A Phase Ib/II, Multicentre, Open Label, Randomized Study of BI 836845 in Combination With Enzalutamide, versus Enzalutamide alone, in Metastatic Castration-Resistant Prostate Cancer (CRPC) Following Disease Progression on Docetaxel-Based Chemotherapy and Abiraterone

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To compare treatment with enzaluatmide plus BI836845 with treatment with enzalutamide only.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms male benign
Study type	Interventional

Summary

ID

NL-OMON43930

Source
ToetsingOnline

Brief title
BI 836845 plus enzalutamide in castrate resistant prostate cancer (CRPC)

Condition

- Reproductive neoplasms male benign

Synonym

castration resistant prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim BV
Source(s) of monetary or material Support: Boehringer Ingelheim BV

Intervention

Keyword: BI836845, enzalutamide, phase II, prostate cancer

Outcome measures

Primary outcome

Radiological progression free survival (PFS), based on investigator assessment

Secondary outcome

-* Overall survival (OS)

-* Time to PSA progression

-* Maximum decrease in PSA

-* Percentage change in PSA at 12 weeks

-* PSA response

-* change in circulating tumor cells (CTC)

- radiological progression free survival (PFS), based on central review

Study description

Background summary

Most man with prostate cancer die from their disease, and new treatment modalities are therefore needed. Pogression of castration resistant prostate cancer (CRCP) is known to involve enhanced signalling by the androgen receptor (AR).

Preclinical and clinical data suggest that inhibition of both the AR and the insullin-like growth factor (IGF) can provide therapeutic benefit in metastatic CPRC. Therefore, the current trial aims to compare the safety and anti-tumor activity of enzalutamide (inhibition of AR) plus BI836845 (inhibition of IGF signalling) versus enzalutamide only in patients with mCRPC who have been pre-treated with docetaxel and abiraterone.

Study objective

To compare treatment with enzaluatmide plus BI836845 with treatment with enzalutamide only.

Study design

This is a randomised, open-label, multi-centre, phase II trial. Worldwide approximately 80 patients will participate, in the Netherlands 6 will be entered. Patients will be randomised between addition of BI836845 to enzalutamide or no addition to enzalutamide in a 1:1 ratio. Treatment will continue until the patient experiences disease progression, withdraws consent or experiences severe toxicities.

Intervention

Patiënts will be randomised in a 1:1 fashion between the following arms:
1) enzalutamide (orally, once daily, continuous intake)
2) enzalutamide (orally, once daily) plus BI836845 (iv infusion, 1x/week)

Study burden and risks

See E4 and E9 of this ABR form.

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

- The patient has histologically, or cytologically, confirmed adenocarcinoma of the prostate.
- Male patient aged, equal to, or more than,18 years old.
- Patients with radiographic evidence of metastatic prostate cancer (stage M1 or D2). Distant metastases evaluable by radionuclide bone scan, CT scan, or MRI within 28 days before the start of study treatment.
- Patients with a PSA, equal to, or more than, 5 ng/mL.
- Patients with prior surgical or chemical castration with a serum testosterone of <50 ng/mL. If the method of castration is luteinizing hormone releasing level hormone (LHRH) agonists, the patient must be willing to continue the use of LHRH agonists during protocol treatment.
- Eastern Cooperative Oncology Group performance status (ECOG PS) 0 or 1.
- Cardiac left ventricular function with resting ejection fraction of at more than 50% as determined by ECHO or MUGA.
- International normalized ratio (INR) <= 2.0 and a partial thromboplastin time (PTT) <= 5 seconds above the ULN (unless on oral anticoagulant therapy). Patients receiving full-dose anticoagulation therapy are eligible provided they meet all other criteria, are on a stable dose of oral anticoagulant or low molecular weight heparin (except warfarin or coumarin-like anticoagulants, which are not permitted).
- Fasting plasma glucose <8.9 mmol/L (<160 mg/dL) and HbA1c <8.0%.
- Patients who have disease progression during, or after, receiving docetaxel and have had at least 12 weeks of treatment and in the opinion of the investigator are unlikely to derive significant benefit from additional docetaxel-based therapy, or were intolerant to therapy with this agent.
- Patients who have disease progression during, or after, receiving abiraterone treatment in any setting.
- Patients must have progressive disease defined as at least one of the following:
a. Progressive measurable disease: using conventional solid tumour criteria RECIST 1.1.

b. Bone scan progression: at least two new lesions on bone scan, plus a rising PSA as described in (c) below.
c. Increasing PSA level: at least two consecutive rising PSA values over a reference value (PSA #1) taken at least 1 week apart. A third PSA (PSA #3) is required to be greater than PSA #2; if not, a fourth PSA (PSA #4) is required to be greater than PSA #2.

Exclusion criteria

- Prior therapy with agents targeting IGF and/or IGFR pathway.
- Patients that have been treated with any of the following within 4 weeks of starting trial treatment: chemotherapy, immunotherapy, biological therapies, molecular targeted, hormone therapy (except LHRH agonists and LHRH antagonists), radiotherapy (except in case of localized radiotherapy for analgesic purpose or for lytic lesions at risk of fracture which can then be completed within 2 weeks prior to study treatment).
- Use of any investigational drug within 4 weeks before start of trial treatment or concomitantly with this trial.
- Patients that have been treated with strong CYP2C8 inhibitors, CYP2C8 inducers within 2 weeks of starting the trial treatment.
- QTcF prolongation >450 ms or QT prolongation deemed clinically relevant by the investigator (e.g., congenital long QT syndrome). The QTcF will be calculated as the mean of the 3 ECGs taken at screening.
- Patients with small cell or neuroendocrine tumours.
- Patients with known or suspected leptomeningeal metastases.
- Uncontrolled or poorly controlled hypertension.
- Patients with epilepsy, seizures, or predisposing factors for seizure as judged by the investigator.
- A history of allergy to human monoclonal antibodies.
- Previous or concomitant malignancies at any other site with the exception of the following:
a.) benign basal cell carcinoma
b.) benign low grade transitional cell carcinoma of the bladder
c.) other effectively treated malignancy that has been in remission for more than 5 years and is considered to be cured
Exclusion criteria only for patients entering phase Ib escalation and phase II:
- Patients that have received prior taxane-based therapy or enzalutamide in any setting will not be eligible.
- Patients who have received more than 2 prior non-docetaxel-containing cytotoxic chemotherapy regimens for Metastatic Castration-Resistant Prostate Cancer (mCRPC).
- Patients who have received a taxane based treatment or abiraterone, within 4 weeks before start of study treatment.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-02-2016
Enrollment:	6
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:	07-05-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	16-10-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	11-04-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-05-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-07-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-01-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-01-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	01-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-08-2018
Application type:	Amendment
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
EudraCT	EUCTR2013-004011-41-NL
ClinicalTrials.gov	NCT02204072
CCMO	NL53285.078.15