A Phase 2, Randomized, Double-Blind Study of Ipilimumab Administered at 3 mg/kg vs 10 mg/kg in Adult Subjects with Metastatic Chemotherapy-Naïve Castration Resistant Prostate Cancer Who are Asymptomatic or Minimally Symptomatic;Pharmacogenetics Blood Sample Amendment Number 01

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON42128

Source
ToetsingOnline

Brief title
Ipilimumab in Adults with Metastatic Prostate Cancer

Condition

- Other condition
- Reproductive neoplasms male malignant and unspecified

Synonym
Castration resistant prostrate cancer

Health condition

prostate disease (excluding infection and inflammation)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Chemotherapy-Naive, Ipilimumab, phase 2, prostrate cancer

Outcome measures

Primary outcome

The primary outcome of this study is defined as the radiographic

progression-free survival (rPFS) of patients with chemotherapy-naive mCRPC

randomized to ipilimumab 3 mg/kg and 10 mg/kg.

Secondary outcome

1. Rate of Severe irAEs

The rate of severe irAEs is defined as the proportion of treated subjects with

Grade 3 or worse irAEs within each treatment arm.

2. Overall Survival (OS)

OS will be defined as the time from the date of randomization until the date of

death. For those subjects who have not died OS will be censored at the last

date the subject was known to be alive.

3. Prostate Specific Antigen Progression-free Survival

Prostate specific antigen progression-free survival (PSA PFS) will be defined as the time from randomization to the earliest date of PSA progression or death, whichever comes earlier. Subjects who did not progress or die will be censored at the last PSA assessment date.

4. Prostate Specific Antigen Response Rate

PSA response rate is defined as the proportion of subjects with a 50% or greater decrease from baseline to the lowest post-baseline PSA result (confirmed 3 weeks later) for each randomised arm.

5. Time to pain progression: (to determine whether there is benefit to taking the study drug). Defined as the time from randomisation to*

a) an increase in daily average pain

b) whether the patient is now taking opioid analgesic (strong pain killers)

c) whether the patient has started to receive radiotherapy for their prostate cancer

d) increase in the patient's analgesic score (assessing the number of pain killers the patient is taking)

Study description

Background summary

For prostate cancer patients with disease that 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. 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 examine how well two different doses of ipilimumab work in patients with prostate cancer who are no longer responding to hormone therapy (castration resistant). 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.

This study is a double blinded study. In this study, patients will receive either 3 mg/kg or 10 mg/kg of ipilimumab as an intravenous (IV) infusion. Neither the patient nor the investigator will know which dose is being administered, except in an emergency. There is a 50% chance that a patient will be assigned to receive the 3 mg/kg dose of ipilimumab and a 50% chance that they will receive the 10 mg/kg dose of ipilimumab.

Study objective

The objective of this study is to determine how well two different doses of ipilimumab work in patients with prostate cancer who are no longer responding to hormone therapy (castration resistant), and whom have the best radiographic progression-free survival rate when treated with a 3mg/kg dose versus a 10mg/kg dose.

Study design

This study is a randomized, double-blind study which will be conducted in 5 phases; a screening phase which will last from 1-28 days; an induction phase where study medication will be administered as 4 separate doses at 3-week intervals on weeks 1, 4. 7 and 10; a maintenance phase where study medication will be administered every 12 weeks, for a maximum treatment duration of 3 years from the first induction dose or, the patient*s disease progresses or, the patient experiences unacceptable side-effects and cannot continue; a toxicity/progression follow up and a survival follow up phase.

Intervention

Ipilimumab is an investigational product in this study. Each patient will receive either a 3mg/kg or 10mg/kg dose of ipilimumab administered by intravenous (IV) infusion which will take about 60 to 100 minutes depending on the patients* body weight.

Study burden and risks

Burden: study procedures (physical exams, blood sampling, intravenous infusions of study medication, MRI/CT scans, bone scans) and regular attendance for hospital visits during the induction phase of the study, followed by visits every 12 weeks until follow up.
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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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 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 in soft tissue lesions (non-bone lesions), per Response Evaluation Criteria In Solid Tumors (RECIST) 1.1.;e) Anti-androgens (enzalutamide, bicalutamide, flutamide, nilutamide) or adrenal androgen production inhibitors (abiraterone, aminoglutethamide or ketoconazole) must be discontinued prior to starting study therapy:
i) Use of abiraterone and/or enzalutamide prior to starting study therapy is allowed
ii) 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;
iii) 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. Asymptomatic is defined as BPI-SF item #3 score of 0 to 1
ii. Minimally symptomatic is defined as BPI-SF item #3 score of 2 to 4;h) If cancer related pain is present, any cancer related pain must not require any opiate analgesics (including codeine and dextropropoxyphene) over the 5-day assessment period prior to randomization;i) 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; ;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 based on the standard Cockroft and Gault formula; ;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, cabazitaxel, or mitoxantrone);;c) Pelvic-targeted radiotherapy within 3 months prior to the start of study therapy. Bone-directed radiotherapy for palliation of painful bone metastases to pelvic region is allowed;;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 as an on-study management of an AE; ;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 systemic, bone-targeted radioisotope therapy (e.g. Radium 223, strontium -89, samarium -153 or similar agents). Use of bisphosphonate and/or denosumab is allowed.;6) Prisoners or subjects who are involuntarily incarcerated; ;7) Subjects who are compulsorily detained for treatment of either a psychiatric or physical (e.g, infectious disease) illness.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	15-04-2015
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ipilimumab
Generic name:	Ipilimumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2015
Application type:	First submission
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	EUCTR2014-002987-34-NL
ClinicalTrials.gov	NCT02279862
CCMO	NL50666.029.14