

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 (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...

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| Ethische beoordeling | Positief advies |
| Status | Werving gestart |
| Type aandoening | - |
| Onderzoekstype | Interventie onderzoek |

Samenvatting

ID

NL-OMON21668

Bron

Nationaal Trial Register

Verkorte titel

Sunitinib rechallenge

Aandoening

Metastatic renal cell cancer - uitgezaaide nierkanker

Sunitinib rechallenge - herbehandeling met sunitinib

Sunitinib - Sunitinib

Ondersteuning

Primaire sponsor: VU Medical Center

Overige ondersteuning: Divisie I Beheer BV

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoekopzet

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.

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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 $\geq 1.5 \times 10^9/L$, platelets $\geq 100 \times 10^9/L$, 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 $\leq 1.5 \times ULN$, ALT and AST $\leq 2.5 \times ULN$ (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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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 $\leq 160/95$ 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.

Onderzoeksopzet

Opzet

| | |
|------------------|-------------------------|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | N.v.t. / één studie arm |
| Blinding: | Open / niet geblindeerd |
| Controle: | N.v.t. / onbekend |

Deelname

| | |
|-------------------------|----------------------|
| Nederland | |
| Status: | Werving gestart |
| (Verwachte) startdatum: | 12-10-2012 |
| Aantal proefpersonen: | 45 |
| Type: | Verwachte startdatum |

Ethische beoordeling

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|-----------------|------------------|
| Positief advies | |
| Datum: | 14-11-2012 |
| Soort: | Eerste indiening |

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

| Register | ID |
|----------------|-------------------------------------|
| NTR-new | NL3527 |
| NTR-old | NTR3711 |
| Ander register | METC VUmc : 2012/259 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

Resultaten

Samenvatting resultaten

N/A