Protocol to obtain tumor biopsies from patients with locally advanced (incurable) or metastatic cancer to improve selection for clinical trials.

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* To stratify cancer patients for participation in clinical trials.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metastases
Study type	Observational invasive

Summary

ID

NL-OMON40487

Source
ToetsingOnline

Brief title
CPCT-05 biopsy protocol patient selection

Condition

- Metastases

Synonym
metastatic cancer, metastatic malignancy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: meerdere financiers (KWF/ NUTS-Ohra/ Barcode for Life)

Intervention

Keyword: Biopsy, Genetic screening, Patient selection

Outcome measures

Primary outcome

* Percentage of screened patients with actionable genetic aberrations, defined as genetic aberrations known to be activating in oncogenes and inactivating in tumor suppressor genes.

Secondary outcome

* Number and nature of (serious) adverse events of the performed histological biopsies.

* Number of samples stored for future related research.

* Number of samples with an adequate microRNA, (phospo)proteomic profiles and organoid cultures that allows biomarker discovery efforts. These profiles will be deposited in the CPCT database.

* Number of samples at progression after initial response to targeted treatment.

Study description

Background summary

Our knowledge on the genetic mutations in cancer is rapidly expanding and we are increasingly testing drugs in mainly metastastic cancer patient populations with rare mutations. Successful examples of this new strategy are ALK inhibitors in ALK translocated NSCLC (less than 5% frequency) and EGFR inhibitors in EGFR mutant NSCLC (approximately 5% frequency). Selecting molecularly stratified patient populations for studies benefits the patient as it increases the odds of obtaining benefit from experimental treatment, especially in early clinical trials. Moreover it increases the speed and

efficacy of drug development as signs of efficacy are picked up in earlier phases. Therefore, broad screening of molecular lesions in the tumors of patients that are being considered for participation in trials is crucial. This pre-selection increases our ability to perform several trials in parallel and thus include more patients in more meaningful trials. With the still dismal prognosis of patients with metastatic cancer, increasing the accrual rate to pivotal trials in selected patient populations is a key factor in improving prognosis.

The advent of Next Generation Sequencing (NGS) platforms enables us to probe a limited number of cancer related genes within 2-4 weeks. We have extensively piloted this approach and are now able to deliver clinically meaningful turn-around-times. This development enables us to use this technology to enrich clinical trials using targeted therapies for patients with specific mutations.

We will obtain tumor biopsies of a metastatic or locally advanced lesion and a peripheral blood sample from all patients included in the trial; the biopsies to obtain information on the tumor related genetic mutations (mutational profile) and the blood samples to assess each patient*s germline DNA background variation. As patients will be asked to undergo an invasive procedure it is important to address the potential safety issues. Review of the literature and our own experience show that tumor biopsies can be performed with only minor complications and acceptable risks. We will recruit patients with metastatic or locally advanced solid tumors from patients that can potentially be included in clinical trials.

Study objective

* To stratify cancer patients for participation in clinical trials.

Study design

This is a diagnostic multicenter study combining histological biopsy of tumor material with DNA sequencing using Ion Torrent®, Next Generation Sequencing (NGS) platform. The study aims improve stratification of cancer patients by obtaining fresh tumor biopsies for next-generation sequencing for participation in clinical trials.

Study burden and risks

Burden in time of study related procedures: - Baseline screening: approximately 3 hours - Blood samples: approximately 5 minutes, preferably combined with other procedures during baseline screening - Histological biopsy: approximately 30 minutes to 4 hours (biopsy itself approximately 15-30 minutes, afterwards observation for a maximum of 4 hours), maximum pre-treatment, on-treatment and post-treatment biopsies Risks of study related procedures: - Blood samples for

pharmacogenetic analysis: small change of pain, hematoma, infection - Histological biopsy: small chance on pain, bleeding, infection, allergic reaction to local anesthetic (lidocaine) or (in case of endoscopic guided biopsy) to midazolam and/or phentanyl, tissue damage.

Participation in this research project contributes towards an improved efficacy of new anti-cancer agents. Nowadays patients often face chances of less than 50% of responding to a certain treatment. We anticipate that genetic screening will improve these odds. The patients participating in this project may already benefit from this improvement. Certainly, future patients will benefit from improved treatment stratification based om knowledge generated in this project.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Patients with cancer who are eligible to enter into a trial with systemic anti-cancer therapy. A CPCT-05 biopsy may be combined with a diagnostic biopsy at all instances, if deemed appropriate for selection for study participation.Exempt from biopsy: glioblastoma patients who have undergone surgery with adequate histological material available for identification of tumor specific mutations.
2. Histologic biopsy can safely be obtained:
a. Patients with safely accessible lesions according to the medical specialist performing the biopsy procedure.
b. Patients not known should not have with known bleeding disorders (such as hemophilia) or bleeding complications from biopsies, dental procedures or surgeries.
c. Patients must not using use any anti-coagulant medication at the time of biopsy: all aspirin derivatives, NSAID*s, coumarines, platelet function inhibitors, heparins (including LMWHs) and oral factor Xa inhibitors are not allowed, unless medication can either be safely stopped or counteracted. If the medical specialist performing the biopsy of a superficial lesion agrees with performing the biopsy procedure while the patient is on anticoagulant therapy other than therapeutically dosed coumarines, LMWHs and oral Xa inhibitors, the biopsy may be performed with caution.
d. Adequate hematology and coagulation status as measured by
:i. Hb > 6.0 mmol/L
Note: Red blood cell transfusions are allowed to increase the Hb.
Platelet count >100 x 109/L
ii. PT < 1.5 x ULN or PT-INR < 1.5
iii. APTT < 1.5 x ULN
iv. On the day of biopsy in patients using coumarines: PT-INR < 1.5
e. Biopsies should be performed at least four weeks after last bevacizumab administration (only in patients previously treated with bevacizumab).
3. Patients not known with contraindications for lidocaine (or its derivatives) or (in case of endoscopic guided biopsy procedure) midazolam and phentanyl.
4. Patients with adequate organ function as measured by:
a. Adequate liver function (only in case of planned liver biopsy):
i. Total bilirubin < 1.5 x ULN (except in case of documented Gilbert*s disease)
b. Adequate renal function (only in case of planned kidney biopsy):
i. Creatinine < 1.5 x ULN or
ii. Creatinine clearance (calculated by Cockroft) > 60 mL/min
5. WHO performance status 0-2
6. Patients age > 18 years, willing and able to comply with the protocol as judged by the investigator with a signed informed consent.

Exclusion criteria

defined as positive selection criteria

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-01-2014
Enrollment:	1500
Type:	Actual

Ethics review

Approved WMO Date:	22-10-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	13-08-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
ClinicalTrials.gov	NCT01904916
CCMO	NL45677.041.13