Kinaseprofiling voor therapieselectie bij uitbehandelde kankerpatiënten.

No registrations found.

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

Summary

ID

NL-OMON22647

Source
Nationaal Trial Register

Brief title
TSAP

Health condition

Gemetastaseerde solide tumoren
Vergevorderde (uitgezaaide of inoperabele) kanker
Advanced solid tumors
Metastasized or inoperable cancer

Sponsors and support

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Source(s) of monetary or material Support: Vitromics BV

Intervention

Outcome measures

Primary outcome

To determine the clinical benefit rate (CBR) of this therapy selection approach, defined by the number of patients demonstrating either a complete or partial response or stable disease after 12 weeks of treatment.

Secondary outcome

1. To compare progression free survival (PFS) using a kinase inhibitor treatment regimen selected by kinase profiling with the PFS of the most recent treatment regimen on which the patient progressed (i.e., patients are their own controls);

2. To determine the relation of Comparative Genomic Hybridization (CGH)-profiles with response to kinase inhibitors;

3. To determine the relation of serum and tissue kinome proteomic and activity profiles with response to kinase inhibitors and survival;

4. To correlate the frequency and phenotype of immunoregulatory cells in blood and tumor tissue with response to kinase inhibitors;

5. To correlate individual pharmacodynamics with response to kinase inhibitors.

Study description

Background summary

In the past decade multiple agents that target specific signalling proteins important for tumor growth and angiogenesis have been developed and have reached clinical approval. Thus far, it is unclear which patients will respond to these agents. Targeted agents induce responses in a subgroup of cancer patients only, and adequate diagnostic tools to predict whether a patient will respond to targeted treatments are not yet available. It is of crucial importance to develop new clinical tests to determine which patients will respond to specific targeted agents. In order to select patients for targeted therapies, several profiling approaches have been explored but to date no adequate and reliable test to predict for response is available. Each patient has a unique genomic and proteomic tumor profile. It is assumed that responses to targeted agents depend on specific receptor and protein signalling activities in tumor tissues. Therefore, we propose that kinase activity profiling may be a potential clinical diagnostic tool to predict for tumor response to targeted therapy with TKI’s.

Study objective

We propose that kinase activity profiling may be a potential clinical diagnostic tool to predict for tumor response to targeted therapy with tyrosine kinase inhibitors (TKI's).

Study design

Upon informed consent for participation in this trial, a tumor biopsy of either the primary tumor or a metastasis will be performed for ex vivo analysis. If this procedure demonstrates significant inhibition of kinase activity compared to the untreated sample, the patient will receive treatment with the most potent kinase inhibitor in this assay.

Patients will be monitored by outpatient clinic visits and laboratory analysis on a 1- to 3-weekly basis.
Treatment will continue until disease progression.

Intervention

Patients will undergo a tumor biopsy for 'ex vivo' treatment of this tumor tissue with clinically available targeted tyrosine kinase inhibitors, such as sunitinib, sorafenib and erlotinib. Inhibition of the kinase activity profiles of ex vivo treated samples will be determined by comparison of their untreated control. If incubation with a targeted agent results in significant signal inhibition, treatment with the most potent inhibitor in this assay will be proposed to the patient. In case of equal inhibition, the least toxic agent will be selected for treatment.

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients presenting with an advanced (unresectable and/or metastatic) solid malignancy for whom no standard treatment is available;

2. Patients should have received at least one prior standard medical treatment regimen for their advanced disease;

3. Patients with progressive disease within 12 weeks prior to the start of study medication based on radiological assessment;

4. At least one tumor lesion should be assessable for biopsy to perform kinase activity analysis;

5. Age ≥ 18 years;

6. Histological or cytological documentation of cancer is required;

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

8. WHO performance status 0 - 2;

9. Life expectancy of at least 12 weeks;

10. Adequate bone marrow, liver and renal function as assessed by the following laboratory requirements to be conducted within 7 days prior to screening:

A. Hemoglobin ≥ 5.6 mmol/L;

B. Absolute neutrophil count (ANC) ≥ 1,500/mm3;

C. Platelet count ≥ 100*109/l;

D. Total bilirubin ≤ 1.5 times the upper limit of normal;

E. ALT and AST ¡Ü 2.5 x upper limit of normal (≤ 5 x upper limit of normal for subjects with liver involvement of their cancer);

F. Serum creatinine ≤ 1.5 x upper limit of normal or a calculated creatinine clearance ≥ 50 ml/min;

G. Activated partial thromboplastin time < 1.25 x ULN;

H. Prothrombin time or INR < 1.25 x ULN.

11. Patients should be able to swallow oral medication;

12. Written informed consent.

Exclusion criteria

1. History of cardiac disease:

A. Congestive heart failure >NYHA class 2;

B. Active Coronary Artery Disease (myocardial infarction more than 6 months prior to screening is allowed);

C. Cardiac arrhythmias requiring anti-arrhythmic therapy (beta blockers or digoxin are permitted);

D. 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 3 separate measurements on at least 2 separate days.

2. Uncontrolled infections (> grade 2 NCI-CTC version 3.0);

3. Subjects with serious non-healing wound, ulcer, or bone fracture;

4. History or clinical evidence of CNS disease, including primary brain tumor and brain metastases;

5. Clinical findings associated, in the judgment of the investigator, with an unacceptably high tumor biopsy risk;

6. Pregnant or breast-feeding subjects. Women of childbearing potential must have a negative pregnancy test performed within 7 days of the start of treatment. Both men and women enrolled in this trial must agree to use adequate barrier birth control measures (e.g., cervical cap, condom, and diaphragm) during the course of the trial. Oral birth control methods alone will not be considered adequate on this study, because of the potential pharmacokinetic interaction between study drug and oral contraceptives. Concomitant use of oral and barrier contraceptives is advised. Contraception is necessary for at least 6 months after receiving the study kinase inhibitor;

7. Concurrent anticancer chemotherapy, immunotherapy or investigational drug therapy during the study or within 4 weeks of the start of study drug;

8. Radiotherapy on target lesions during study or within 4 weeks of the start of study drug. Palliative radiotherapy will be allowed;

9. Concomitant use of dexamethasone, anti-convulsants and anti-arrhythmic drugs other than digoxin or beta blockers;

10. Major surgery within 28 days of start of treatment. The surgical wound should be fully healed prior to the start of study drug. In subjects who experienced wound healing complications during therapy, treatment should be withheld until the wound is fully healed;

11. Substance abuse, medical, psychological or social conditions that may interfere with the subject's participation in the study or evaluation of the study results;

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

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-09-2010
Enrollment:	43
Type:	Anticipated

Ethics review

Positive opinion

Date:	04-08-2010

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	NL2353
NTR-old	NTR2460
Other	METC VUmc : 2010/124
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A