Evaluation of the activity of temsirolimus with FLT-PET in patients with renal cell cancer

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Primary objectiveAssessment of the duration of PFS after treatment with temsirolimus in heavily pre-treated metastatic RCC patientsSecondary objectivesEvaluation of the FLT-PET and FDG-PET:Measurement of 18F-FLT-PET-signal and FDG-PET-signal, and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON33063

Source
ToetsingOnline

Brief title
temsirolimus-RCC-imaging

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
kidney cancer, renal cell carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Carcinoma, FDG-PET, FLT-PET, Renal Cell, temsirolimus

Outcome measures

Primary outcome

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Secondary outcome

n.a.

Study description

Background summary

The prognosis of metastatic renal cell carcinoma (mRCC) patients has improved the last couple of years, due to the treatment with angiogenesis inhibitors and mTOR inhibitors. First line and second line therapy is nowadays standard. However, responses on third or fourth line therapy, in RCC patients participating in phase I studies have been observed. As yet the optimal sequence of therapeutic agents in mRCC is not known and data on progression free survival of third or fourth line treatment are not available. More and more patients with metastatic RCC will receive multiple sequential treatments. A large proportion of those patients will remain in a good condition and have a good quality of life. Those are the candidates for new lines of therapy.
In the evaluation of new treatments the difficulty lies in the way of assessment of activity of new drugs. In the past, chemotherapy induced real volume responses, whereas with the new targeted agents volume reponse may take a long period of time (more than 6 months is not exceptional), or will never induce a real decrease in tumor volume, while the patient may benefit from a long period of stable disease. All these new drugs are costly and not without side effects, and therefore there is an urgent need for new end points of therapy, better reflecting the activity of the drug.
In first line poor prognosis metastatic RCC patients mTor inhibition with temsirolimus has become standard therapy based on an improvement in PFS and OS. Also for temsirolimus RECIST criteria have been used. However, by using the RECIST criteria for the evaluation of efficacy only the change in tumour volume is assessed. Temsirolimus is an antiproliferative anti cancer drug and proliferation might be assessed by FLT PET or FDG PET.
Until now only very limited data have been published on the role of FDG PET and FLT PET after mTor inhibitors. FLT PET seems promising in mice glioblastoma in

mice treated with mTor inhibitors. Another very recent paper reports the value of FDG PET as suurogate marker of everolimus activity, also in mice. Only one clinical study in which FDG PET was used in patients treated with mTor inhibitors had included patients with a mixture of diagnoses.
Therefore, we propose to investigate in a systematic way whether molecular imaging with FLT-PET and/or FDG-PET is a better predictor of response and progression free survival (PFS) than evaluation by standard anatomical imaging by CT-scan in RCC patients treated with temsirolimus. Furthermore, we propose to investigate the optimal way of assessment of molecular characteristics of the tumor (metabolism, proliferation) by comparing FLT-PET with FDG-PET.

Study objective

Primary objective
Assessment of the duration of PFS after treatment with temsirolimus in heavily pre-treated metastatic RCC patients

Secondary objectives
Evaluation of the FLT-PET and FDG-PET:
Measurement of 18F-FLT-PET-signal and FDG-PET-signal, and signal changes during treatment with temsirolimus
Correlation of 18F-FLT-PET-signal and FDG-PET before, and signal changes during treatment with treatment outcome (clinical response and PFS).
Response rate
Toxicity

Study design

Open-label, multicenter phase II trial of temsirolimus (standard schedule: 25 mg weekly, by 1-hour i.v. infusion) with translational research in part of the patients.

Intervention

temsirolimus (standard schedule: 25 mg weekly, by 1-hour i.v. infusion)

Study burden and risks

nvt

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

1. patients with histologically confirmed, advanced (stage IV or recurrent disease) RCC who have received at least one prior angiogenesis inhibitor for their disease.
2. Karnofsky performance status >= 70.
3. At least 1 measurable lesion that can be accurately measured in at least 1 dimension with the longest diameter >= 10-mm when measured by spiral computerized tomography (CT, 5-mm slice thickness contiguous)
4. Age >= 18 years.
5. Absolute neutrophil count (ANC) >= 1.5 x 109/L (1500 cells/mm3), platelet count >= 100 x 109/L (100,000 cells/ mm3), hemoglobin >= 8.0 g/dL (5.0 mmol/L).
6. Adequate renal function (serum creatinine >= 1.5 times the ULN) or creatinin clearance of >= 50 ml/min
7. Adequate hepatic function (bilirubin <= 1.5 times the ULN, aspartate transaminase (AST) <= 3 times the ULN [<= 5 times the ULN if liver metastases are present]).
8. Fasting serum cholesterol <= 350 mg/dL (9.0 mmol/L), triglycerides <= 400 mg/dL (4.56 mmol/L).
9. Subjects receiving cytochrome P450 (CYP) 3A4 inducers or inhibitors must be on stable doses for at least 1 week prior to randomization.
10. Life expectancy of at least 8 weeks.

11. Negative pregnancy test for female patients of childbearing potential
12. Women and men enrolled into this trial must use adequate birth control measures during the course of the trial and must continue for 3 months after the last dose of temsirolimus.
13.Signed and dated written informed consent form

Exclusion criteria

1. Subjects with central nervous system (CNS) metastases. Subjects with a prior history of CNS metastases will be eligible if the screening magnetic resonance imaging (MRI)/CT (with contrast) indicates no residual disease.
2. Prior investigational therapy/agents within 2 weeks of randomization.
3. Prior treatment with a mTOR inhibitor
4. History of other prior malignancy in past 5 years, other than basal cell carcinoma, squamous cell carcinoma of the skin, or cervical carcinoma in situ.
5. Not recovered from prior surgery and/or surgery or radiation therapy within 4 weeks of randomization.
6. Immunocompromised subjects, including subjects known to be human immunodeficiency virus (HIV) positive, hepatitis B positive, or hepatitis C positive.
7. Active infection or serious intercurrent illness.
8. Presence of unstable angina or myocardial infarction within the previous 6 months (prior to screening), use of ongoing maintenance therapy for life-threatening arrhythmia, known pulmonary hypertension, or pneumonitis.
9. Pregnant or nursing women, women who are of childbearing potential who are not using an effective contraceptive method, or men with partners of childbearing potential who are not using an effective contraceptive method. (A woman of childbearing potential is defined as a woman who is biologically capable of becoming pregnant.)
10. Any other major illness that, in the investigator's judgment, will substantially increase the risk associated with the subject's participation in this study

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-08-2009
Enrollment:	50
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Torisel
Generic name:	temsirolimus
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-05-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-07-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-06-2011
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
EudraCT	EUCTR2009-012802-38-NL
CCMO	NL28298.091.09