Development of a platform for next-generation DNA sequencing based personalized treatment for cancer patients: Protocol to obtain biopsies from patients with locally advanced or metastatic cancer.

Published: 01-08-2011
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Primary objective:- To recruit patients to clinical intervention trials based on the mutational profiles of their individual cancer genome to improve treatment efficacy or intend to develop future predictors for response.Secondary objectives:- To...

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

Summary

ID

NL-OMON53030

Source
ToetsingOnline

Brief title
CPCT - 02 biopsy protocol

Condition

- Metastases

Synonym
Locally advanced or metastatic solid tumors

Research involving

Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Biopsy, Locally advanced or metastatic disease from solid tumors, Next-generation DNA sequencing, Personalized cancer treatment

Outcome measures

Primary outcome

Percentage of patients enrolled in clinical intervention trials based on the

mutational profile of their cancer genome

Secondary outcome

Secondary endpoints:

- Percentage of samples with sufficient DNA for sequencing analysis

- Percentage of samples with an adequate mutational profile to allow enrollment

in trials

- Database of all (anonymized) data obtained using this protocol

- Differences in mutational profile pre, post and during treatment

- Number and nature of all (serious) adverse events of the performed

histological biopsies

- 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 filled in questionnaires, sufficient for performing e.g. health

economic analysis or PROM research.

Study description

Background summary

A major challenge for researchers in cancer care is to expedite the development of new therapeutics. This research was set up by foundation CPCT (Centre for Personalized Cancer Treatment) to achieve this goal. Foundation CPCT was founded by three large cancer centers in the Netherlands: Dept. of Medical Oncology from the University Medical Center Utrecht, Netherlands Cancer Center - Antoni van Leeuwenhoek hospital and the Erasmus Medical Center - Cancer institute.

The current and future generation anti-cancer drugs are developed to specifically activate or deactivate deregulated gene products or signaling pathways in cancer cells. The development of such *targeted* agents is an exciting new opportunity that promises to deliver more anti-cancer efficacy and less toxicity. Although targeted therapy has been a breakthrough in medical oncology leading to the development of a portfolio of potentially successful new drugs, it has not yet delivered the much needed relief for large patient populations. We believe that the development of these agents is mainly hampered by our lack of successful patient selection.

The CPCT aims to select patients for clinical trial participation based on the results of Next Generation Sequencing (NGS) information obtained from tumor material. The advent of NGS platforms enables us to probe a significant proportion of the cancer genome and thus to develop a realistic view on the complex genetic changes in cancer cells. The CPCT aims to use NGS platforms to improve the selection of patients for targeted therapy trials.

We will obtain a tumor biopsy and peripheral blood sample from all patients included in the trial; the biopsy to obtain information on the tumor related genetic mutations (mutational profile) and the blood sample 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 shows that in general tumor biopsies can be performed with only minor complications and acceptable risks. We will recruit patients with all metastatic and locally advanced solid tumors and we aim to use the information obtained from DNA sequencing to stratify patients for inclusion in clinical trials. The final personalized treatment decision will be made dependent on the availability of trials and the expected predictive value of the mutational profile.

Study objective

Primary objective:
- To recruit patients to clinical intervention trials based on the mutational profiles of their individual cancer genome to improve treatment efficacy or intend to develop future predictors for response.

Secondary objectives:
- To determine the amount of biopsy samples with sufficient DNA for analysis
- To determine the amount of biopsy samples with an adequate mutational profile
- To collect and anonymously interpret all mutational profiles obtained using this protocol
- To determine changes in the mutational profile under the influence of systemic treatment
- To explore and analyze the individual microRNA,(phospho)proteomic profiles and organoid cultures in patients with cancer to develop future predictors for response to systemic treatment.
- To explore the correlation between mutational profiles in solid tumor biopsies and liquid biopsies (circulating tumor DNA)
- To measure the effect of testing and treatment on the patients* motivation, utility, QoL, productivity and informal care by means of questionnaires

Study design

This is a diagnostic study combining histological biopsy of tumor material with DNA sequencing using the SOLiDTM Next Generation Sequencing (NGS) platform. The study aims to obtain a more accurate pre-treatment stratification of cancer patients by obtaining fresh tumor biopsies for next-generation sequencing to obtain a mutational profile.

The study is a Dutch multicenter study and will be executed in the hospitals as described in C9 of this ABR form.

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 and (optional and if applicable, see CPCT-02 Study manual) post-treatment biopsies.
- Additional questionnaires for patients with pancreas cancer and FOLFIRINOX (included >= amendment 16): approximately 30 minutes
- Additional ctDNA bloodsamples for patients with bladdercancer and

Pembrolizumab (included >= amendment 18): approximately 25 minutes (5 minutes per bloodample: in total five additional bloodsamples will be taken)

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

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

* Patient with the following locally advanced or metastatic cancer for whom a new line of therapy is indicated starting within 3 months after biopsy:

- Metastatic Pancreas Cancer: FOLFIRINOX (Folinic acid [leucovorin] + Fluorouracil [5-FU] + Irinotecan + Oxaliplatin)
- Metastatic Bladder Cancer (including Renal Cell Cancer and all types of Urothelial Cell Cancer): Pembrolizumab
* Measurable metastatic or locally advanced lesion(s), according to RECIST 1.1 criteria.. Guidelines for response evaluation are given in appendix A.
* Metastatic or locally advanced lesion(s) of which a histological biopsy can safely be obtained.
* Patients age > 18 years, willing and able to comply with the protocol as judged by the investigator with a signed informed consent.

Patients must meet selection criteria 3 not only prior to baseline biopsy, but also prior to the (optional and if applicable, see CPCT-02 Study manual) post-treatment biopsies.

Exclusion criteria

No locally advanced or metastatic cancer.
Age below 18 years

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):	17-08-2011
Enrollment:	7500
Type:	Actual

Ethics review

Approved WMO Date:	01-08-2011
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-10-2011
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-03-2012
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-09-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-07-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-09-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-09-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-12-2014

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-03-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-03-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-04-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-04-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-06-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-06-2015

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-05-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-06-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-07-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-07-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-07-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-07-2016

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-08-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-09-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-10-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-10-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-11-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-11-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-11-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-12-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-12-2016

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-02-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-03-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-04-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-04-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-05-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-05-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-06-2017

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-06-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-07-2018

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-11-2022
Application type:	Amendment
Review commission:	METC NedMec

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	NCT01855477
CCMO	NL35781.041.11

Study results

Results posted: 17-01-2024

First publication
13-12-2023