The Prostate CARE Study: Capecitabine (Xeloda??) combined with Rhenium-188-HEDP in hormone refractory prostate cancer patients with bone metastases; a Capecitabine phase I dose escalation study and phase II efficacy study.

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

Summary

ID

NL-OMON30787

Source
ToetsingOnline

Brief title
The Prostate CARE Study

Condition

- Metastases
- Prostatic disorders (excl infections and inflammations)

Synonym
Prostate cancer that has spread to the bone

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: bone metastases, capecitabine, prostate cancer, rhenium

Outcome measures

Primary outcome

The MTD of capecitabine will be determined. Efficacy will be determined from

PSA scores.

Secondary outcome

Biodistribution will be compared to historical data of single Re-188-HEDP

therapy. Efficacy will be determine from pain scores, analgesic consumption,

symptom evaluation and HRQOL scores.

Study description

Background summary

Prostate cancer is currently one of the most common malignancies worldwide. About 50-70% of patients with prostate cancer present a locally advanced stage and about 15-30% have bone metastases at the time of diagnosis. Metastatic disease may also develop after treatment for localized disease. Although a vast majority of patients initially respond to hormone treatment most, if not all, patients subsequently relapse and progresses from an androgen-dependent to an androgen-independent state. Approximately 65% of patients with bone metastases suffer from bone painand require palliative treatment.
Rhenium-188-HEDP is a radiopharmaceutical that has an affinity for skeletal tissue and that concentrates in areas of bone turnover secondary to invasion by tumor. It is used for the treatment of metastatic bone pain.
Capecitabine inhibits tumor growth and has a proven efficacy in patients with

colorectal and breast cancer. As Capecitabine has proven radiosensitizing properties in other tumors, it might be a potential radiosensitizer for the combined use with Re-188-HEDP in prostate cancer patients, without unacceptable hematotoxicity. This combined treatment may lead to improved pain palliation and thus to a better quality of life.

Study objective

The primary aim of the phase I part of this study is to establish the safety profile and to determine the maximum tolerated dose of capecitabine combined with Re-188-HEDP.
The primary aim of the phase II part of this study is to obtain insight in the efficacy of Re-188-HEDP combined with capcitabine, as reflected by PSA.
Secondary objectives of the study are to determine the biodistribution of Re-188-HEDP when combined with capecitabine; to study heamtological toxicity; to monitor pain and analgesic consumption; to monitor quality of life.

Study design

This will be a combined phase I/II, uncontrolled, non-randomized, open-label study in hormone refractory prostate cancer patients with osteoblastic bone metastases.

Intervention

In phase I, after a screening procedure, three cohorts of 3 succesive patients will be treated with 3 dosage levels of capecitabine and a fixed dose of Re-188-HEDP (37MBq/kg). If a dose limiting toxicity occurs the cohort will be increased to 6 patients. If at least 3 patients out of 6 (in one cohort) have a dose limiting toxicity, the maximum tolerated dose can be determined (i.e. the previous dosage level).
In phase II, after a screening procedure, all patients will undergo combined treatment with the MTD of capecitabine combined with a fixed dose of Re-188-HEDP.
In both phases the patient will undergo 1 total body scintigraphy 6 hours after administration of re-188-HEDP, and urine collection during 8 hours.
Bloodsamples for safety will be taken each week. A bloodsample for PSA measurement will be taken in weeks 1, 5 and 9. Patients will be asked to keep a pain an medication diary throughout the study, and to fill out a HRQOL questionnaire before treatment and in weeks 5 and 9.

Study burden and risks

The extra burden to the patient consists of:
1 screening visit
1 hospital admission for treatment with Re-188-HEDP

1 total body scan
2 outpatient visits
10 bloodsampling for safety and/or PSA
3 urine samples for saftey
keeping a pain and medication diary during 8 weeks
3 HRQOL questionnaires
The possible risks are related to the side effects of both capecitabine and Re-188-HEDP and the possibility of bruising from bloodsampling or intravenous injection.
The radiation dose from Re-188-HEDP (mean dose 1400 mSv) does not form a large risk to the patient and does not impose any restrictions for medical investigations or treatments with radiation the patient may need in the future.

The patient may benefit from pain relief.

Contacts

Public
Academisch Medisch Centrum

Heidelberglaan 100
3508 GA Utrecht
Nederland
Scientific
Academisch Medisch Centrum

Heidelberglaan 100
3508 GA Utrecht
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

Histologically documented prostate cancer; presence of more than one osteoblastic bone metastases; hormone refractory disease; bone pain; life expectancy of at least 3 months; informed consent.

Exclusion criteria

Previous chemotherapy within 6 weeks prior to screening; prior treatment with systemic radiotherapeutic bone agent within a specified period; previous external beam radiotherapy within a specified period; active CNS or epidural brain metastases. ANC < 2 10^9/L; Platelet count < 150 10^9/L; Hb < 6 mmol/L; PSA > 5 microgram/L.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-06-2007
Enrollment:	33
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Rhenium-188-HEDP
Product type:	Medicine
Brand name:	Xeloda

Generic name:	capecitabine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-11-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-03-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-10-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	31-03-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2006-004564-32-NL
CCMO	NL15388.041.06