Randomized, Double-Blind, Phase 3 Trial to Compare the Efficacy of Ipilimumab vs Placebo in Asymptomatic or Minimally Symptomatic Patients with Metastatic Chemotherapy-Naïve Castration Resistant Prostate Cancer

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The objective of this study is to compare the overall survival of patients with prostate cancer who are no longer responding to hormone therapy (castration resistant) and who have not yet received chemotherapy live longer (overall survival) when...

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

Summary

ID

NL-OMON38019

Source
ToetsingOnline

Brief title
CA184-095 Ipilimumab vs placebo in Chemotherapy-Naïve Prostate Cancer

Condition

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

Synonym
Castration Resistant Prostate Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharma Industry

Intervention

Keyword: Chemotherapy-Naïve, Ipilimumab, Phase III, prostate cancer

Outcome measures

Primary outcome

The primary outcome of this study is overall survival defined as the time from

date of randomisation to the date of death.

Secondary outcome

The secondary outcomes of the study are to assess the time the patient is free

from disease progression, assess how long it takes for patients to develop pain

symptoms and how long it takes until they need treatment with standard

chemotherapy.

Study description

Background summary

Prostate cancer patients who*s disease has spread outside the prostate and who are no longer responding to hormone therapy (castration resistant) but who are experiencing no or only minor symptoms, it is often appropriate to watch and wait until they develop painful symptoms before starting treatment with standard chemotherapy, docetaxel. This form of standard of care is known as 'watchful waiting'. Treatment with chemotherapy is not necessarily appropriate at this stage and treating doctors may decide to watch and wait and keep a close eye on the patient to see if the cancer and symptoms begin to develop.

The purpose of this study is to determine if patients with prostate cancer who

are no longer responding to hormone therapy (castration resistant) who have not received chemotherapy live longer when treated with ipilimumab, an investigational drug, than those treated with a dummy treatment (placebo). Ipilimumab is a class of medicine which attempts to use the body*s own immune system to stimulate a response to disease. The study will look at how safe ipilimumab is and how well it works.

Study objective

The objective of this study is to compare the overall survival of patients with prostate cancer who are no longer responding to hormone therapy (castration resistant) and who have not yet received chemotherapy live longer (overall survival) when treated with ipilimumab than those treated with a dummy drug (placebo).

Study design

This study is a randomized, double-blind study which will be conducted in 4 stages;
A screening phase which will last from 1-28 days; an induction phase lasting approximately 24 weeks, where study medication will be administered on weeks 1, 4. 7 and 10; a maintenance phase where study medication will be administered every 12 weeks until the patient decides to stop treatment, the patient*s disease worsens or the patient experiences unacceptable side-effects and can not continue; a follow up phase to monitor the patient*s survival until the study ends or the patient decides to withdraw.

Intervention

Ipilmumab is an investigational product in this study. Each patient will receive either ipilimumab or placebo administered by intravenous (IV) infusion which will take about 90 minutes.

Study burden and risks

Burden: study procedures (physical exams, blood sampling, intravenous infusions of study medication) and regular attendance for hospital visits during the induction phase of the study, followed by visits every 6 weeks for the first 24 weeks and then every 12 weeks after in the maintenance phase.
Risks: possible adverse events of ipilimumab
Benefit: potential improvement of overall survival.
Group relatedness: knowledge gain from this study may also help other patients in the future.

Contacts

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

a) Histologic or cytologic confirmation of adenocarcinoma of the prostate: ;b) Have been treated by orchiectomy or are receiving a LH-RH analog, and have a testosterone level less than 50ng/dl: ;c) Metastatic disease by any 1 of the following modalities: CT, MRI, bone scan:;d) Progression during hormonal treatment. For eligibility purposes, progressive disease is defined as: ;i) Rising PSA values at a minimum of 1-week intervals and a 2.0 ng/ml minimum starting value
ii) Progression per bone scan: the appearance of 2 or more new lesions
iii) Progression per target lesions/measurable disease: nodal or visceral disease progression, per modified RECIST. Only lymph nodes greater than 2 cm will be considered to assess a change in size qualifying for disease progression. ;e) Anti-androgens (bicalutamide, flutamide, nilutamide) or adrenal androgen production inhibitors (aminoglutethamide or ketoconazole) should be discontinued prior to starting study therapy:

i) For subjects with a history of response to an anti-androgen or adrenal androgen production inhibitor and subsequent progression while on that anti-androgen should be assessed for anti-androgen withdrawal response for 4 weeks, and must demonstrate progression off anti-androgen prior to enrolment;
ii) For subjects that have never responded to anti-androgens, observation for anti-androgen withdrawal response is not necessary; however, a 2 week washout period is required prior to start of study therapy;f) ECOG Performance Status 0-1: ;g) Asymptomatic or minimally symptomatic.
i) Minimally symptomatic disease will be defined as the following:
(1) If cancer related pain is present, the pain must be rated by the patient as * 4 according to item #3 of the BPI-SF (*[on a scale of 0 to 10]...describe your pain at its worst in the last 24 hours.*) for all days during the 5 day assessment period prior to randomization;
(2) Any cancer related pain must not require any opiate analgesics (including codeine and dextropropoxyphene) over the 5 day assessment period prior to randomization.;h) Men > 18 years of age or minimum age of consent per local regulations.

Exclusion criteria

1) Sexually active fertile men not using effective birth control if their partners are women of child-bearing potential (WOCBP). ;2) Visceral (liver, lung or brain) metastases are not permitted;;3) Medical History and Concurrent Diseases
a) Autoimmune disease: subjects with a documented history of inflammatory bowel disease, including ulcerative colitis and Crohn*s disease are excluded from this study.
Subjects with a history of symptomatic disease (eg, rheumatoid arthritis, autoimmune thyroiditis (eg, Hashimoto*s disease), autoimmune hepatitis, systemic progressive sclerosis (scleroderma), Systemic Lupus Erythematosus, autoimmune vasculitis (eg, Wegener*s Granulomatosis); Subjects with motor neuropathy considered of autoimmune origin (eg, Guillain-Barré Syndrome) are excluded from this study. Patients with vitiligo are eligible to enter the study.;b) Less than 1 year since resolution of * Grade 2 toxicity related to pelvic-targeted therapy (e.g radiation enteritis);;c) Dementia, altered mental status, or any psychiatric condition that would prohibit the understanding or rendering of informed consent or completing questionnaires; ;d) A serious uncontrolled medical disorder that, in the opinion of the investigator, would impair the ability of the subject to receive protocol therapy; ;e) Prior malignancy active within the previous 3 years except for locally curable cancers that have been apparently cured and needing no subsequent therapy, such as basal or squamous cell skin cancer, superficial bladder cancer or carcinoma in situ of the breast;;f) Known HIV or Hepatitis B or Hepatitis C infection. ;4) Physical and Laboratory Test Findings
a) Inadequate hematologic function defined by an absolute neutrophil count (ANC) < 1,500/mm3, a platelet count < 100,000/mm3, or a haemoglobin level < 9 g/dL; ;b) Inadequate hepatic function defined by a total bilirubin level * 2.5 times the upper limit of normal (ULN), AST and ALT levels * 2.5 times the ULN or * 5 times the ULN if liver metastases are present; ;c) Inadequate renal function defined by a serum creatinine level * 2.5 times the ULN; ;d) Inadequate creatinine clearance defined as less than 50 mL/min; ;5) Prohibited Treatments and/or Therapies
a) Prior treatment with any immunotherapy for prostate cancer, including autologous

prostate cancer vaccine sipuleucel-T (Provenge®);;b) Prior or ongoing cytotoxic therapy for metastatic prostate cancer (eg, docetaxel,
mitoxantrone, estramustine);;c) Pelvic-targeted radiotherapy within 3 months prior to the start of study therapy;;d) Chronic use of immunosuppressants and/or systemic corticosteroids (used in the management of cancer or non-cancer-related illnesses). However, during the course of the study, use of corticosteroids is allowed if used for treating irAEs, or adrenal insufficiencies; ;e) Any non-oncology vaccine therapy used for the prevention of infectious diseases (for up to 4 weeks prior to or after any dose of blinded study drug); ;f) Prior treatment with any inhibitor or agonist of T cell costimulation; ;g) Prior radioisotope therapy (e.g. strontium -89, samarium -153 or similar agents; ;6) Prisoners or subjects who are involuntarily incarcerated; ;7) Subjects who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness.

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):	08-12-2010
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	None
Generic name:	Ipilimumab

Ethics review

Approved WMO Date:	23-08-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-10-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-03-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-07-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-12-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2012

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-09-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-04-2015
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	EUCTR2009-016217-23-NL
ClinicalTrials.gov	NCT01057810
CCMO	NL31584.029.10