

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-naïve, 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 or recurrence, but 12 months 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 of 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)
	metc-ldd@lumc.nl

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

Approved WMO	
Date:	23-03-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	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