A phase I/II trial of Cabazitaxel +/- Rhenium-188 HEDP in patients with metastatic castration resistant prostate cancer who progressed on or after a docetaxel containing treatment. The ReCab trial

Published: 01-08-2012
Last updated: 26-04-2024

Primary objectives:To establish a safe and effective dosing schedule for repeated administration of Rhenium-188 HEDP combined with Cabazitaxel in order to proceed with a Randomised Phase 2 trial designed to determine the clinical value of Rhenium-...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON44670

Source
ToetsingOnline

Brief title
ReCab Trial

Condition

- Metastases

Synonym
prostate cancer - bone metastases

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Sanofi-aventis,TEVA Pharma

Intervention

Keyword: bone metastases, Cabazitaxel, prostate cancer, Rhenium-188-HEDP

Outcome measures

Primary outcome

Primary objectives:

To establish a safe and effective dosing schedule for repeated administration of Rhenium-188 HEDP combined with Cabazitaxel in order to proceed with a Randomised Phase 2 trial designed to determine the clinical value of Rhenium-188 HEDP/Cabazitaxel using progression free survival as the primary endpoint.

Phase I:

The Dose Limiting Toxicity (DLT) period is defined as 7 weeks from administration of Rhenium. In no DLT occurs in this period, patients can be included in the next dose level. If a DLT occurs in 1 of the 3 patients in a particular treatment level, the group will be expanded to 6 patients. If 2 or more of the group experience a DLT, we will treat the next 3 patients at the previous dose level (i.e. If DLT in >2/6 at dose level 2, 3 patients will be treated at dose level 1). If none of the group of 3 or <1/6 experience DLT, 3 patients will be treated at the next dose level. The final group of 3 patients

will be treated at a planned dose of 6 cycles of cabazitaxel 25mg/m2 and 2 cycles of Rhenium-188 HEDP (40 MBq/kg).

DLT is defined as:

- Hematological:

- Neutropenia: Grade 4 > 7days. Grade 3 when failure of count recovery to allow for next cycle on time.

- Thrombopenia: All grade 4. Grade 3 when failure of count recovery to allow for next cycle on time.

- Anemia: All grade 4.

-Non-hematological:

- All grade 4

- All grade 3 except for nausea, vomiting or diarrhea unless not recovered to allow for next cycle on time.

N.B. Patients with grade 4 neutropenia >7 days during the first or second cycle cabazitaxel will be excluded from the phase I study

Phase II:

Progression Free Survival (PFS) will be the primary efficacy endpoint.

Secondary endpoints are: PSA response, overall survival, pain response, and quality of life

Secondary outcome

Secondary objectives:

Evaluate overall survival, PSA response, clinical benefit response (pain and

Quality of life), toxicity, RNA-expression profiles on trombocytes

Study description

Background summary

Prostate cancer is very common and often leads to bone metastases. Although initially most patients respond to androgen deprivation, after approximately 18 months the cancer will become hormone refractory leading to progressive disease. Since 2004 Docetaxel became standard chemotherapy for men with metastatic CRPC leading to survival benefit. Several trials have shown evidence of the disease modifying potential of bone seeking radionuclides. Recent studies have shown an improvement of survival and quality of life when Rhenium-186 HEDP was given in high dosage or repeatedly. Recently results of our dosefinding trial (XRP6976J/6213) showed that combined therapy with Docetaxel and Rhenium-186 HEDP is generally well tolerated in patients with metastatic bone disease from prostate cancer. A phase II study (DOCET_L_04935) will be conducted using 3 cycles of Docetaxel 75mg/m2 followed by Rhenium-188 HEDP 2500MBq, followed by another 3 cycles of Docetaxel, followed by Rhenium-188 HEDP 1250MBq.

Cabazitaxel is a promising new drug to be used for the treatment of castrate resistant prostate cancer (CRPC) after progression on Docetaxel therapy.
In this study, we build upon previous results and we aim to test wheather the combination of Cabazitaxel with repeated Rhenium-188 HEDP is feasible and leads to better PFS, OS and pain control compared to Cabazitaxel alone in patients with mCRPC after progression of disease after first line docetaxel. We start with a phase I dosefinding trial, immediately followed by a phase II trial if the envisaged schedule is feasible.

Study objective

Primary objectives:
To establish a safe and effective dosing schedule for repeated administration of Rhenium-188 HEDP combined with Cabazitaxel in order to proceed with a Randomised Phase 2 trial designed to determine the clinical value of Rhenium-188 HEDP/Cabazitaxel using progression free survival as the primary endpoint.

Secondary objectives:
Evaluate overall survival, PSA response, clinical benefit response, toxicity and RNA-expression profiles on trombocytes. Second side study will investigate the influence of lipegfilgrastim on the incidence of neutropenic fever.

Study design

Trial design phase I (see appendix)
Trial design phase II:
Arm A: Cabazitaxel (20 or 25mg/m2) d1, q3 for a maximum of 10 cycles
Arm B: Cabazitaxel (20 or 25mg/m2) d1, q3 for a maximum of 10 cycles + Rhenium-188 HEDP (dose schedule phase I)
All patients will receive 10 mg prednisone daily during Cabazitaxel treatment.

In phase II, an extra randomasation (1:1) will be performed; arm A will not receive lipegfilgrastim after the first cycle of cabazitaxel, patients in arm B will receive 1 injection of lipegfilgrastim after the first dose of cabazitaxel.

Intervention

Randomization:

Phase II
Arm A: Cabazitaxel (20 or 25mg/m2) d1, q3 for a maximum of 10 cycles
Arm B: Cabazitaxel (20 or 25mg/m2) d1, q3 for a maximum of 10 cycles + Rhenium-188 HEDP (dose schedule phase I)
All patients will receive 10 mg prednisone daily during Cabazitaxel treatment.

Side study; randomastion for lipegfilgrastim (1:1)

Study burden and risks

Burden:

- Blood tests will be done every weeks instead of 3-weekly during the phase I part only. In the phase II part of the trial bloodtest will be performed before every cycle according to standard care.
- Patients in arm B will have two extra visits to the hospital (hospital stay 0.5 days)
- Additional bloodsamples: after the two cycles of rhenium (2x), during follow-up (4x) and in case the patient participates in a side study (optional): 3 times 9 ml. For the last no additional venapunctures are necessary, but blood will be drawn during a regular punction.
- Patients will be asked to fill in questionairies about quality of life

Risks:

The most important risk is hematological toxicity, especially leucopenia and thrombocytopenia. However, our phase I study combining rhenium and docetaxel showed that combining of rhenium and Docetaxel is generally well tolerated and

hematological toxicity is self limiting. Therefore we suspect that the combination of cabazitaxel with Rhenium will also be feasible.

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

Castration resistant prostate cancer with bone metastases

Exclusion criteria

patients with predominant visceral metastases. Bone marrow insuffiency

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-06-2016
Enrollment:	86
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Jevtana
Generic name:	Cabazitaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lonquex
Generic name:	Lipegfilgrastim
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rhenium-188-HEDP
Generic name:	Rhenium-188-HEDP

Ethics review

Approved WMO Date:	01-08-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-09-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-10-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-06-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	07-06-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-10-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-02-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-07-2017
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
Other	10793
EudraCT	EUCTR2011-005116-28-NL
CCMO	NL38495.100.12