A RANDOMIZED, DOUBLE-BLIND, PHASE 3 TRIAL COMPARING IPILIMUMAB VS. PLACEBO FOLLOWING RADIOTHERAPY IN SUBJECTS WITH CASTRATION RESISTANT PROSTATE CANCER THAT HAVE RECEIVED PRIOR TREATMENT WITH DOCETAXEL

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

Summary

ID

NL-OMON36426

Source
ToetsingOnline

Brief title
CA184-043 IPILIMUMAB PLUS RADIOTHERAPY IN PROSTATE CANCER

Condition

- Reproductive neoplasms female malignant and unspecified
- Congenital reproductive tract and breast disorders

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: IPILIMUMAB, PHASE III, PROSTATE CANCER, RADIOTHERAPY

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 and assess how many patients have had a 50% decrease

from baseline in their level of prostate specific antigen.

Study description

Background summary

Most, if not all castration resistant prostate cancer patients present with bone metastases which may be very painful and the bones are at risk of fractures. These patients receive bone radiotherapy as standard of care to provide pain relief. Ipilimumab is a class of medicine which attempts to use the body*s own immune system to stimulate a response to disease. The hypothesis is that the combination of standard radiotherapy to symptomatic bone metastasis with Ipilmumab will amplify the immune response generated by the radiotherapy and result in systemic anti-tumour activity leading to an improvement in the patient*s overall survival.

Study objective

The objective of this study is to compare the overall survival of patients with castration resistant prostate cancer who have progressed after receiving docetaxel treatment, when they are treated with bone directed radiotherapy plus Ipilimumab compared to patients who are treated with bone directed radiotherapy plus 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. After receiving radiotherapy, 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

Public
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NL
Scientific

Bristol-Myers Squibb

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Signed Written Informed Consent
a) Willing and able to give informed consent. ;2. Target Population
a) Histologic or cytologic confirmation of adenocarcinoma of the prostate:
b) At least 1 symptomatic bone metastasis which can be irradiated, or at least 1 asymptomatic bone metastasis which, in the clinical judgment of the investigator, is appropriate to be irradiated (eg, risk of fracture or cord compression):
c) Have been treated by orchiectomy or are receiving a GnRH agonist/antagonist, and have a testosterone level less than 50ng/dl:
d) If applicable, must have discontinued anti-androgens at least 2 weeks prior to randomization. Medications considered to be anti-androgens include; Flutamide, Bicalutamide (Casodex), nilutamide, aminoglutethimide, ketoconazole, diethylstilbestrol, megestrol acetate (Megace), and finasteride (Proscar).
Additionally, any natural substance that might have anti-androgen activities, including but not limited to St John*s Wort, Saw Palmetto, or PC-SPES, must be discontinued prior to randomisation;
e) Must have received at least 1 prior regimen containing docetaxel for the treatment of metastatic CRPC consisting of at least 2 cycles of docetaxel.
f) ECOG Performance Status: Subjects must have ECOG PS 0-1.
g) Subjects must have progressed during docetaxel treatment or within 6 months of receiving, a docetaxel-containing regimen. If the subject received an additional anti-cancer therapy after docetaxel, they must also demonstrate signs of progression on that therapy. 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.
3. Age and Sex
a) Men > 18 years of age or minimum age of consent per local regulations.

Exclusion criteria

1) Sex and Reproductive Status
a) Sexually active fertile men not using effective birth control if their partners are women of child-bearing potential (WOCBP).
2) Target Disease Exceptions
a) Subjects with radiological evidence of brain metastasis.
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, as are subjects with a history of rheumatoid arthritis, systemic progressive sclerosis (scleroderma), Systemic Lupus Erythematosus, autoimmune vasculitis
(eg, Wegener*s Granulomatosis);
b) Motor neuropathy considered of autoimmune origin (eg, Guillain-Barre
Syndrome);
c) Patients with a prior history of pelvic (prostate) radiation associated with significant radiation proctitis within 12 months prior to the planned first infusion of blinded study drug. For the purpose of this protocol, radiation proctitis is defined as diarrhoea that reached a level of Grade 2 or Grade 3, that occurred within 1 month of radiation treatment, and that was of 7 days duration or longer.
d) Dementia, altered mental status, or any psychiatric condition that would prohibit the understanding or rendering of informed consent or completing questionnaires;
e) A serious uncontrolled medical disorder that, in the opinion of the investigator, would impair the ability of the subject to receive protocol therapy;
f) Any other malignancy from which the subject has been disease-free for less than
5 years, with the exception of adequately treated and cured basal or squamous cell skin cancer, or superficial bladder cancer;
g) 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;

e) Usage of greater than 120 mg of morphine (or equivalent) over a 24 hour period within 3 days of randomization, unless narcotic usage is necessitated by a symptomatic bone lesion that is likely to be palliated by protocol-specified radiotherapy.
5) Prohibited Treatments and/or Therapies
a) More than 2 prior systemic anti-cancer regimens (including re-treatment with docetaxel) for metastatic CRPC;
b) 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, or if administered at doses of prednisone 5 mg BID or equivalent;
c) 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);
d) Prior treatment with any inhibitor or agonist of T cell costimulation;
e) Prior strontium or samarium;
f) Prior treatment on BMS study CA180227: A Randomized Double-Blind
Phase 3 Trial Comparing Docetaxel Combined with Dasatinib to Docetaxel Combined with Placebo in Castration-Resistant Prostate Cancer.
6) Other Exclusion Criteria
a) Prisoners or subjects who are involuntarily incarcerated;
b) 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):	02-12-2009
Enrollment:	40

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	geen
Generic name:	Ipilimumab

Ethics review

Approved WMO Date:	22-07-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-11-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-02-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-03-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2010

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-12-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-04-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-08-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-09-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2011
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:	18-06-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2013
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:	27-02-2014
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:	26-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-05-2015

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	EUCTR2008-003314-97-NL
ClinicalTrials.gov	NCT-00861614
CCMO	NL28137.029.09