Prediction of response to kinase inhibitors based on protein phosphorylation profiles in tumor tissue from advanced renal cell cancer patients.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26770

Source
Nationaal Trial Register

Brief title
Phosphoproteomics for prediction of response to treatment in kidney cancer

Health condition

Phosphoproteomics - phosphoproteomics
Response prediction - therapieselectie
renal cell cancer - nierkanker
kinase inhibitors - kinaseremmers

Sponsors and support

Primary sponsor: VU Medical Center
Source(s) of monetary or material Support: VitrOmics Health Services BV (VHS)

Intervention

Outcome measures

Primary outcome

The phosphoproteomics profile of the tumor biopsy before treatment will be determined and correlated with radiological response and progression-free survival.

Secondary outcome

1. The relationship between the PamChip kinase activity profile for the initiation of therapy and progression-free survival;

2. The relationship between the genetic mutation profile of the primary tumor based on MPS and progression-free survival;

3. The relationship between the serum peptide profile before and during treatment and progression-free survival;

4. The relationship between the number and type of immune regulatory cells in blood and tissue and progression-free survival;

5. The relationship between genetic polymorphisms and pharmacokinetic parameters and progression-free survival;

6. The relationship between protein profile tumorexosomen from urine and serum and progression-free survival.

Study description

Background summary

The rapid development of agents blocking kinases has established the use of molecularly targeted therapy as the preferred treatment approach for patients with metastatic renal cell cancer (RCC). Five kinase inhibitors (sunitinib, everolimus, temsirolimus, sorafenib and pazopanib) are now approved for clinical use. Response rates differ among these agents, importantly depending on line of treatment. In first-line treatment sunitinib results in 47% objective response rates, where in second-line after cytokines 34% responds. Thus far, it is unclear which patient with advanced renal cell cancer will respond to targeted therapy. In order to select patients for targeted therapies, several profiling approaches have been explored but to date no adequate and reliable test is available. It is assumed that responses to targeted agents depend on specific receptor and protein signalling activities in tumor tissues. Therefore, we propose that protein phosphorylation profiling with phosphoproteomics may be a potential clinical diagnostic tool to predict for tumor response to targeted therapy.

Study objective

The rapid development of agents blocking kinases has established the use of molecularly targeted therapy as the preferred treatment approach for patients with metastatic renal cell cancer (RCC). Five kinase inhibitors (sunitinib, everolimus, temsirolimus, sorafenib and pazopanib) are now approved for clinical use. Response rates differ among these agents, importantly depending on line of treatment. In first-line treatment sunitinib results in 47% objective response rates, where in second-line after cytokines 34% responds. Thus far, it is unclear which patient with advanced renal cell cancer will respond to targeterd therapy. In order to select patients for targeted therapies, several profiling approaches have been explored but to date no adequate and reliable test is available. It is assumed that responses to targeted agents depend on specific receptor and protein signalling activities in tumor tissues. Therefore, we propose that protein phosphorylation profiling with phosphoprotemics may be a potential clinical diagnostic tool to predict for tumor response to targeted therapy. This approach is expected to increase efficacy, reduce costs an d prevent toxicities from (ineffective) targeted agents.

Study design

A feasability analysis will be performed when 20 patients are included.

Intervention

In this study, a fresh tumor biopsy from a metastasis or a primary tumor will be taken. In all subjects subsequent standard treatment will be initiated according to current clinical guidelines. In addition to this biopsy, collection of urine and blood is performed upon inclusion and the same procedure is optional on 2 other time points during treatment.

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients with advanced (unresectable and/or metastatic) renal cell cancer;

2. Patients who will start treatment with sunitinib, pazopanib, sorafenib, axitinib or everolimus;

3. At least one tumor lesion should be accessible for biopsy. bone metastases are excluded as possible biopsy site;

4. Age >- 18 years;

5. Patients must have at least one measurable lesion. Lesions must be evaluated by CT-scan or MRI according to Response Evaluation Criteria in Solid Tumors (RECIST);

6. WHO performance status 0 - 2;

7. Able to provide written informed consent.

Exclusion criteria

1. Clinical findings associated with an unacceptably high tumor biopsy risk, according to the judgement of the investigator;

2. Radiotherapy on target lesions during study or within 4 weeks of the start of study drug;

3. Any condition that is unstable or could jeopardize the safety of the subject and their compliance in the study.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial

Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-11-2012
Enrollment:	225
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	NL3526
NTR-old	NTR3710
Other	METC VUmc : 2012/109
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A