Zoledronic Acid to Maintain Bone Mass After Denosumab Discontinuation: AfterDmab

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1. Primary objective: to investigate changes in BMD of the lumbar spine (LS) one year after treatment discontinuation in denosumab-treated women and in denosumab-treated women who received a single infusion of zoledronic acid after treatment...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON43199

Source
ToetsingOnline

Brief title
After Dmab

Condition

- Other condition

Synonym
Osteoporosis

Health condition

Osteoporosis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Denosumab, Osteoporosis, Zoledronic Acid

Outcome measures

Primary outcome

Lumbar spine and hip BMD at 24 months (12 months after discontinuation)

Secondary outcome

- Markers of bone turonover at T= 6 months, 12 months, 15 months, 18 months and

24 months

- Number of fractures at T=24 months

Study description

Background summary

Denosumab, a monoclonal antibody against the receptor activator of nuclear factor *-* ligand (RANKL), is a potent antiresorptive agent [1] commonly prescribed in patients with postmenopausal osteoporosis. In phase 3 clinical studies long-term treatment with denosumab increased bone mineral density (BMD) continuously with more than 80% of patients with osteoporosis (T-score < -2.5) attaining BMD values in the range of osteopenia (T-score between-1.0 and -2.5) or even in the normal range [2]. Such increases are associated with decreases in fracture risk and raise the possibility of treatment discontinuation. However, in phase 2 clinical studies, discontinuation of denosumab resulted in a rebound response of bone turnover markers, which rose above baseline at 3 months and remained elevated until reaching again baseline levels within approximately 30 months after the last dose. Bone mineral density (BMD) gains were also lost and BMD values readched original baseline values after 2 years off-treatment [3, 4]. In contrast, bisphosphonates remain within the skeleton acting for several months or even years after discontinuation [4] while maintaining BMD despite the cessation of treatment [5,6]. We hypothesize, therefore, that a single intravenous dose of the potent bisphosphonate

zoledronic acid after discontinuation of denosumab therapy in patients who have reached osteopenic or normal BMD values will consolidate the effect of denosumab on BMD and will prevent bone loss .

Study objective

1. Primary objective: to investigate changes in BMD of the lumbar spine (LS) one year after treatment discontinuation in denosumab-treated women and in denosumab-treated women who received a single infusion of zoledronic acid after treatment discontinuation.

2. Secondary objective : to investigate Changes in BMD of the femoral neck (FN) of the non-dominant hip and changes in bone turnover markers and parameters of bone metabolism throughout the study.

Study design

2 year Interventional, parallel assignment, open label, randomized clinical trial.
Patients will be recruited at the outpatient clinics for Metabolic Bone Diseases of the 424 General Military Hospital, Thessaloniki, Greece, at the Department of Endocrinology of the 251 General Airforce and VA Hospital, Athens, Greece and at the outpatient of the LUMC Center for Bone Quality, Leiden, the Netherlands
Postmenopausal Caucasian women treated with denosumab who become osteopenic with treatment (BMD T-score of > -2.5 and < -1.0 at the LS and/or the non-dominant FN) will be randomly assigned to a single intravenous infusion of zoledronic acid 5mg (Zol group, n=40) or only calcium/d3 supplements (Denosumab group, n=40) after discontinuation of the therapy.

Intervention

Treatment with zoledroninezuur after denosumab discontinuation.

Study burden and risks

The burden will be minimal. Currently there is no information nor policy about the follow-up treatment of patients previously treated with denosumab, a commonly prescribed anti-osteoporotic drug. This study aims to provide more insight if follow up treatment is needed and integrates with the standard care of our Co-ordinated Care Trajectory Osteoporosis.

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

Postmenopausal women with osteoporosis (T-score <-2.5) who reached a T score of >-2.5 on the LS spine and/or Fn Neck while on treatment with denosumab attending the outpatient clinic and willing to participate.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:;i) secondary osteoporosis; ii) diseases that could affect bone metabolism other then osteoporosis; iii) medications that could affect bone metabolism; iv) history of any antiosteoporotic treatment other than denosumab prior to randomization.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-10-2016
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aclasta
Generic name:	Zoledronic Acid
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-03-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	02-06-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	10-07-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2016-000852-91-NL
ClinicalTrials.gov	NCT02499237
CCMO	NL57170.058.16