Radium-223 Dichloride (Alpharadin) in Castration-Resistant (Hormone-Refractory) Prostate Cancer Patients with Bone Metastasis

Published: 06-03-2013
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To provide access to Radium-223 dichloride to patients diagnosed with CRPC/HRPC with bonemetastasis.

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

Summary

ID

NL-OMON39188

Source
ToetsingOnline

Brief title
Ra-223 dichloride in treatment of CRPC/HRPC patients with bone metastasis

Condition

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

Synonym
Castrate-resistant prostate cancer, Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Bayer

Source(s) of monetary or material Support: Bayer Healthcare

Intervention

Keyword: Castration-Resistant, Prostate Cancer, Radiotherapy

Outcome measures

Primary outcome

- To assess the acute and long-term safety of Ra-223 dichloride

- To assess the overall survival of this patient population

Secondary outcome

Not applicable

Study description

Background summary

A prior Phase III study (Alsympca) was terminated by the Independent Data Monitoring Committee (IDMC) based on the results of a preplanned interim analysis that evaluated overall survival. The results from the interim analysis revealed significant improvement of overall survival in subjects treated with Ra-223 Cl2 compared with placebo.
The study described in the current protocol was designed to explore the acute and long-term safety of treatment with Ra-223 Cl2, 50 kBq/kg body weight, when administered at 4-week intervals.

Study objective

To provide access to Radium-223 dichloride to patients diagnosed with CRPC/HRPC with bonemetastasis.

Study design

This is an international prospective, interventional, open-label, multicenter study.

Upon obtaining signed informed consent, screening evaluations will be performed to confirm eligibility and to obtain baseline safety data.
During the treatment period, study medication will be administered every 4

weeks and may be delivered on an outpatient basis. Patients will be evaluated at each visit, prior to receiving Ra-223 dichloride for treatment emergent Grade 3-4 adverse events (AEs), all treatment emergent AEs of any grade leading to drug discontinuation, all grades of treatment-related AEs, serious adverse events (SAEs), and skeletal-related events (SREs); laboratory values; and for changes in bone pain (quality of life [QoL]) as measured by patient assessment using a validated questionnaire.
During the follow-up period, patients will be evaluated every 6 months for long-term safety including hematologic effects of Ra-223 dichloride on peripheral blood counts, SREs, treatment-related AEs and SAEs, and occurrence of secondary malignancies. If the patient can no longer travel to the clinical site, he will be followed up for survival only.
Adverse events will be categorized in regards to their relationship to treatment with Ra-223 Cl2, seriousness, NCI-CTCAE v4.03 grading, action taken, and outcome.

Intervention

Not applicable.

Study burden and risks

It is expected that patients will complete the treatmentschedule. This means that they will receive 6 injections van Radium-223 dichloride, at 4 week intervals. It is expected that patients will stay in the study for about 38 weeks.
Safety of the product: according to the protocol, the safety of the product will be evaluated as follows:
During the treatment period, study medication will be administered every 4 weeks and may be delivered on an outpatient basis. Patients will be evaluated at each visit, prior to receiving Ra-223 Cl2 for treatment emergent Grade 3-4 adverse events (AEs), all treatment emergent AEs of any grade leading to drug discontinuation, all grades of treatment-related AEs, serious adverse events (SAEs), and skeletal-related events (SREs); laboratory values; and for changes in bone pain (quality of life [QoL]) as measured by patient assessment using a validated questionnaire.
During the follow-up period, patients will be evaluated every 6 months for long-term safety including hematologic effects of Ra-223 Cl2 on peripheral blood counts, SREs, treatment-related AEs and SAEs, and occurrence of secondary malignancies. If the patient can no longer travel to the clinical site, he will be followed up for survival only.

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

• Has provided written informed consent. Subjects must be able to understand and be willing to sign the written informed consent form (ICF). A signed ICF must be appropriately obtained prior to the conduct of the any trial- specific procedure. ;• Age >= 18 years;• Histologically or cytologically confirmed prostate cancer;• Patients diagnosed with progressive bone predominant metastatic CRPC/HRPC with at least two skeletal metastases on imaging with no lung, liver, and/or brain metastasis (lymph node only metastasis is allowed). A standard of practice bone scan for the documentation of at least 2 skeletal metastases can be used as long as it is within 3 months of planned start of treatment. If no bone scan within a 3 month window is available, then a technetium-99m bone scan will be obtained at screening (within 28 days of planned start of study drug).;• Progressive disease is defined either by: ;o The appearance of new bone lesions. If progression is based on new lesion(s) on bone scan only without an increase in PSA, PSA values from 3 assessments within the last 6 months must be provided; OR;o In the absence of a new bone lesions by 2 consecutive increases in serum PSA over previous reference value, which should not be more than 6 months before screening, each measured at least 1 week apart with the last PSA >=5 ng/mL. (The reference value time

point 1, is defined as the last PSA measured before increases are documented, with subsequent values obtained a minimum of 1 week apart. If the PSA at time point 3 is greated than the PSA at time point 2, then the eligibility has been met. If the PSA at time point 3 is not greater than the PSA at time point 2 but the PSA value at time point 4 and/or time point 5 is greater than the PSA at time point 2, the patient is eligible assuming that other criteria are met) ;• No intention to use cytotoxic chemotherapy within the next 6 months;• Life expectancy >= 6 months;• ECOG PS 0-2;• Adequate hematological, liver and renal function;o Absolute neutrophil count (ANC) >= 1.5 x10^9/L;o Platelet count >= 100 x10^9/L ;o Hemoglobin >=10.0 g/dL (100 g/L; 6.2 mmol/L);o Total bilirubin level <= 1.5 x institutional upper limit of normal (ULN);o Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) <= 2.5 x ULN ;o Creatinine <= 1.5 x ULN;o Albumin > 25 g/L;• Willing and able to comply with the protocol, including follow-up visits and examinations

Exclusion criteria

• Treatment with an investigational drug within previous 4 weeks, or planned during the treatment period or follow-up;• Eligible for first course of docetaxel, i.e., patients who are fit enough, willing, and who are located where treatment with docetaxel is available;• Treatment with cytotoxic chemotherapy within previous 4 weeks, prior to screening, or failure to recover from AEs due to cytotoxic chemotherapy administered more than 4 weeks previous prior to screening (however, ongoing neuropathy is permitted);• Treatment with any prior anticancer therapy (including therapeutic vaccines), other than the permitted Standard of Care therapies (please refer to section 6.9), are allowed provided that they are completed 28 days before treatment or 5.5 half-lives of the drugs involved have elapsed before treatment start.;• Prior hemibody external radiotherapy is excluded. Patients who received other types of prior external radiotherapy are allowed provided that the bone marrow function is assessed and meets the protocol requirements for hemoglobin, absolute neutrophil count and platelets.;• Received systemic therapy with radionuclides (e.g., strontium-89, samarium-153, rhenium-186, or rhenium-188, or radium-223 dichloride) for the treatment of bony metastases ;• Other malignancy treated within the last 3 years (except non-melanoma skin cancer or low-grade superficial bladder cancer) ;• Visceral metastases as assessed by abdominal or pelvic computed tomography (CT) (or other imaging modality based on institutional standard of care);• Presence of brain metastases;• Lymphadenopathy exceeding 6 cm in short-axis diameter;• Any size pelvic lymphadenopathy if it is thought to be a contributor to concurrent hydronephrosis.;• Imminent or history of spinal cord compression based on clinical findings and/or magnetic resonance imaging (MRI). Patients with history of spinal cord compression should have completely recovered.;• Any other serious illness or medical condition, such as but not limited to:;o Any infection >= NCI-CTCAE v.4.03 Grade 2 ;o Cardiac failure New York Heart Association (NYHA) Class III or IV;o Crohn*s disease or ulcerative colitis;o Bone marrow dysplasia;• Fecal incontinence

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-10-2013
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Xofigo
Generic name:	Radium-223 dichloride

Ethics review

Approved WMO Date:	06-03-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-07-2013

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-12-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-03-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-03-2014
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	EUCTR2012-000075-16-NL
ClinicalTrials.gov	NCT01516762
CCMO	NL40865.091.13