# An Exploratory Phase 2, open-label, single-arm, efficacy and imaging Study of Oral Enzalutamide (MDV3100) Androgen Receptor (AR)-Directed Therapy in Chemo-Naïve patients with Progressive Prostate Cancer who have failed Androgen Deprivation Therapy (CRPC patients)

Published: 30-03-2015
Last updated: 14-04-2024

1. To evaluate the feasibility of 18F-FDG PET/CT, or WB MRI or both to determine metastatic tumour load before and after treatment with Enzalutamide in CRPC patients. 2. To evaluate how these 2 imaging modalities perform compared to traditional…

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Metastases |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON45038

**Source**
ToetsingOnline

**Brief title**
Xtandi in Chemo-Naïve CRPC patients failing Androgen Deprivation Therapy

### Condition

- Metastases

**Synonym**
metastatic prostate cancer

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Dit investigator-initiated onderzoek wordt gedeeltelijk ondersteund door een grant van Astellas

## Intervention

**Keyword:** Anti-androgen failure, Chemo-naive, Prostate cancer

## Outcome measures

**Primary outcome**

Progression-Free Survival (PFS) at 6 and 12 months: defined as the time from the date of randomization to the date of radiological progression or death (patients will be followed beyond the fixed time point of 12 months for continued response cq recurrence, but 12 month*s is the last fixed primary endpoint assessment). Radiological progression is defined by any of the following criteria: Soft tissue lesions: Progressive disease on 18F-FDG PET/CT or MRI by RECIST 1.1.

Bone or bone marrow lesions: Progressive disease on PET/CT or MRI as evidenced by new lesions or an increase in size of 25% of the sum of target lesions.

Conversion of the 18F-FDG PET signal of the metastases at 2 weeks, 2 or 6 months compared to baseline PET which by comparing it to PFS at 6 and 12 months may be an indicator or drug response. Radiological PFS at 6 and 12 months will be compared to a) PET signal conversion and to b) PSA measurements, and changes

in number of lesions on the bone scan (conventional work up).

**Secondary outcome**

Biochemical (PSA) response defined as prostate-specific antigen (PSA) nadir.

PSA progression. PSA kinetics measured by PSA doubling time (regular PSA measurements).

Progression of bone lesions detected with bone scan according to Prostate Cancer Working Group 2 (PCWG2) criteria. Radiologically confirmed spinal cord compression or pathological fracture due to malignant progression. A Symptomatic Skeletal Event (SSE) is defined as external beam radiation therapy (EBRT) to relieve skeletal pain, new symptomatic pathologic bone fracture, occurrence of spinal cord compression or tumour-related orthopedic surgical intervention, or change of anti-neoplastic therapy to treat bone pain.

CTC measurements and comparison with radiological PFS at 6 and 12 months.

Circulating testosterone (T), dihydrotestosterone (DHT), sex hormone binding globulin (SHBG), androstenedione, DHEA, luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin and estradiol assessed as temporal changes of absolute values and temporal percentage changes of baseline values.

Biomarker assessment / correlative: (next to PSA) biomarkers of bone turnover, Alkaline Phosphatase, PTH, Ca, Phosphate, 25 (OH)Vitamin D, beta-CTX (beta-crosslaps), PN1P.

The safety of Enzalutamide as assessed by serious adverse events (SAEs), severity of adverse events (AEs) graded by National Cancer Institute*s Common Terminology Criteria for Adverse Events (NCI-CTCAE), discontinuation due to AEs, as well as new clinically significant changes in physical exam findings,

vital signs, laboratory values, and ECGs.

Time to symptomatic progression (including death due to prostate cancer)

Time to first radiological or symptomatic progression

Time to initiation of salvage systemic therapy, including chemotherapy, or

palliative radiation

Quality of life measured by the Functional Assessment of Cancer

Therapy-Prostate (FACT-P) questionnaire and by the EuroQol 5-Dimension QoL

Instrument (EQ-5D)

Changes in Karnofsky score/ECOG score

Changes in visual analogue scale (VAS) for tumour-related pain

Changes in BMD as measured by DXA scan

# Study description

**Background summary**

The detection of tumour deposits/metastatic sites in metastatic prostate cancer is notoriously difficult and the conventionally used PSA (reflecting tumour mass and differentiation grade of prostate cancer cells scored as Gleason score in primary tumours) and bone scintigraphy do not provide accurate information with regard to responses to treatment. There is an unmet need for robust and reproducible imaging technology allowing accurate quantification and qualification of bone plus soft tissue metastases and which are useful to early predict responses and early detect progressive disease cq. heterogeneity in tumour responses to novel agents. Importantly, emerging imaging modalities such as PET/CT or WB MRI theoretically offer advantage over traditional PSA measurements plus bone scan, but this has never been established in a prospective study. Therefore, we aim to perform an exploratory study in which both modalities will be evaluated and compared head-to-head.
Clinical practice is hampered by the poor methods and criteria to assess progression with the risk of prematurely discontinuing effective therapy in patients with metastatic castrate resistant prostate cancer (mCRPC) because of apparent initial progression on bone scan. Ineffective treatment may be stopped earlier if we have methodology to accurately predict favourable or lack of

favourable responses, whereas early prediction of favourable responses will allow better patient selection and true patient-tailored treatment. This will be an asset for drug development programmes and result in decreased costs.

### Study objective

1. To evaluate the feasibility of 18F-FDG PET/CT, or WB MRI or both to determine metastatic tumour load before and after treatment with Enzalutamide in CRPC patients.
2. To evaluate how these 2 imaging modalities perform compared to traditional serial PSA measurements and bone scan in assessing metastatic tumour load, progressive disease and response to treatment in CRPC patients.

### Study design

Prospective Open-label Observational Cohort Study

### Intervention

Oral Enzalutamide

### Study burden and risks

The study will be performed mainly using routine treatment practice. However, the patients will be requested to undergo more imaging sessions which are basically non-invasive and virtually without risk.

## Contacts

**Public**
Leids Universitair Medisch Centrum

Albinusdreef 2 na
Leiden 2333 ZA
NL
**Scientific**
Leids Universitair Medisch Centrum

Albinusdreef 2 na
Leiden 2333 ZA
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Adult metastatic prostate cancer patients who are progressive on first-line ADT for metastatic disease and who have at least one measurable metastasis on either 18F-FDG PET/CT or WB MRI or both.

## Exclusion criteria

Previous chemotherapy, impaired liver/kidney/bone marrow function, susceptibility for seizures

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 25-06-2015 |
| Enrollment: | 60 |
| Type: | Actual |

### Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Xtandi |
| Generic name: | Enzalutamide |
| Registration: | Yes - NL intended use |

## Ethics review

| | |
|---|---|
| Approved WMO Date: | 30-03-2015 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

| | |
|---|---|
| Approved WMO Date: | 18-05-2015 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

| | |
|---|---|
| Approved WMO Date: | 23-03-2016 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

| | |
|---|---|
| Approved WMO Date: | 24-09-2018 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |

# 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 |
|---|---|
| EudraCT | EUCTR2014-001161-27-NL |
| ClinicalTrials.gov | NCT02814968 |
| CCMO | NL52067.058.15 |