A Phase 3 study to evaluate the efficacy and safety of docetaxel and prednisone with or without lenalidomide in subjects with castrate-resistant prostate cancer.

Published: 19-11-2009
Last updated: 04-05-2024

Am2: Primary Objective* To compare the Overall Survival (OS) benefit of docetaxel and prednisone with and without lenalidomide as first-line combination therapy in chemo-naïve metastatic CRPC Secondary Objectives* Progression-Free Survival (PFS), *...

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

Summary

ID

NL-OMON43687

Source
ToetsingOnline

Brief title
Study with lenalidomide in patients with CRPC.

Condition

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

Synonym
prostate cancer that can't be treated surgically

Research involving
Human

Sponsors and support

Primary sponsor: Celgene Corporation
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Castrate-resistant prostate cancer, Docetaxel, Lenalidomide

Outcome measures

Primary outcome

During the survival follow-up, second primary malignancies and additional

treatments for prostate cancer will be obtained.

Secondary outcome

N/A for Amendment 3

Study description

Background summary

Prostate cancer is the most common form of noncutaneous cancer diagnosed in American and European men. Among American men prostate cancer is the second leading cause of death and the most common cancer-related cause of death in European men.
A docetaxel-based regimen is now the accepted standard of care for patients with CRPC (NCCN Guidelines 2008). Despite the survival advantage conferred by docetaxel-based regimens, rapid disease progression and a significantly shortened lifespan still exhibits by most patients with CRPC.
Lenalidomide has been assessed for pharmacological activity in a variety of preclinical and in vitro models. Evidence that lenalidomide is both anti-angiogenic and a potent immunomodulator provides the non-clinical rationale for evaluating lenalidomide in prostate cancer. Based on the in vitro activity and expected plasma levels at the suggested study treatment dose we expect lenalidomide to enhance T cell activation as well as reduce the immune suppressive activity of Tregs, potentially providing increased benefit for patients receiving lenalidomide in combination with docetaxel and prednisone therapy for castrate-resistant prostate cancer patients.
Multiple phase 1 and phase 2 clinical trials have been performed with lenalidomide, as both a single agent and combination therapies, in subjects

with advanced prostate cancer. These studies have demonstrated lenalidomide to be both tolerable and active in this disease indication suggesting that lenalidomide should be further examined in larger trials of advanced prostate cancer patients. More in Protocol chapter 5 (p16-19)

Study objective

Am2:
Primary Objective
* To compare the Overall Survival (OS) benefit of docetaxel and prednisone with and without lenalidomide as first-line combination therapy in chemo-naïve metastatic CRPC
Secondary Objectives
* Progression-Free Survival (PFS), * Objective Response Rate , * Safety of lenalidomide in combination with docetaxel and prednisone
Exploratory Objectives
* PSA response, PSA progression, PSA doubling time and PSA velocity, * Biomarker analysis , * Pharmacokinetic analysis
* Change in Analgesic Use, * Patient-Reported Outcomes

Under Am.3
* To continue to collect information on Second Primary Malignancies (SPMs) and additional treatments for prostate cancer in all randomized subjects during survival follow-up
* To continue to provide docetaxel and prednisone to CRPC subjects randomized at non-US sites who were ongoing in the CC-5013-PC-002 (Amendment 2, Version dated 09-Jun-2011) protocol when the decision was made to discontinue lenalidomide/placebo and are experiencing benefit as per investigator discretion

Study design

This is a Phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group efficacy and safety study in chemo-naïve subjects with metastatic CRPC.

Approximately 1015 subjects meeting inclusion criteria will be randomized 1:1 into one of two treatment arms:
* DP Treatment Arm: docetaxel, prednisone and placebo
* DPL Treatment Arm: docetaxel, prednisone and lenalidomide

Amendment 3:
Subjects that were ongoing in the CC-5013-PC-002 (Amendment 2, Version dated 09-Jun-2011) protocol when the decision was made to discontinue lenalidomide/placebo and are experiencing benefit as per investigator discretion will continue to receive docetaxel and prednisone up to 10 cycles,

unacceptable toxicity, disease progression, or discontinue for any reason. For patients enrolled outside the USA and who are beyond 10 cycles, an additional 2 cycles can be provided to allow the switch to commercial supply or other further therapies at the discretion of the treating physician.
All subjects (US and non-US) who have discontinued treatment will be followed for survival for Second Primary Malignancies (SPMs) and additional treatments for prostate cancer every 90 days until death or up to 5 years following the last patient randomized (21-Nov-2011).
Patients will be unblinded after database lock. Prior to locking the database, any unblinding requests will be discussed between the Investigator and Sponsor on a case by case basis.

Intervention

The 21-day treatment cycles will consist of docetaxel administered as an IV infusion for approximately 60 minutes (as per package insert) at a dose of 75 mg/m2 to all subjects on Day 1 of each cycle and prednisone at a dose of 5 mg oral BID administration as per the current approved standard of care for this disease indication. Pre-treatment for docetaxel will be administered according to institutional standards.
Lenalidomide will be administered at 25 mg orally, QD for Days 1*14 of each cycle. An identical matching placebo will be administered Days 1-14 in the control arm. Neither lenalidomide nor placebo will be taken on days 15-21 in either treatment cycle. Rationale for this treatment dose selection is found in Section 5.2.2.2.

Amendment 3:
For patients enrolled outside the USA and who are beyond 10 cycles, an additional 2 cycles can be provided to allow the switch to commercial supply or other further therapies at the discretion of the treating physician.

Study burden and risks

Subjects will need to be treated in the clinic on Day 1 of each cycle with docetaxel and will have a physical exam, blood collection, urine collection, complete Quality of Life questionnaires, and every 3rd cycle will be tumor assessments. Subjects will be required to also have exams and blood collections on Day 14 of the first cycle. Following treatment discontinuation subjects will be contacted every 90 days for survival and other treatment information.
Overall this results in little added burden to these subjects that most would not experience if undergoing Standard of Care treatment for Castrate-Resistant Prostate Cancer.

Contacts

Public
Celgene Corporation

Morris Avenue 86
Summit NJ 07901
US
Scientific
Celgene Corporation

Morris Avenue 86
Summit NJ 07901
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Amendment 3: screening and recruitment was completed under protocol amendment 2. Below are criteria from Am2.;Subjects Must Meet All of the Following Inclusion Criteria to be Eligible for Enrollment Into The Study:
1. Understand and voluntarily sign an Informed Consent Form (ICF)
2. Males * 18 years of age at the time of consent
3. Able to adhere to the study visit schedule and requirements of the protocol
4. ECOG performance status of * 2
5. Life expectancy of * 12 weeks
6. Willingness to participate in HRQoL and pain assessments and have ability to complete PRO and pain assessments without assistance or with minimal assistance from trained site personnel and/or caregiver
7. Effective castration defined as serum testosterone levels < 50 ng/dL

* Primary testicular androgen suppression (e.g., LHRH agonists or antagonists) should be continued during study treatment for subjects who have not had a bilateral orchiectomy
8. Histologically confirmed adenocarcinoma of the prostate and:
* Prostate cancer that is unresponsive or refractory to hormonal therapy AND
* Metastatic disease confirmed by bone scan, Computer Tomography (CT) scan, Magnetic Resonance Imaging (MRI) or X-ray
9. Have documented disease progression while receiving or following hormonal therapy for treatment of advanced prostate cancer despite castrate levels of serum testosterone due to orchiectomy or luteinizing hormone-releasing hormone (LHRH) agonist as determined by at least one of the following criteria:
* Serum PSA level * 2ng/mL that has increased from a reference value (the last value immediately prior to the first rise) on at least two consecutive PSA measurements obtained at least 1 week apart prior to randomization
* Progression of measurable disease
Measurable disease is defined as at least one measurable lesion * 10 mm in longest diameter by CT or MRI (or 20 mm by chest X-ray) and/or lymph nodes * 15 mm short axis
Progression of measurable disease is defined as an increase of * 20% in the sum of the diameters of target lesions from the time of maximal regression with an absolute increase of * 5mm, OR the appearance of * 1 new lesion
* Unequivocal progression of non-measurable disease
Non-measurable disease is defined as all lesions < 10mm in the longest diameter or pathological lymph nodes *10 mm to < 15 mm short axis
Unequivocal progression of existing lesions is defined as an increase in overall disease burden based on the change in non-measurable disease that is comparable in magnitude to the increase that would be required to declare disease progression for measurable disease
And by 2 or more new bone lesions as detected by bone scan
10. All subjects:
* Must be counseled about pregnancy precautions and risks of fetal exposure. See Appendix 21.7.2 Lenalidomide Risks of Fetal Exposure, Pregnancy Testing Guidelines and Acceptable Birth Control Methods, and Appendix 21.7.3 Lenalidomide Education and Counseling Guidance Document
* Must agree to use a condom (specified in the appropriate country specific appendix) during sexual contact with a female of childbearing potential (FCBP), even if they have had a vasectomy, while participating in this study, during dose interruptions, and for a period of 28 days following the last dose of study drug
* Must agree to refrain from donating semen or sperm while participating in this study and for a period of 28 days following the last dose of study drug
* Must agree to refrain from donating blood or plasma while participating in this study and for a period of 28 days following the last dose of study drug
* Must agree not to share study drug with anyone during participation in the study;Additional Criteria:
Before Starting Study Drug:
* Subjects should understand the potential teratogenic risk if engaged in sexual activity with a female of childbearing potential
* Subjects should understand the need for the use of a condom if engaged in sexual activity with a woman of childbearing potential
* Subjects should be instructed never to give this medicinal product to another person and to

return any unused capsules to their pharmacist at the end of treatment.

Exclusion criteria

Amendment 3: screening and recruitment was completed under protocol amendment 2. Below are criteria from Am2.;Key Exclusion Criteria
Presence of any of the Following will Exclude a Subject from Enrollment into the Study:
1. A history of clinically significant (as determined by the investigator) medical, surgical, or psychiatric disease that would place the subject at an unacceptable risk for study entry
2. Prior therapy with thalidomide, lenalidomide (CC-5013) or pomalidomide (CC-4047)
3. Prior chemotherapy for prostate cancer
* Treatment with estramustine will be allowed if last treatment is more than 28 days prior to randomization, and subject has recovered from side effects
* Adjuvant and/or neoadjuvant treatment will be allowed if completed > 3 years prior to randomization and provided the treatment was a non-taxane based regimen
4. Use of any other experimental drug or therapy within 28 days prior to randomization
5. Prior radiation to * 30% of bone marrow as determined by review of Appendix 21.4 and/or consulation with radiation specialist
6. Any other radiation therapy within 28 days prior to randomization
* Subjects receiving prior radiation must have recovered from acute toxicity or any side effects due to radiation treatments prior to randomization
7. Prior use of Strontium-89 at any time or Samarium-153 within 56 days prior to randomization
8. Surgery within 28 days prior to randomization (minimally invasive procedures for the purpose of diagnosis or staging of the disease are permitted)
9. Concurrent antiadrogen therapy as follows:
* Treatment with antiandrogens (e.g. flutamide), aminoglutethimide, megestrol or diethylstilbestrol (DES) must be discontinued at least 4 weeks prior to randomization
* Treatment with bicalutamide and nilutamide must be discontinued at least 6 weeks prior to randomization
* Subjects exhibiting clinical symptoms and/or radiologic evidence of rapidly progressive disease will be allowed to initiate treatment if in the clinical judgment of the investigator a 4- or 6-week delay for anti-androgen washout would compromise the health and safety of the study subject
* Subjects without prior orchiectomy should continue treatment with LHRH agonists or antagonists
* Bisphosphonates may be used if treatment was initiated at least 28 days prior to randomization
* Concurrent therapy with steroids or hormones for adrenal insufficiency or nondisease-related conditions (e.g., insulin for diabetes) are allowed
10. Any of the following laboratory values:
* Hemoglobin < 9 g/dL
* Absolute neutrophil count (ANC) < 1.5 x 109 cells/L
* Platelet count < 100 x 109 cells/L
* Creatinine clearance <50mL/min by Cockcroft-Gault formula

* Total bilirubin > 1.0 x ULN
* Serum aspartate amino transaminase (AST)/SGOT and/or alanine transaminase (ALT)/SGPT > 1.5 x ULN concomitant with alkaline phosphatase > 2.5 x ULN
11. Must not have had significant active cardiac disease within the previous 6 months including:
* History of uncontrolled hypertension (i.e., BP > 160/90 mm Hg) despite anti-hypertensive therapy
* New York Heart Association class II-IV congestive heart failure
* Unstable angina
* Myocardial infarction
12. Clinically significant peripheral arterial occlusive disease (i.e., claudication on less than 1 block)
13. Thrombotic or thromboembolic events within the past 6 months, including any of the following:
* Deep Vein Thrombosis or Pulmonary Embolism within the preceding 6 months
* Transient ischemic attack
* Cerebrovascular accident
* Any other arterial thrombotic event
14. Current or history of peripheral neuropathy of *grade 2
15. History of severe hypersensitivity reaction to drugs formulated with polysorbate 80
16. Paraplegia
17. History of symptomatic central nervous system (CNS) or brain metastases
* Subjects who have remained asymptomatic for 90 days and demonstrate no active CNS involvement as shown by CT, MRI, or lumbar puncture are not excluded
* If required, CT, MRI, or lumbar puncture should be performed during the screening process
18. History of malignancies other than prostate cancer within the past 5 years, with the exception of treated basal cell/squamous cell carcinoma of the skin
19. Concurrent use of alternative cancer therapies during study treatment. Subjects taking alternative therapies for cancer must stop taking these therapies prior to randomization. Alternative therapies are not allowed during study treatment This includes alternative therapies such as, but not limited to:
*Saw Palmetto
*DHEA
*Lycopene
*PC-SPES (all types)
*Vitamins and/or dietary supplements used at therapeutic doses for treatment of prostate cancer including: Vitamin D, Selenium and
*The use of dietary supplements at daily recommended levels or for vitamin/mineral deficiencies is not an exclusion criterion
*Citrus pectin.

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):	06-04-2010
Enrollment:	136
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Prednisone
Generic name:	Prednisone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Revlimid
Generic name:	Lenalidomide
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	Docetaxel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	19-11-2009

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-03-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-07-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-10-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	15-10-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-10-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-01-2011
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-04-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-04-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	03-08-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-03-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-08-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-03-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-06-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	06-06-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-08-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-10-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2008-007969-23-NL
ClinicalTrials.gov	NCT00988208
CCMO	NL30305.060.09