Pilot study on the determination of intratumoral concentrations of kinase inhibitors in patients with advanced solid malignancies

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The main objective of this pilot study is to determine intratumoral concentrations of kinase inhibitors upon 2 weeks of treatment in tumor tissue of patients.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON36159

Source
ToetsingOnline

Brief title
Intratumoral kinase inhibitor concentrations in advanced cancer patients

Condition

- Other condition
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Advanced solid tumors, metastasized/inoperable cancer

Health condition

alle vormen van gevorderde, dwz inoperabele of uitgezaaide, solide tumoren

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Advanced solid cancer, Kinase inhibitor, Pharmacokinetics, Targeted therapy

Outcome measures

Primary outcome

To determine intratumoral kinase inhibitor concentrations upon 2 weeks of

treatment.

Secondary outcome

To determine kinase inhibitor concentrations in plasma, serum and PBMC's upon 2

weeks of treatment.

To determine intra-dermal kinase inhibitor concentrations upon 2 weeks of

treatment.

To determine per patient whether 2 weeks of treatment with kinase inhibitors

induces significant change of (1) phosphoproteomic profiles in tumor tissue;

(2) kinase activity in tumor tissue; (3) markers for antiangiogenic and

antiproliferative activity in tumor tissue; (4) serum peptide profiles

Study description

Background summary

In the past decade multiple agents targeting specific signaling proteins important for tumor growth and angiogenesis, including (tyrosine) kinase inhibitors and monoclonal antibodies, have been developed and have reached clinical approval. Thus far, it is unclear which patients will respond to these agents and why targeted agents are only effective in a small subgroup of cancer patients. Clinically applicable diagnostic tools to predict whether a patient will respond to targeted agents are not yet available. It is assumed that responses to these agents depend on specific receptor and protein signaling activities in tumor tissues. Our general hypothesis is that (phospho)proteomic and kinase activity profiling in tissue before and during treatment with kinase inhibitors may provide more insight in which markers can be clinically used to predict response to this type of targeted therapy.
We hypothesize that intratumoral drug concentrations will provide the most reliable and relevant data when used in in vitro assays to determine changes of (phospho)proteomic and kinase activity profiles in tumor tissue. To date, literature on intratumoral kinase inhibitor concentrations is not available. Results of this pilot study will be used for the design of a study aimed at determining biological and early clinical response in tumor tissue upon 2 weeks of treatment with kinase inhibitors.

Study objective

The main objective of this pilot study is to determine intratumoral concentrations of kinase inhibitors upon 2 weeks of treatment in tumor tissue of patients.

Study design

Single center, non-randomized interventional pilot study.

Intervention

Patients will be cohort-wise treated with clinically available kinase inhibitors for 2 weeks prior to standard palliative treatment. Five patients will be included in each of seven drug cohorts. Biopsies will be performed to determine intratumoral drug concentrations and to compare tissue (phospho)proteomic and kinase activity profiles before and during therapy.

Study burden and risks

Enrolment in this study will require 2 weeks of treatment with a clinically approved kinase inhibitor prior to standard palliative treatment. As much as possible, we aim to include patients who will receive standard treatment with one of the study kinase inhibitors. However, not all study drugs are administered as monotherapy standardly. Adverse events as a result of the kinase inhibitor treatment may occur. A tumor biopsy prior to and during

treatment will be taken. This biopsy may cause physical discomfort. During therapy, follow-up until start of palliative treatment will include laboratory analysis on a visit to the outpatient clinic. Before starting standard palliative treatment, potential antitumor activity of two weeks kinase inhibitor treatment can not be ruled out. Results of this study will be used for personalized treatment selection strategies that may prevent unnecessary toxicity of ineffective therapy in the future.

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

Advanced solid malignancy, minimum age 18 years, indication for palliative treatment, measurable disease with at least one lesion accessable for biopsy

Exclusion criteria

Cardiovascular conditions including congestive heartfailure NYHA class >2, recent myocardial infarction or uncontrolled coronary artery disease, cardiac arrhythmias requiring anti-arrhythmic therapy, uncontrolled hypertension; uncontrolled infections; serious non-healing wound, ulcer or bone fracture, pregnant or breast feeding.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-08-2011
Enrollment:	35
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Afinitor
Generic name:	everolimus
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Nexavar
Generic name:	sorafenib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Sutent
Generic name:	sunitinib

Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tarceva
Generic name:	erlotinib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Votrient
Generic name:	pazopanib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	10-05-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2011
Application type:	First submission
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	EUCTR2011-000219-21-NL
CCMO	NL35441.029.11