Phase 1b/2 Study to Assess the Safety and Efficacy of AMG 102 in Combination with Mitoxantrone and Prednisone in Subjects with Previously Treated Castrate Resistant Prostate Cancer

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The objective of the study (phase 2) is to evaluate the effectiveness of AMG 102 in combination with Mitoxantrone and Prednisone in previously treated subjects with castrate resistant prostate cancer.

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

Summary

ID

NL-OMON33942

Source
ToetsingOnline

Brief title
AMG 102, MP in Subjects with Castrate Resistant Prostate Cancer

Condition

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

Synonym
Prostate Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: AMG 102, CastrateResistant, ProstateCancer

Outcome measures

Primary outcome

Phase 2;

To estimate with adequate precision the effect of the addition of AMG 102 to MP, compared with placebo + MP, as assessed by the hazard ratio (HR) for overall survival (OS) of previously treated subjects with castrate resistant prostate cancer (CRPC).

Secondary outcome

Phase 2;

- Progression free survival (PFS), objective response rate (ORR) as measured by modified RECIST, percentage changes in prostate specific antigen (PSA) level and response rates.

- Patient reported outcomes, including pain.

- The incidence of adverse events, laboratory abnormalities.

- The incidence of anti-AMG 102 antibody formation.

- Pharmacokinetics (PK): Cmax and Cmin for AMG 102

Study description

Background summary

In this study, the experimental study drug AMG 102, in combination with Mitoxantrone and Prednison, is evaluated for the treatment of patients with previously treated Castrate Resistant Prostate Cancer. AMG 102 is a fully human monoclonal antibody against hepatocyte growth factor that blocks binding of HSF/SF to it's receptor c-Met, inhibiting HGF/c-Met-driven activities in cells. The expression of c-Met has been linked to disease progression in prostate cancer, so AMG 102 might delay the progression. AMG 102 is being tested in combination with Mitoxantrone and Prednison (standard of care) to see if it delays disease progression. AMG 102 is not approved by any regulatory organisation.

Study objective

The objective of the study (phase 2) is to evaluate the effectiveness of AMG 102 in combination with Mitoxantrone and Prednisone in previously treated subjects with castrate resistant prostate cancer.

Study design

This study has two parts; In Phase 2 the Dutch hospitals will participate. Phase 2 is a randomized, double-blind portion of this study designed to evaluate the efficacy, safety and PK of AMG 102 in combination with Mitoxantrone and Prednisone (MP) in subjects with previously treated Castrate Resistant Prostate Cancer. Phase 2 will commence upon identification of the appropriate dose of AMG 102. Assuming the 15 mg/kg Q3W dose level is determined, 135 subjects will be rendomized in a 1:1:1 ration to receive MP+15 mg/kg AMG 102 (arm A), MP+7.5 mg/kg (arm B) or MP+placebo (arm C), for a maximum of 12 cycles. If the outcome of the Phase 1 study is that the appropriate dose of AMG 102 is 7.5 mg/kg or 5 mg/kg , than 90 subjects will be randomized in a 1:1 ratio receiving MP+7.5/5 mg/kg or MP+placebo.
There will be a 28 days screening period, a 12 cycle (Q3W) treatment period, after the end of treatment a safety follow up in 30 days, a 60 day follow up and a long term follow up of 36 months (Q3M) after the 30 day safety follow up.

Intervention

All Participating patients will receive AMG 102 Q3W in dose 15, 7.5, 5mg/kg or placebo on day 1 of each cycle.

Study burden and risks

During the screening the following assessments will be done; - ECG, MUGA/ECHO, blood samples, bone scan, CT/MRI, physical exam
During the treatment phase; the estimated treatment period will be 36 weeks. the patient should visit the hospital every three weeks (12 times) for medication dosing and laboratory assessments. Also some questinaires needs to

be filled out. In cycle 5, 9 and 12 radiological assessments will be done.
The risks of participation are small. Patients might receive AMG 102 and therefore have a chance on a possible positive effect of AMG 102. The treatment options for this patient population are small. If there are situations that are not acceptable (for the patient or the investigator) the patient is always able to stop with the study.

Contacts

Public
Amgen

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Pathologically confirmed adenocarcinoma of the prostate
* Radiographic evidence of metastatic disease
* Progressive disease meeting at least one of the following criteria:
1) a sequence of at least 2 rising PSA values measured at a minimum of 1

week apart with a 2 ng/mL minimum starting value, or
2) progression according to RECIST criteria for measurable lesions, or
3) appearance of 2 or more new lesions on bone scan.
* History of prior taxane-based chemotherapy for metastatic prostate cancer; no more than one prior chemotherapy regimen for CRPC is allowed (estramustine will be considered as chemotherapy)
* ECOG Performance status 0 or 1
* Life expectancy * 3 months
* Men * 18 years of age

Exclusion criteria

* Treatment with external beam radiotherapy * 14 days before enrollment or radiopharmaceutical * 8 weeks
* * 4 weeks since receipt of most recent prior chemotherapy, non-GnRH analog hormonal therapy (except for continuing corticosteroids) or other systemic therapy to treat prostate cancer and <6 weeks since receipt of prior bevacizumab.
* Subjects with evidence of an antiandrogen withdrawal response must demonstrate objective or PSA progression following the response.
* Known CNS metastases (epidural disease is allowed if it has been treated and there is no progression in the treated area).
* Significant cardiovascular disease (CHF class III or IV, uncontrolled angina, MI within 6 months of enrollment); patients with medically stable atrial fibrillation may be included.
* LVEF < 50% by MUGA or ECHO
* Treatment of infection with systemic anti-infectives within 7 days before enrollment (with the exception of uncomplicated urinary tract infection)
* Concurrent or prior (within 7 days of enrollment) anticoagulation therapy, except that use of low dose coumarin-type anticoagulants or heparins for prophylaxis against central venous catheter thrombosis is allowed

Study design

Design

Study phase:	2
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):	16-06-2009
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AMG102
Generic name:	AMG102
Product type:	Medicine
Brand name:	Novantronel
Generic name:	Mitoxantrone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-03-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-04-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-07-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2009
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-07-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-09-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-10-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-12-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-12-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2008-004355-30-NL
ClinicalTrials.gov	NCT-nummernognietbekend
CCMO	NL25740.029.08