An Exploratory Phase 2, open-label, single-arm, efficacy and imaging Study of Oral Enzalutamide (MDV3100) Androgen Receptor (AR)-Directed Therapy in Hormono-Sensitive patients with Metastatic Prostate Cancer.

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

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

Summary

ID

NL-OMON50224

Source
ToetsingOnline

Brief title
NA

Condition

- Renal and urinary tract neoplasms malignant and unspecified

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: Enzalutamide, Imaging, Metastatic 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-choline 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 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), P1NP.

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 prostate cancer 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 patients with metastatic prostate cancer.
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 metastatic prostate cancer.

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 with the addition of Enzalutamide, which has been shown safe and efficacious in large trials. Also, the patients will be requested to undergo more imaging sessions which are basically non-invasive and virtually without risk.

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

Adult metastatic hormone-sensitive prostate cancer patients with progressive metastatic disease requiring treatment and who have at least one measurable metastasis on either PET/CT or WB MRI or both.

Exclusion criteria

Previous androgen deprivation therapy within the last 6 months / Known or suspected brain metastasis or active leptomeningeal disease / Evidence of clinically relevant liver/kidney disease/bone marrow failure / history of seizure or any condition that may predispose to seizure / history of loss of consciousness or transient ischemic attack within 12 months of enrollment /

Contra-indication for MRI (e.g. pacemaker).

Study design

Design

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

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 outside 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:	06-05-2015
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:	18-04-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2014-001162-10-NL
ClinicalTrials.gov	NCT02815033
CCMO	NL52114.058.15