zr-bevacizumab

PET scan and the scan performed after 2 and 6 weeks of treatment with sunitinib

or bevacizumab plus interferon in patients with RCC.

Secondary outcome

The secondary endpoint is progressive disease according to Response Evaluation

Criteria in Solid Tumors (RECIST) criteria, after 3 months of treatment.

Study description

Background summary

The majority of renal cell carcinomas is characterized by profound angiogenesis because of inactivation of the Von Hippel Lindau gene. Treatment with angiogenesis inhibitors results in doubling of progression free survival in the metastatic setting.
Currently it is not possible to predict which individual patient will benefit from anti-angiogenic therapy. A predictive biomarker for efficacy of angiogenesis inhibitors is urgently needed as it may spare the patients unnecessary side effects, safes costs for the society as angiogenesis inhibitors are expensive agents and for research purposes, a predictive biomarker may speed up development of combination therapies, of individual titration of the dose, and save time and patients during early clinical studies of new agents. Angiogenesis inhibitors may fail because 1) the target for the drug is absent, 2) the drug does not reach the target or 3) angiogenesis is not sufficiently inhibited. Serum VEGF increases abruptly after start sunitinib

while free serum VEGF decreases after start bevacizumab, a phenomenon that is not understood and may not reflect tumour VEGF production. Non-invasive measurement of VEGF in the tumour and its surroundings by 89Zr-bevacizumab labelled PET imaging can potentially give insight in presence of the target for bevacizumab and tumour dependency on angiogenesis. Change in 89Zr-bevacizumab uptake early during treatment with angiogenesis inhibitors may be a predicitive biomarker for clinical benefit.

Study objective

The primary objective of the study is to evaluate the feasibility of 89Zr-bevacizumab PET imaging as a biomarker before and during treatment with sunitinib or bevacizumab plus interferon in patients with RCC.

Study design

This is a pilot study for evaluation of 89Zr-bevacizumab PET imaging as a biomarker during treatment with sunitinib or bevacizumab plus interferon in patients with RCC.
Patients who will start treatment with:
arm A: sunitinib 50 mg orally once daily for 28 days followed by 14 days rest,
or
arm B: bevacizumab intravenously (IV) 10 mg/kg q 14 days in combination with IFNα2a subcutaneously (SC) 9MIU 3 times a week, are eligible for this study.
89Zr-bevacizumab PET imaging will be performed before start of treatment and after 2 and 6 weeks of treatment.
The primary endpoint is change in SUVmax between the baseline scan and the scan after 2 and after 6 weeks.

Patients will be injected intravenously with 37 MBq, protein dose 1-10 mg 89Zr-bevacizumab at day -4 or -3, at day 10 or 11 and at day 38 or 39. Subsequently, images will be made at day 1, day 15 and day 43, on these days blood will be drawn for determination of VEGF related biomarkers.

Study burden and risks

Patients will be intravenously injected at 3 time points with 37MBq. This results in a cumulative radiation dose of 54 mSv for female patients and 45 mSv for male patients. According to ICRP 62 this radiation dose falls in category III (moderate risk).
Life expectancy of the patients is limited because of their incurable renal cell carcinoma, making the risk of development of a secondary malignancy clinically likely not relevant.
Patients have to pay 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 at 3 time points.

There is no direct benefit for the patients in this study. If 89Zr-bevacizumab 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

•locally advanced irresectable or metastatic renal cell cancer
•no untreated brain metastases (CT or MRI not necessary in the absence of symptoms)
•no uncontrolled hypertension
•no clinically significant cardiovascular events or disease during the last 12 months
•no surgery in the last 4 weeks
•no treatment with bevacizumab or another monoclonal antibody with anti-angiogenic

properties in the last 4 months
•no treatment with a tyrosine kinase inhibitor during the last 4 weeks
•measurable disease with x-ray or CT scan, at least one site of disease must be unidimensionally measurable as follows:
X ray >= 20 mm
Spiral CT scan >= 10 mm
Non-spiral CT scan >= 20 mm
•>= 18 years
•clear cell histology component
•absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial
•before patient randomization, written informed consent must be given according to GCP, and local regulations

Exclusion criteria

Are formulated as "no existence of" in inclusion criteria

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):	01-11-2008
Enrollment:	26
Type:	Anticipated

Medical products/devices used

Product type:	Medicine

Brand name:	89Zr-bevacizumab
Generic name:	89Zr-bevacizumab

Ethics review

Not available

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	EUCTR2008-005519-17-NL
ClinicalTrials.gov	NCT00831857
CCMO	NL24452.042.08