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

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21668

Source
Nationaal Trial Register

Brief title
Sunitinib rechallenge

Health condition

Metastatic renal cell cancer - uitgezaaide nierkanker
Sunitinib rechallenge - herbehandeling met sunitinib
Sunitinib - Sunitinib

Sponsors and support

Primary sponsor: VU Medical Center
Source(s) of monetary or material Support: Divisie I Beheer BV

Intervention

Outcome measures

Primary outcome

To investigate the proportion of patients with mRCC retreated with sunitinib that is

progression-free at 3 months.

Secondary outcome

1. To assess the clinical benefit rate (ORR and SD), mPFS and OS in individuals retreated with sunitinib;

2. To assess the effects of sunitinib rechallenge on LAMP1/2 proteins in PBMCs and tumor tissue;

3. To assess the immunological effects of sunitinib rechallenge on the number and activation state of circulating DC, MDSC and Tregs;

4. To study phosphoproteomic profiles of tumors before rechallenge and at the time of progression;

5. To assess sunitinib drug levels and tumor tissue concentrations of sunitinib;

6. 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 after failure of second-line treatment. However, these data are retrospective. A prospective trial to investigate a rechallenge with sunitinib is needed to determine whether this strategy is of benefit for patients with mRCC with prior clinical benefit to sunitinib but who stopped treatment because of overt clinical resistance.

Study objective

To determine whether sunitinib rechallenge in patients with mRCC, who had benefit (defined as stable disease for at least 6 months) from prior treatment with sunitinib and who progressed on both sunitinib and second-line therapy (or were without treatment for a period of more than 3 months), can again be of clinical benefit.

Study design

We aim to study 14 patients in stage I and 31 patients in stage II. If at interim analysis (end of stage I) at least 8 of the 14 patients are progression free (CR, PR or SD according to RECIST 1.1) it would be worth continuing research and an additional 31 patients will be accrued. If 7 or less of the first 14 patients are progression-free, this study will be terminated due to lack of acceptable clinical benefit to retreatment with sunitinib. In case a minimum of 25 of the total of 45 patients will be progression free at 3 months, we will reject the null hypothesis that retreatment with sunitinib has no clinical activity. Based on Simon's two-stage design, this trial will have 90% power to detect that sunitinib retreatment results in a progression-free percentage in 70% of patients at 3 months of treatment versus the estimated null progression-free rate of 40% at three months with a 5% Type I error rate.

Intervention

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

Contacts

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Eligibility criteria

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);

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 type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-10-2012
Enrollment:	45
Type:	Anticipated

Ethics review

Positive opinion

Date:	14-11-2012
Application type:	First submission

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
NTR-new	NL3527
NTR-old	NTR3711
Other	METC VUmc : 2012/259
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A