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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)

Submission date
19/12/2005

Recruitment status
No longer recruiting

Registration date
19/12/2005

Overall study status
Completed

Last Edited
20/04/2015

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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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
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Sponsor information

Organisation
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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