Phase II study of sunitinib rechallenge in patients with metastatic renal cell carcinoma.

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To determine whether sunitinib rechallenge in patients with mRCC, who had benefit from prior treatment with sunitinib and who progressed on both sunitinib and second-line therapy (or a period of more than 3 months without treatment), can again...

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

Summary

ID

NL-OMON41227

Source
ToetsingOnline

Brief title
Sunitinib Rechallenge

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
advanced or metastatic kidney cancer, renal cell cancer

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Divisie I Beheer BV

Intervention

Keyword: metastatic renal cell cancer, sunitinb rechallenge, sunitinib

Outcome measures

Primary outcome

To investigate the proportion of patients that is progression-free at 3 months upon retreatment with sunitinib.

Secondary outcome

(1) To assess the clinical benefit rate, median progression-free survival and overall survival in individuals retreated with sunitinib. (2) To assess the effects of sunitinib rechallenge on (a) expression of LAMP1/2 proteins in circulating mononuclear cells and in tumor tissue (b) the number and activation state of circulating DC, MDSC and Tregs (c) sunitinib drug levels (d) sunitinib tumor tissue concentrations (e) intratumoral phosphoproteomic profiles. (3) To evaluate the effect of retreatment with sunitinib on the quality of life.

Study description

Background summary

Targeted therapies are associated with (acquired) resistance after a median of 5-11 months of treatment, resulting in disease progression, while almost no tumors are intrinsically resistant in the first line setting. We recently published that tumor cell resistance to sunitinib may be directly related to lysosomal sequestration of sunitinib. This resistance mechanism was shown to be transient, since a drug-free culture period could normalize the lysosomal storage capacity for sunitinib and resulted in recovery of drug sensitivity.
In two reports it has been suggested that patients with mRCC who responded to sunitinib in the first-line setting may benefit from rechallenge with sunitinib treatment after second-line treatment failure. However, these data are retrospective. A prospective trial to investigate rechallenge with sunitinib is needed to determine whether this strategy is of benefit for patients with mRCC

with prior clinical benefit to sunitinib but stopped treatment because of overt clinical resistance.

Study objective

To determine whether sunitinib rechallenge in patients with mRCC, who had benefit from prior treatment with sunitinib and who progressed on both sunitinib and second-line therapy (or a period of more than 3 months without treatment), can again induce a meaningful clinical benefit.

Study design

A multi-center single arm phase II study.

Intervention

Patients will be treated in repeated 6-week cycles with 50 mg sunitinib orally daily for 4 weeks followed by 2 weeks off.

Study burden and risks

The most common adverse events due to sunitinib treatment are fatigue, diarrhea, nausea, skin and hair discoloration, hand-foot syndrome, rash, hypertension, fever, mucositis/stomatitis, vomiting, dyspepsia, abdominal pain, constipation, taste alteration, headache, back pain, extremity pain, cough, dyspnea, anorexia, and bleeding.

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 or cytologically confirmed clear-cell mRCC.
2. Patients who progressed on first-line treatment with sunitinib and who had clinical benefit defined as a response (according to RECIST 1.1 criteria) or SD for more than 6 months on this treatment.
3. Patients who progressed after second-line treatment (mTOR inhibitor or other treatment as long as patients are not treated with a VEGF targeted TKI, see exclusion criteria), or who progressed after a treatment-free interval of at least 3 months since discontinuation of first-line sunitinib treatment.
4. Patients with radiological (and/or clinical) confirmed progressive disease according to RECIST 1.1 criteria.
5. Measurable or evaluable disease as defined by RECIST 1.1.
6. WHO performance status 0-2.
7. Life expectancy of at least 12 weeks.
8. Age 18 years or older.
9. Able to receive oral medication.
10. Able to provide written informed consent.
11. Adequate hematologic function: ANC * 1.5 x 109/L, platelets * 100 x 109/L, Hb * 6.0 mmol/L.
12. Patients with brain metastases are eligible if they have been stable for at least two months post-radiation therapy or surgery.
13. No other current malignant disease, except for basal cell carcinoma of the skin.
14. Adequate hepatic function: serum bilirubin * 1.5 x ULN, ALT and AST * 2.5 x ULN (or * 5 times ULN if liver metastases are present).
15. Renal function: estimated glomerular filtration rate * 40 ml/min.
16. Patients with reproductive potential must use effective contraception. Female patients must have a negative pregnancy test.

Exclusion criteria

1. Patients treated with any VEGF targeted TKI (sorafenib, pazopanib, axitinib, dovitinib) as second-line treatment after progression on first-line sunitinib treatment.
2. Uncontrolled hypertension. Blood pressure must be *160/95 mmHg at the time of screening on a stable antihypertensive regimen. Blood pressure must be stable on at least 2 separate measurements on at least 2 separate days.
3. Active infection or serious intercurrent illness.
4. Presence of unstable angina, recent myocardial infarction (within the previous 3 months), evidence of or symptoms compatible with cardiac failure class III or IV according to the New York Heart Association Functional Classification.
5. Macroscopic hematuria.
6. Presence of any significant central nervous system or psychiatric disorder(s) that would hamper the patient*s compliance.
7. Any other major illness that, in the investigator*s judgment, substantially increases the risk associated with the subject*s participation in the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-04-2013
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Sutent

Generic name:	Sunitinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-09-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2012-002891-15-NL
CCMO	NL41280.029.12