Reduced dose-density of denosumab for maintenance therapy of unresectable giant cell tumor of bone: a multicenter phase II study "REDUCE"

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

Summary

ID

NL-OMON47949

Source
ToetsingOnline

Brief title
REDUCE

Condition

- Skeletal neoplasms malignant and unspecified

Synonym
Giant Cell Tumor

Research involving
Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)

Source(s) of monetary or material Support: Amgen Ltd,EORTC

Intervention

Keyword: Denosumab, Giant Cell Tumor of Bone, Phase II

Outcome measures

Primary outcome

o Progression free survival (overall)

o Overall survival

o Denosumab treatment duration

o ONJ incidence (overall)

o Safety and tolerability (Common Terminology Criteria for Adverse Events

(CTCAE) v 5.0)

o Visual Analogue Scale (VAS) pain score

Secondary outcome

OS, denosumab duration, side effects and visula pain scale

Study description

Background summary

At this moment 4 wkly denosumab is the standard, however this may lead to serious side effects mainly osteonecrosis of the jaw. The idea is to increase the interval of denosumab to 12 wkly in order to decrease the side effects while mainting efficacy

Study objective

The primary objective of the trial is to evaluate the risk versus benefit of denosumab in maintenance setting in patients requiring long-use (>1 year) of denosumab. For that purpose, the treatment schedule with reduced dose density (120mg SC 12 weekly instead of 4-weekly) will be investigated, starting after 1-year (12-15 months) of denosumab full dose, as per current label. The impact

on incidence of ONJ without compromising disease control will ben assessed. Secondary objectives are to assess the effect of the reduced dose density schedule on patient clinical and self-reported outcomes, and on the toxicity profile of the treatment

Study design

this is a multicenter phase 2 single-arm trial. Patients will be registered in this study after at least 12 months and at most 15 months of treatment with denosumab, given in a full dose of 120 mg SC on day 1 of every 4 weeks. After registration, patients will receive the study treatment which consists of the reduced dose density schedule denosumab 120 mgSC on day 1 of every 12 weeks.

Intervention

12 wkly instead of wkly denosumab

Study burden and risks

same as with 4-weekly denousmab, but less inhjections (12 wkly instead of 4-wkly)

Contacts

Public
EORTC

Avenue du Mounier 83 11
Brussel 1200
BE
Scientific
EORTC

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Histologically proven primary or metastatic unresectab~e GCTB or resectable GCTB but not a candidate for
surgery, excluding primary or metastatic GCTB in the jaw.
Evidence of active disease at time of registration based on local
investigator's assessment
* Age >_ 18 years old and skeletally mature (ie, radiographic evidence of at least 1 mature long bone (e.g.
humerus with closed growth epiphyseal plate)
* Patient must have received denosumab before entering this trial:
- The duration of treatment with full dose denosumab (120 mg SC) as per current label must be at least 12
months and patient may have received up to 15 months of denosumab.
- And patient must have received at least 12 doses of denosumab 120 mg before entering into this trial.
* ECOGNVHO PS 0-2
* Albumin-adjusted serum calcium level >_ 2.0 mmollL (8.0 mg/d L)
* Representative formalin fixed, paraffin embedded tumor blocks or unstained tissue slides,either from the primary tumor or a metastatic lesion, must be available for histological central review.
* Women of child bearing potential (WOCBP) must have a negative serum pregnancy test within 7 days prior to the first reduced dose of study treatment.
WOCBP should use adequate birth control measures, as defined by the investigator, during the study
treatment period and for at least 5 months after the last treatment cycle. A highly effective method of birth
control is defined as a method which results in a low failure rate (i.e. less than 1 %per year) when used
consistently and correctly. Such methods include:
- Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of
ovulation (oral, intravaginal, transdermal)
- Progestogen-only hormonal contraception associated with inhibition of

ovulation (oral, injectable, implantable)
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion
- Vasectomized partner
- Sexual abstinence (the reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient)
Female subjects who are breast feeding should discontinue nursing prior to the first dose of study treatment and until 5 months after the last study treatment.
* Before patient registration, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion criteria

het Engels
* Currently receiving other GCTB specific treatment (eg, radiation, chemotherapy, or embolization)
* Concurrent bisphosphonate treatment and calcitonin
* Known or suspected current diagnosis of underlying malignancy including high-grade sarcoma,
osteosarcoma, fibrosarcoma, malignant giant cell sarcoma
* Known diagnosis of second malignancy within the past 5 years (subjects with definitively treated basal cell carcinoma and cervical carcinoma in situ are permitted)
* Creatinine clearance < 30 mL/min
* Hemoglobin < 10.0 g/dL or 6.2 mmol/L
* Prior history or current evidence of osteonecrosis/osteomyelitis of the jaw
* Active dental or jaw condition which requires oral surgery, including tooth extraction Non-healed dental/oral surgery
* Planned invasive dental procedure for the course of the study
* Known hypersensitivity to the active substance or to any of the excipients (glacial acetic acid, sodium hydroxide, sorbitol (E420), polysorbate 20)
* Treatment with other investigational device or drug 30 days prior to registrationKnown hypersensitivity to products to be administered during the study (calcium and/or vitamin D)
* Unstable systemic disease including active and uncontrolled infection, uncontrolled hypertension, unstable
angina, congestive heart failure, or myocardial infarction within 6 months before registration
* Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-02-2020
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	Denosumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	05-09-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	10-04-2020
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	29-04-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2018-002096-17-NL
ClinicalTrials.gov	NCT03620149
CCMO	NL67850.058.19