A randomized, double-blind, placebo controlled Phase III study of ODM-201 versus placebo in addition to standard androgen deprivation therapy and docetaxel in patients with metastatic hormone sensitive prostate cancer

Published: 17-10-2016
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Main:Overall survivalSecondary:Time to castration resistant prostate cancer Time to initiation of subsequent antineoplastic therapy Symptomatic skeletal event free survival (SSE-FS) Time to first symptomatic skeletal event (SSE) Time to initiation...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON45459

Source
ToetsingOnline

Brief title
BAY Arasens

Condition

- Reproductive neoplasms male malignant and unspecified
- Prostatic disorders (excl infections and inflammations)

Synonym
hormone-sensitive, Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Bayer AG
Source(s) of monetary or material Support: Farmaceutisch Industrie

Intervention

Keyword: Metastatic hormone sensitive prostate cancer

Outcome measures

Primary outcome

Overall survival

approximately 70 months

From date of randomization until death from any cause, during treatment and

during active and long term follow-up

Secondary outcome

Time to castration resistant prostate cancer

approximately 70 months

Approximately every 12 weeks (according to standard of care) up to the time of

PSA progression by soft tissue lesion or progression by bone lesions, whatever

come first.

Time to initiation of subsequent antineoplastic therapy

approximately 70 months

Every 12 weeks up to the date of first subsequent antineoplastic therapy for

prostate cancer.

Symptomatic skeletal event free survival (SSE-FS)

approximately 70 months

Every 12 weeks up to the first occurrence of SSE or death from any cause, whatever comes first

SSE is defined as external beam radiation therapy (EBRT) to relieve skeletal symptoms, or new symptomatic pathologic bone fracture, or occurrence of spinal cord compression or tumor-related orthopedic surgical intervention, whichever comes first.

Time to first symptomatic skeletal event (SSE)

approximately 70 months

Every 12 weeks up to the first occurrence of SSE.

SSE is defined as EBRT to relieve skeletal symptoms, or new symptomatic pathologic bone fracture, or occurrence of spinal cord compression or tumor-related orthopedic surgical intervention, whichever comes first.

Time to initiation of opioid use

approximately 70 months

Every 12 weeks up to the opiod use.

Time to pain progression

approximately 70 months

Every 12 weeks up to the first date a subject experiences a pain progression.

Pain to be assessed with a patient reported questionaire.

Time to worsening of physical symptoms of disease

approximately 70 months

Every 12 weeks up to the first date a subject experiences an increase in

physical symptoms.

Physical symptoms of disease to be assessed with a patient reported

questionaire.

Number of participants with adverse events as a measure of safety

approximately 70 months

Study description

Background summary

ADT remains the mainstay of treatment in metastatic hormone sensitive prostate cancer (mHSPC). Recent randomized trials have shown a significant improvement in overall survival for subjects with mHSPC treated with docetaxel in addition to ADT. However, subjects ultimately progress and die of castration resistant prostate cancer (CRPC). Darolutamide (ODM-201) is a novel non-steroidal androgen receptor (AR) inhibitor lacking a significant agonist action on AR and with a very high binding affinity to the AR. In phase I-II clinical studies, darolutamide(ODM-201) has demonstrated a very favorable safety profile, with no dose-limiting toxicities, and substantial antitumor activity in mCRPC, with effect on both serum PSA and soft tissue and bone lesions. A phase III trial is ongoing to compare darolutamide (ODM-201) versus placebo in men with non-metastatic CRPC. The clinical data obtained so far provide the rationale to explore the efficacy of darolutamide (ODM-201) in mHSPC, where novel therapeutic strategies are needed to improve the outcome of subjects before castration resistance occurs. This randomized phase III study aims to demonstrate that the addition of darolutamide (ODM-201) to ADT and docetaxel chemotherapy significantly prolongs OS over placebo in mHSPC subjects.

Study objective

Main:
Overall survival

Secondary:
Time to castration resistant prostate cancer
Time to initiation of subsequent antineoplastic therapy
Symptomatic skeletal event free survival (SSE-FS)
Time to first symptomatic skeletal event (SSE)
Time to initiation of opioid use
Time to pain progression
Time to worsening of physical symptoms of disease
Safety

Study design

Randomized, double blind, placebo controlled, multicenter phase III study.

Intervention

You have an equal chance of being in either of these two treatment groups:

• Treatment 1
ODM-201 600 mg (2 x 300 mg tablets) twice daily for a total daily dose of 1200 mg to be taken with food

• Treatment 2
Placebo - *sugar pills* which look like the real ODM-201 tablets but do not contain any active study drug to be taken with food.

in Addition to Standard Androgen Deprivation Therapy and Docetaxel

Study burden and risks

Burden: Due to the event driven study design a definitive treatment period per individual patient cannot be guaranteed.
The average treatment period is estimated at approximately 2 years and 7 months and the maximum treatment period per individual patient is estimated at approximately 2 to 3 years.

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

- Histologically or cytologically confirmed adenocarcinoma of prostate.
- Metastatic disease
- Candidates for ADT and docetaxel.
Started ADT with or without first generation anti androgen, but no longer than 12 weeks before randomization
- An Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate bone marrow, liver and renal function

Exclusion criteria

- Prior treatment with: LHRH agonist/antagonists; second generation androgen receptor (AR) inhibitors such as enzalutamide, ARN-509, darolutamide (ODM-201); other investigational AR inhibitors; CYP17 enzyme inhibitor such as abiraterone acetate or oral ketoconazole as antineoplastic treatment for prostate cancer, chemotherapy or immunotherapy for prostate cancer prior to randomization.
- Treatment with radiotherapy/radiopharmaceuticals within 2 weeks before randomization.
- Had any of the following within 6 months before randomization: stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, congestive heart failure (New York Heart Association Class III or IV)
- Had a prior malignancy. Adequately treated basal cell or squamous cell carcinoma of skin or

superficial bladder cancer that has not spread behind the connective tissue layer (i.e., pTis, pTa, and pT1) is allowed, as well as any other cancer for which treatment has been completed * 5 years before randomization and from which the subject has been disease-free
- Gastrointestinal disorder or procedure which is expected to interfere significantly with absorption of study treatment.
- Inability to swallow oral medications

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-11-2016
Enrollment:	42
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Darolutamide (ODM-201)
Generic name:	nvt

Ethics review

Approved WMO

Date:	17-10-2016

Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-01-2017
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-03-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-03-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-06-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-08-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-09-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-10-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-10-2017

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-11-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-11-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-05-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-07-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-08-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-10-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-12-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-02-2020

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-03-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-10-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-04-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-05-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-12-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-01-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-04-2022

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2015-002590-38-NL
CCMO	NL58831.028.16