Effectiveness of Zometa® treatment for the prevention of bone metastases in high risk prostate cancer patients: a randomised, openlabel, multicentre study of the European Association of Urology (EAU) in Cooperation with the Scandinavian Prostate Cancer Group (SPCG) and the Arbeitsgemeinschaft Urologische Onkologie (AUO)

Submission date	Recruitment status No longer recruiting	Prospectively registered		
19/12/2005		☐ Protocol		
Registration date	Overall study status	Statistical analysis plan		
19/12/2005	Completed	[X] Results		
Last Edited	Condition category	Individual participant data		
20/04/2015	Cancer			

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

Mr C Caris

Contact details

CuraTrial SMO & Research P.O. Box 30016 Arnhem Netherlands 6803 AA +31 (0)26 3890677 c.caris@uroweb.org

Additional identifiers

EudraCT/CTIS number 2004-001786-18

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers CZOL446G DE08; NTR355

Study information

Scientific Title

Effectiveness of Zometa® treatment for the prevention of bone metastases in high risk prostate cancer patients: a randomised, open-label, multicentre study of the European Association of Urology (EAU) in Cooperation with the Scandinavian Prostate Cancer Group (SPCG) and the Arbeitsgemeinschaft Urologische Onkologie (AUO)

Acronym

ZEUS

Study objectives

Zoledronic acid (Zometa®) is a third-generation nitrogen-containing bisphosphonate which has been approved in Europe and the US for the treatment of bone metastases (4 mg Zoledronic acid intravenous [iv]/month) in a broad range of tumours and for the treatment of malignancy-related hypercalcaemia.

In animal models, bisphosphonates have been shown to reduce and even to prevent the development of bone metastases. The hypothetical mechanisms for this antitumour effect by bisphosphonates are:

- 1. The inhibition of osteoclastic bone resorption prevents the release of tumour-promoting growth factors from the bone matrix
- 2. Inhibition of the adhesion of tumour cells to bone matrix
- 3. Inducing tumour cell apoptosis

It is expected that in the present study Zometa® in addition to the prevention of bone metastases will show its potential in preventing hormone therapy induced bone loss.

On 20/04/2015 the following changes were made to the trial record:

- 1. The overall trial end date was changed from 15/01/2011 to 17/01/2014.
- 2. The following countries were added to the countries of recruitment: Germany, Denmark, Sweden, Norway, Finland, Belgium, Greece, Italy, Turkey, Switzerland, France, Spain

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval received from local medical ethics committee

Study design

Multicentre randomised controlled parallel group trial

Primary study design

Interventional

Secondary study design

Randomised parallel trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Prostate cancer

Interventions

Patients will be randomised between standard treatment plus Zometa®; 4 mg infusions every 3 months for a total of 48 months or standard treatment only.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Zometa®

Primary outcome measure

The primary outcome parameter is the proportion of patients who develop bone metastases during the study.

Secondary outcome measures

- 1. Time to first bone metastasis
- 2. Overall survival
- 3. Time to PSA doubling
- 4. Safety
- 5. Bone mineral density (sub study in selected centres)
- 6. Biochemical markers of bone turnover (sub study in selected centres only)

Overall study start date

15/01/2004

Completion date

17/01/2014

Eligibility

Key inclusion criteria

- 1. Male patients aged 18+ years, Eastern Cooperative Oncology Group (ECOG) = 0 (Karnofsky performance status greater than 90)
- 2. M0 prostate cancer patients who previously received local curative treatment (e.g. surgery, radiotherapy) or no local curative treatment. Duration between local curative treatment and starting of the study drug must not be longer than 6 months.
- 3. At least one of the following conditions must be present:
- 3.1. Gleason Score 8 10
- 3.2. pN+
- 3.3. Prostate specific antigen (PSA) equal to or higher than 20 ng/ml at diagnosis
- 4. Patients receiving androgen deprivation by orchiectomy or administration of GnRH analogue ± anti-androgens or no androgen deprivation. Hormone therapy regimen will depend on standard medical management of prostate cancer patients i.e. when corresponding to standard medical management, patients on hormone treatment at study entry can later be withdrawn and patients not on hormone treatment at study entry can later start with androgen deprivation. Intermittent hormone treatment is allowed when corresponding to standard medical management. Patients should not be under hormonal ablation for longer than 6 months before the first study drug infusion. Neoadjuvant androgen deprivation is allowed as long as the duration between start of androgen deprivation and start of study drug is no longer than 6 months.
- 5. Life expectancy of greater than 6 months
- 6. Signed informed consent prior to initiation of any study procedure

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Male

Target number of participants

1300

Key exclusion criteria

- 1. Patients with known visceral metastasis or bone metastases in bone scan
- 2. Prior treatment with bisphosphonates
- 3. Chemotherapy to treat prostate carcinoma
- 4. Anti-androgen monotherapy is not allowed
- 5. Use of other investigational drugs (drugs not marketed for any indication) within 6 months before start of study
- 6. History of noncompliance to medical regimens and patients who are considered potentially unreliable or incapable of giving informed consent as judged by the investigator
- 7. Serum creatinine greater than 3 mg/dl (265 µmol/l)

- 8. History of other malignant neoplasm within previous five years with exception of non-melanomatous skin cancer which has been satisfactorily treated
- 9. Other known concurrent, severe medical disorder jeopardising the life of the patient in the immediate future (myocardial infarction in previous six months, angina pectoris despite treatment, uncontrolled severe arterial hypertension, progressive cardiac or respiratory failure)

Date of first enrolment 15/01/2004

Date of final enrolment 15/01/2011

Locations
Countries of recruitment Belgium
Denmark
Finland
France
Germany
Greece
Italy
Netherlands
Norway
Spain
Sweden
Switzerland
Türkiye

Study participating centre CuraTrial SMO & Research Arnhem Netherlands 6803 AA

Sponsor information

Organisation

European Association of Urology (The Netherlands)

Sponsor details

P.O. Box 30016 Arnhem Netherlands 6803 AA +31 (0)26 3890680 EAU@uroweb.org

Sponsor type

Research organisation

ROR

https://ror.org/00m9mc973

Funder(s)

Funder type

Not defined

Funder Name

Not provided at time of registration

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2015		Yes	No