Quantification of Circulating tumor DNA derived Structural variants to assess treatment response in metastatic prostate cancer patients

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON43524

Source
ToetsingOnline

Brief title
Circus study

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
prostate cancer, prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Gelden van de afdeling Interne Oncologie

Intervention

Keyword: ctDNA, prostate cancer, structural variants

Outcome measures

Primary outcome

The primary endpoint is the rate of mPC patients with quantifiable tumor-specific SVs in ctDNA from plasma taken pre-treatment; quantifiable is: the number of SV copies per milliliter plasma (load) is above the lower limit of detection (LLD).

Secondary outcome

Secondary, exploratory endpoints include the overlap in SVs between tumor biopsy samples pre- and post-treatment, the longitudinal assessment of SV load under influence of systemic treatment and the interval between detected variations in SV load PSA response and imaging modality markers.

Study description

Background summary

Prostate cancer (PC) is the most common malignancy in men worldwide. At diagnosis approximately 17% displays initial metastasized disease and an additional 20-40% of PC patients will have metastatic disease (mPC) within 10 years after primary curative treatment. Several treatment modalities are available to prolong progression free and overall survival, however it has proven to be ambiguous to accurately monitor treatment response with the current available response markers like prostate specific antigen (PSA) and radiological imaging. With the discovery of circulating tumor DNA (ctDNA) a new approach to non-invasively and safely obtain tumor-derived DNA has become available. To use ctDNA as a highly sensitive and specific marker for early therapy response we aim to detect and quantify somatic structural variants (SVs) in ctDNA from mPC patients. SVs are widespread in cancer and comprise

small and large aberrations in genome structure. In PC predominant alterations in involved signaling pathways are often caused by SVs. We hypothesize that the load of circulating SVs is correlated with the metastatic prostate tumor load. If so, variations in the concentration of tumor-specific SVs can potentially serve as a new marker for measuring early therapy response and for detecting minimal residual disease. If we can improve treatment response monitoring, especially in the early phase, we will be able to advise patients promptly and more precisely on the following treatment.

Study objective

The primary objective of this study is to assess the rate of mPC patients with quantifiable individualized SVs in ctDNA from plasma taken pre-treatment. Secondary objectives include SV characterization in tumor biopsies, exploration of the concordance between SVs in ctDNA and tumor biopsies and the investigation whether SV load in ctDNA correlates with tumor load and can predict early treatment response.
Study design: Prospective, longitudinal, observational study.

Study design

Prospective, longitudinal, observational study.

Study burden and risks

Of all patients every 3 to 4 weeks 2x 10 ml blood will be drawn up to disease progression occurs. As part of the CPCT-02 protocol a pre-treatment biopsy of a metastatic lesion and/or locally advanced tumor site and an optional biopsy after disease progression will be performed. Treatment response and disease progression will be assessed according to current clinical guidelines. The risk of longitudinal blood collections by venipuncture is negligible.

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

- metastasized castration resistant prostate cancer
- participation in CPCT-02 study
- age * 18 years
- written informed consent

Exclusion criteria

- not meeting the inclusion criteria

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-04-2016
Enrollment:	285
Type:	Actual

Ethics review

Approved WMO Date:	08-03-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL56192.078.16