Probing Intercellular heterogeneity in Circulating TUmor cells of de novo metastatic Hormone Sensitive Prostate CanceR patiEntS

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Primary objective: 1. To establish whether obtaining CTCs of mHSPC patients by DLA for single cell genotyping and phenotyping warrants further clinical exploration. Secondary objectives: 1. To investigate the number of CTCs in peripheral blood of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive and genitourinary neoplasms gender unspecified NEC
Study type	Observational invasive

Summary

ID

NL-OMON49282

Source
ToetsingOnline

Brief title
PICTURES

Condition

- Reproductive and genitourinary neoplasms gender unspecified NEC

Synonym
Metastatic hormone sensitive prostate cancer, metastatic prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: NWO

Intervention

Keyword: Biomarker, Circulating tumorcells, Prostate cacncer

Outcome measures

Primary outcome

The primary endpoint of this study is:

- The percentage of patients from who 30 single viable CTCs can be isolated from the DLA product.

Secondary outcome

Secondary endpoints of this study are:

- The number of CTC in mHSPC patients obtained in peripheral blood and obtained by DLA

- The correlation between the number of CTC at baseline and after six months of treatment (defined as 6 months from start treatment for mHSPC) to clinical outcome (defined as time to start mCRPC treatment, time to first line therapy for CRPC, time to mCPRC as defined by PCWG3 and overall survival)

- The level of PSA secretion and cell stress factors on single CTCs after drug exposure

- The percentage of patients from whom chromosomal profiles of single CTCs can be successfully generated

- The levels of ctDNA in mHSPC patients obtained in peripheral blood at baseline and after six months.

Exploratory endpoints of this study are:

- The intra-patient and inter-patient heterogeneity in genotype and phenotype

of single CTCs

- The correlation between genotypic and phenotypic characterization of single

CTCs

- The correlation between genomic heterogeneity and phenotypic heterogeneity of

individual cancer cells in poor and well responding mHSPC patients.

Study description

Background summary

The treatment of de novo mHSPC has evolved rapidly in the last years. After the identification of a robust
survival benefit for 6 cycles of docetaxel added to Androgen Deprivation Therapy (ADT) we now know
that the androgen receptor targeting drugs: abiraterone/ prednisone and enzalutamide render robust
survival gains if started immediately concomitantly with ADT. The median progression free survival of
these patients is estimated between 18 and 24 months, a major improvement, which also poses a
number of challenges. First of all, we still see patients that recur relatively quickly after therapy
initiation. These patients are difficult to identify upfront, so here we urgently need a real predictive
biomarker.

Study objective

Primary objective:
1. To establish whether obtaining CTCs of mHSPC patients by DLA for single cell genotyping and phenotyping warrants further clinical exploration.

Secondary objectives:
1. To investigate the number of CTCs in peripheral blood of mHSPC patients.
2. To investigate the number of CTCs obtained by DLA in mHSPC patients.
3. To correlate CTC count at baseline and after six months of therapy to clinical outcome.

4. To develop a protocol enabling the isolation and identification of viable CTCs in DLA
products of mHSPC patients.
5. To measure the excretion of PSA and cell stress factors on single CTCs with or without exposure to drugs.
6. To generate DNA copy number profiles of single CTCs in mHSPC patients.
7. To investigate the levels of ctDNA in mHSPC patients

Exploratory objective:
1. To identify mHSPC patients that respond poorly and those that respond well by combined phenotyping and genotyping of individual cancer cells.

Study design

This is a prospective, exploratory, multi center cohort study

Study burden and risks

The patients included in this study will undergo a DLA procedure which will take a maximum of a couple of hours. A maximum volume of 5L peripheral blood will be processed with the use of an Optia Spectra Cell Separator. This study will not benefit the patients included. The most common adverse events which could be expected are pain or bruising at the site of venipuncture (1-5%), apprehension or fainting associated with venipuncture (1-5%), fluid imbalance (0.01-0.1%) and citrate anticoagulant infusion-related symptoms resulting in tingling or buzzing around the mouth or fingers (20-50%). All patients will receive intravenous calcium to prevent this. The risks associated with participation are considered negligible. All safety measures and procedures will be performed according to local guidelines.

Participation in this study requires additional blood draw, the total needed blood volume varies, but has a maximum of 70ml. The risk of this limited amount of blood being drawn is minimal. The risks are considered negligible.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

dr. Molewaterplein 40
Rotterdam 3015GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

dr. Molewaterplein 40
Rotterdam 3015GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- De novo mHSPC patient, no prior treatment for prostate cancer, including local treatments and ADT
- Intention to start treatment with ADT + docetaxel or ADT + Second Generation Androgen Receptor Targeted therapy
- Age >=18 years
- WHO performance status <=2.
- >= 2 adequate peripheral veins as access point for leukapheresis.

Exclusion criteria

- Known hypersensitivity to the anticoagulant used for apheresis
- Inadequate cardiac function or severe cardiovascular comorbidity
* Heart failure NYHA class III/IV
- Hemoglobin level < 6.0 mmol/L
- Coagulation disorders as defined by one of the following:
* Coagulation disorder in medical history
* Platelet count < 40 x 109/L;
Patients without anticoagulant therapy which affects PT or APTT, when:
* PT > 1.5 x ULN or PT-INR > 1.5 x ULN
* APTT > 1.5 x ULN
Patients with anticoagulant therapy which affects PT or APTT, when:
* PT or APTT > 1.5 x the upper limit of the desired therapeutic window

* Total bilirubin > 2.5 x ULN
- Known chronic viral infections
- Second active malignancy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-09-2020
Enrollment:	134
Type:	Actual

Ethics review

Approved WMO

Date:	16-07-2020
Application type:	First submission
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	NL73860.078.20