A Randomized, Double-blind, Multicenter, Phase 2 Study of a Human Monoclonal Antibody to Human aV Integrins (CNTO 95) in Combination With Docetaxel and Prednisone for the First-Line Treatment of Subjects With Metastatic Hormone Refractory prostate Cancer

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Evaluate the efficacy and safety of treatment with CNTO 95 in combination with docetaxel and prednisone compared with docetaxel and prednisone without CNTO 95 in subjects with metastatic HRPC.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive and genitourinary neoplasms gender unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON31063

Source
ToetsingOnline

Brief title
C1034T08

Condition

- Reproductive and genitourinary neoplasms gender unspecified NEC

Synonym
1/ Metastatic Hormono-resistant Prostate Cancer 2/ Metastatic HRPC

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Centocor B.V.

Intervention

Keyword: anti-integrins, docetaxel, monoclonal antibody, prostate cancer

Outcome measures

Primary outcome

Primary endpoint is progression-free survival (PFS), defined as the time from

the date of randomization until the first documented sign of disease

progression (radiographic, clinical, or both) or death due to any cause,

whichever occurs sooner.

Secondary outcome

• Tumor response rate

• PSA response rate

• Overall survival

• Change from baseline in ECOG performance status

Study description

Background summary

CNTO 95 is an antibody made by Centocor. Antibodies are substances in the body that fight infection. CNTO 95 works by blocking substances on cells called integrins that are involved in formation of new blood vessels (angiogenesis). More specifically, cancer drugs like CNTO 95, work by preventing the formation of blood vessels that feed tumors. These types of cancer drugs are called anti-angiogenic drugs. When new blood vessels are stopped from being made,

tumors cannot get the food and oxygen they need to grow. As a result anti-angiogenic drugs may stop tumors from growing and spreading.

In laboratory studies, CNTO 95 appeared to slow tumor growth without significant side effects. However, laboratory studies do not always predict how the drug will work in humans. Before this study, CNTO 95 was given to over 50 people with different types of advanced cancer that did not respond to standard treatment. The reported side effects are described in the Risks section.

In this study the combination of CNTO 95 with docetaxel and prednisone will be tested to see if it is safe and to see what effects it has on your cancer. Docetaxel and prednisone are approved chemotherapy (cancer drug) for HRPC. In previous studies at least 6 patients received CNTO 95 in combination with docetaxel and prednisone. It is too early to know if CNTO 95 works, either alone or in combination with docetaxel and prednisone.

Study objective

Evaluate the efficacy and safety of treatment with CNTO 95 in combination with docetaxel and prednisone compared with docetaxel and prednisone without CNTO 95 in subjects with metastatic HRPC.

Study design

Randomized, Double-blind, Multicenter, Phase 2 Study of a Human Monoclonal Antibody to Human αv Integrins (CNTO 95) in Combination With Docetaxel and Prednisone for the First-Line Treatment of Subjects With Metastatic Hormone Refractory Prostate Cancer.

Intervention

Not Applicable.

Study burden and risks

Safety information is available for over 50 subjects who received doses up to 10 mg/kg CNTO 95. The side effects most frequently observed were fever, chills, drowsiness, and headache. Less frequently reported side effects were abdominal pain, constipation, liver enzyme increases, low blood salt levels, pain, nausea, loss of appetite, vomiting, coughing and diarrhea.
Subjects receiving CNTO 95 had mild to moderate headaches, chills, fever or a combination on the day of infusion. These all improved within a few hours.

Risk of CNTO 95 and docetaxel given in combination:
So far at least 6 patients have been treated with the above mentioned combination. No increase of the side effects of either CNTO 95 or docetaxel has

been observed. These data however are too limited to know if these drugs will affect each other or affect the potential side effects of either drug listed above.

Contacts

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Scientific
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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. Are male >= 18 years of age.
2. Have histologically or cytologically confirmed adenocarcinoma of the prostate.
3. Have radiologic or clinical evidence of metastatic disease.
4. Have progressive hormone-refractory disease after orchiectomy or gonadotropinreleasing hormone analog and/or antiandrogen treatment within 6 months prior to the first study agent administration, documented by at least 1 of the following:
a. Transaxial imaging (CT or MRI) tumor progression

b. Rise in 2 consecutive PSA values obtained at least 14 days apart
c. Radionucleotide bone scan with at least 2 new lesions
5. Have an ECOG score <= 2.
6. Have adequate bone marrow, liver, and renal function, defined as follows:
a. Absolute neutrophil count (ANC) >= 1.5 × 109/L
b. Hemoglobin >= 10 g/dL (without transfusion)
c. Platelets >= 100 × 109/L
d. AST and ALT < 2.5 × ULN
e. Alkaline phosphatase < 5 × ULN
f. Total bilirubin within normal limits
g. Creatinine <= 1.5 mg/dL
h. Activated partial thromboplastin time (aPTT) and prothrombin time (PT) <= 1.5 × ULN
7. Have testosterone < 50 ng/mL for subjects without surgical castration. Testosterone level will not be documented for subjects who have been surgically castrated.
8. Have serum PSA >= 5.0 ng/mL.
9. Have a life expectancy > 12 weeks.
10. Have at least 4 weeks from previous major surgery to date of first study agent administration. Subjects must have recovered or stabilized from previous surgery.
11. Have discontinued flutamide > 4 weeks prior to the first study agent administration, or have discontinued nilutamide or bicalutamide > 6 weeks prior to the first study agent administration.
12. Use appropriate contraception (eg, condom) for the duration of the study and for 3 months after the last study treatment.
13. Provide signed and dated informed consent(s) prior to any study-specific procedures and agree to comply with all protocol-specified procedures.

Exclusion criteria

1. Have known CNS metastases.
2. Had prior systemic nonhormonal therapy for HRPC.
3. Received any investigational drug/agent within 30 days or 5 half-lives, whichever is longer.
4. Had a prior malignancy (other than prostate cancer) except for adequately treated superficial bladder cancer, basal cell or squamous cell carcinoma of the skin, or other cancer for which the subject has been disease-free for >= 5 years.
5. Have known HIV seropositivity or known hepatitis B or C infection.
6. Have planned major surgery during the study.
7. Had prior radiotherapy to > 25% of the marrow-containing skeleton.
8. Have peripheral neuropathy > Grade 1.
9. Have a history of uveitis.
10. Have taken any over-the-counter or herbal treatment for prostate cancer within 4 weeks prior to the first study agent administration.
11. Have a serious concurrent illness or significant cardiac disease characterized by

significant ischemic coronary disease, significant arrhythmias (requiring active treatment), or congestive heart failure New York Heart Association (>= NYHA II) or myocardial infarction within the previous 6 months.
12. Have any uncontrolled medical condition, serious infection, or the presence of clinically significant laboratory abnormalities that places the subject at unacceptable risk by participating in the study or confounds the ability to interpret data from the study.
13. Requires hematopoietic growth factors or transfusion of blood products to meet eligibility criteria.
14. Had prior use of radionucleotide therapy (eg, Strontium89, Samarium).
15. Undergoing concurrent immunotherapy, biotherapy, radiotherapy, investigational therapy, or steroid therapy other than that included in this protocol (except for topical or inhaled steroids, or unless clinically indicated [eg, for reactions to IV contrast, allergic reactions that develop during the study, severe nausea, vomiting]).
16. Requires concurrent anticoagulation therapy (except for low-dose prophylaxis).
17. Have known hypersensitivity to docetaxel or its components.
18. Have a history of anaphylaxis or severe allergic reaction(s) to human Ig therapy or polysorbate 80 (formulation components of CNTO 95).
19. Has history of bleeding diathesis.
20. Had recurrent arterial or venous thromboembolism within 6 months preceding enrollment.

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):	27-04-2007

Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Not Applicable
Generic name:	Not Applicable
Product type:	Medicine
Brand name:	Prednisone
Generic name:	Prednisone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-04-2007
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-09-2007
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-01-2008
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-03-2008
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	15-04-2008
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-10-2008
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-03-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-03-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2006-005766-39-NL
CCMO	NL17045.091.07