The effect of sorafenib (Bay-43-9006) on 111Indium labeled chimeric monoclonal antibody G250 or 111Indium labeled bevacizumab uptake in patients with clear cell RCC (ccRCC).

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Primary objectivesDetermine the effect of Sorafenib (Bay 43-9006) on the uptake of In-111 labeled chimeric monoclonal antibody G250 (In-111-cG250) by RCC lesions.Determine the effect of Sorafenib (Bay 43-9006) on the uptake of In-111 labeled...

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

Summary

ID

NL-OMON30815

Source
ToetsingOnline

Brief title
effect of sorafenib on imaging of ccRCC

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
angiogenesis, kidney cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: bevacizumab, clear cell renal cell carcinoma, monoclonal antibody cG250, sorafenib

Outcome measures

Primary outcome

Primary objective

To determine the effect of sorafenib treatment on In-111-cG250 uptake of the

tumor

To determine the effect of sorafenib treatment on In-111-bevacizumab uptake of

the tumor

Secondary outcome

Secondary objective

Immunohistochemical analysis of CA-IX expression, (p)VHL status, HIF1-a, VEGF

and PDGF expression, apoptosis and necrosis of surgical specimen, to

investigate whether the clinical effect of sorafenib is based on angiogenesis,

or if other mechanisms play a role.

Study description

Background summary

Sorafenib is one the new drugs developed to interfere in the growth factor signal transduction in tumors. It inhibites the ras/raf kinase pathway and VEGF and PDGF receptors. In this way, it stops tumorcell proliferation as well as angiogenesis.

Antiangiogenic compounds appear to be able to decrease the tumor microvascular density (TMD) and interstitial fluid pressure (IFP), suggestive for normalization of tumor vasculature. Normalization of tumor vasculature is correlated with a reduction of hypoxia and IFP and as a result of this, higher efficacy of radiotherapy and improved drug delivery to the tumor.
The monoclonal antibody cG250 has been extensively investigated in our institute, it recognizes the HIF-inducible gene product CA-IX ubiquitously expressed in clear cell Renal Cell Carcinoma (ccRCC). Multiple studies have convincingly demonstrated the ability of radiolabeled cG250 to effectively image tumors in vivo.
Bevacizumab is a humanized monoclonal anti-VEGF antibody. It depletes VEGF from plasma, thereby inhibiting angiogenesis. Recently, radiolabeled bevacizumab has been shown to visualise ccRCC in vivo.
Surgically excised tumor tissue will be analysed morphologically, molecularly, (immuno)histochemically for different markers in ccRCC
This will be correlated to the radioimmunoscintigraphy.
Hypothesis:
We aim to explore the effect of sorafenib on tumor G250/CAIX and VEGF expression, by determining the tumoral uptake of In-111 labeled G250, In-111 labeled bevacizumab. These images can be compared to the histologically analysed surgical specimen and may lead to a better understanding of the mode of action of sorafenib.

Study objective

Primary objectives
Determine the effect of Sorafenib (Bay 43-9006) on the uptake of In-111 labeled chimeric monoclonal antibody G250 (In-111-cG250) by RCC lesions.
Determine the effect of Sorafenib (Bay 43-9006) on the uptake of In-111 labeled bevacizumab (In-111-bevacizumab) by RCC lesions.

Secondary objectives
Increase the understanding in the mode of action of Sorafenib (Bay 43-9006) on a histological level.

Study design

Pilot study, single center, with a sequential enrollment of patients: first 10 patients will recieve Indium labeled cG250 and the next 10 patients will recieve Indium labeled bevacizumab.

Intervention

20 patients:
All patients will undergo two PET-scans and will take from week 2-5 every day 400mg sorafenib orally.

10 patients will recieve 200 MBq/10 mg 111In-cG250 in 50 ml isotonic saline/5 % Human serum albumin (HAS) as a continuous intravenous (iv.) infusion in 10 minutes, after which on day 2-4 and on day 5-7 gammascans will be made. This will happen in week 1 and in week 5.
10 patients will recieve 200 MBq/1 mg 111In-bevacizumab in 50 ml isotonic saline/5 % Human serum albumin (HAS) as a continuous intravenous (iv.) infusion in 10 minutes, after which on day 2-4 and on day 5-7 gammascans will be made. This will happen in week 1 and in week 5.

Study burden and risks

Burden of the studie comprises of:
-Week 0: screening, extensive anamnesis en physical examination, EKG, blood test
-Week 1: Indium-cG250/bevacizumab injection (day 1), two scans (day 1 and day 5-7)
-Week 1: After last scan; consultation with investigator, start sorafenib treatment
-Week 2-5: Daily use of 400mg sorafenib
-Week 4: screening side-effects sorafenib
-Week 5: Indium-cG250/bevacizumab injection (day 1), two scans (day 1 and day 5-7)
-Week 5: After last scan; stop sorafenib treatment
-Week 12: follow-up visit with investigator

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

-Renal cell carcinoma patients planned for surgery (nephrectomy/metastectomy)
-Karnofsky > 60 %
-age over 18 years
-signed informed consent

Exclusion criteria

-Known subtype other than clear cell RCC
-Pre-exposure to murine/chimeric antibody therapy
-Chemotherapy, immunotherapy or radiation therapy within 4 weeks prior to start of study. Palliative limited field external radiation for fracture prevention is allowed
-Diabetes Mellitus

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):	01-11-2006
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Indium-111
Product type:	Medicine
Brand name:	Avastin
Generic name:	Bevacizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Nexavar
Generic name:	Sorafenib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rencarex
Generic name:	cG250

Ethics review

Approved WMO Date:	09-03-2007
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-10-2007
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-07-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
Other	-
EudraCT	EUCTR2006-006833-42-NL
CCMO	NL14551.091.07