

# 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...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruiting
<b>Health condition type</b>	Reproductive and genitourinary neoplasms gender unspecified NEC
<b>Study type</b>	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 cancer

## **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**

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### **Scientific**

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## 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  $\geq 18$  years
- WHO performance status  $\leq 2$ .
- $\geq 2$  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  $< 40 \times 10^9/L$ ;
- Patients without anticoagulant therapy which affects PT or APTT, when:
- \* PT  $> 1.5 \times$  ULN or PT-INR  $> 1.5 \times$  ULN
  - \* APTT  $> 1.5 \times$  ULN
- Patients with anticoagulant therapy which affects PT or APTT, when:
- \* PT or APTT  $> 1.5 \times$  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