A Randomized Open-Label Study to Evaluate the Safety and Efficacy of Denosumab and Monthly Actonel® Therapies in Postmenopausal Women Transitioned from Weekly or Daily Alendronate Therapy

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bone disorders (excl congenital and fractures)
Study type	Interventional

Summary

ID

NL-OMON38276

Source
ToetsingOnline

Brief title
Evaluate Safety Efficacy Denosumab Actonel Therapies in PMO

Condition

- Bone disorders (excl congenital and fractures)

Synonym
Postmenopausal Osteoporosis

Research involving

Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: Denosumab, monthly Actonel, Postmenopausal Women

Outcome measures

Primary outcome

The primary objective of the study is to evaluate the effect of denosumab 60mg every 6 months (Q6M) compared with Actonel 150mg monthly (QM) on total hip Bone Mineral Density (BMD) at 12 months in postmenopausal women transitioning from previous alendronate therapy

Secondary outcome

To evaluate the effect of denosumab 60mg Q6M en Actonel 150 mg QM on CTX (C-terminal telopeptide) , a subset of subjects, at 1 month . Further to evaluateBMD at the femoral neck at 12 months and the BMD at the lumbar spine at 12 months.

And to evaluate safety objectives as the effect and tolerability of denosumab 60mg Q6M and Actonel 150 mg QM , measured by evaluating adverse events and laboratory parameters over 12 months.

Study description

Background summary

protocol 20080099 is a Randomized Phase 3b Open-Label Study to Evaluate the Safety and Efficacy of Denosumab and Monthly Actonel® Therapies in Postmenopausal Women Transitioned from Weekly or Daily Alendronate Therapys.

Bisphosphonates (BPs) are currently the most commonly utilized treatment forosteoporosis in Europe. Alendronate is generally prescribed as a first line therapy. However difficult dosing regimens and multiple sie-effects limit drug adherence. Most patients, who discontinue BP therapy, do so within the first year of treatment. Poor adherence is common and is associated with poor outcomes and increased treatment costs and is likely associated with a lack of effectiveness.

Study objective

The primary objective of the study is to evaluate the effect of denosumab 60mg every 6 months (Q6M) compared with Actonel 150mg monthly (QM) on total hip Bone Mineral Density (BMD) at 12 months in postmenopausal women transitioning from previous alendronate therapy,who have a low adherence to or stopped previously with alendronate.

Study design

The study consist of two parts.
Firts part is to define of the patient is eligible for the study. Second part is the studyphase and the study conduct is 12 months. The total study period is 13 months, and the first month is the screeningperiod. As a result of a positive outcome of the screening the patient will be allocated to one of the arms.
Approximately 800 subjects will be randomized across approximately 75 sites in a 1:1 ratio to either open label :

• Denosumab 60 mg (subcutane injection every 6 months during 12 months
or
• Actonel® 150 mg oral (one 75 mg tablet on reach of 2 consecutive days each month during 12 months

Patienten zullen ook calcium- en vitamine D-supplementen krijgen die men dagelijks moet innemen.

In total 800 patients are participating in this trial. There is a sub-study , called CTX sub-study for bone turnovermarkers. 250 patients of 800 patients will be approached by selected centers. This means these patients have 1 addditional vist and have to perform additional bloodassessments to assess bonemarkers.

Intervention

denosumab 60mg SC every 6 months (Q6M) and Actonel 150mg monthly (QM)

Study burden and risks

Load for patients

The following procedures will be performed per visit schedule outlined in Appendix A, page 59 of the protocol:Physical examination, vital signs, DXA, hematology,serum chemistry and anti denosumab antibody and serum CTX for the subgroup. Adverse events and concomitant medications will be recorded through participation.

The patients have to visit 4 times the site(inclusive screeningvisit) during the 12 months. For patients, participating the sub-study have to vperform in total 5 visit. At a maximum 28 out of the 100 patients in The Netherlands will partcipate at the CTX study. These patients will be approached by two sites.

More than 13,500 patients have been treated with denosumab in clinical studies. Denosumab has been generally well tolerated.
The following adverse events occurred slightly more frequently (at least 1% more) in patients receiving denosumab than placebo in patients participating in completed large clinical studies:
• Very common adverse events: joint pain, pain in extremity
• Common adverse events: reports of high cholesterol, muscle and bone pain, dizziness, cough, osteoarthritis, cataracts, eczema, muscle pain, difficulty emptying the bladder and decreased skin sensation.

Temporary lowering of blood calcium levels below normal has been observed very rarely in subjects treated with denosumab,The risk of this happening may be higher in subjects with severe kidney disease.
Skin infections such as cellulitis by denosumab does not appear to increase the occurrence of infection when compared to placebo,, in one large study, skin infections that required hospitalization were observed more in patients treated with denosumab than in placebo. Skin infections leading to hospitalization were observed uncommonly in patients receiving denosumab .Some patients receiving bisphosphonates for treatment of bone loss or spread of cancer to their bones may experience osteonecrosis.Osteonecrosis has been reported in patients with cancer involving the bones who received denosumab.
The development of antibodies to denosumab in patients has been uncommon and has had no clinical effects and has not reduced the effect of denosumab on bones. Refer herwith also to section potential risks and discomforts of the patient informed consent

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Ambulatory, postmenopausal women (based) on medical history) aged 55 years or older at screening :
-postmenopause will be defined as no vaginal bleeding or spotting for a least 12 months
2. received at least 1 prescription of oral alendronate therapy (weekly or dialy) as a first treatment for post menopausal osteoporosis in the 18 months prior to screening. Use of raloxifene, calcitonin or HRT prior to alendronate treatment will be allowed. Prior and/or current use of vitamin D and calcium will be allowed.
3,Subject has demonstrated 1 of the following :
-has stopped oral alendronate therapy (is denoted as non-persistent) at least one month before the screening visit
-is still taking oral alendronate therapy but demonstrates low adherence to therapy assessed by a score of less than 6 on the Osteoporosis Specific Morisky Medication Adherence

Scale(OS-MMAS)
4.Provide signed informed consent before any study-specific procedures are conducted

Exclusion criteria

1. any prior or current use of medications prescribed for osteoporosis treatment other than: oral daily or weekly alendronate, calcium and vitamin D
prior use of raloxifene, calcitonin or HRT before alendronate therapy was initiated will be allowed. Use of these therapies must have stopped prior to initiating oral alendronate and their current use is not allowed.;Any prior or current use of medications prescribed for osteoporosis treatment other than:
-oral daily or weekly alendronate, calcium and vitamin D
prior use of raloxifene, calcitonin, or HRT before alendronate therapy was initiated will be allowed. Use of these therapies must have stopped prior to initiating oral alendronate and their currentn use is not allowed

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):	22-10-2009
Enrollment:	98
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Not applicable

Generic name:	Denosumab

Ethics review

Approved WMO Date:	04-08-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-09-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-10-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-10-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-11-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-11-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-12-2009
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-12-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-02-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-02-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-03-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-03-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-03-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-03-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	

Date:	14-04-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-04-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-05-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-05-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-05-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-06-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-06-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-06-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

	Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-06-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-07-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-07-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-08-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-08-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-07-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-08-2011

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-10-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-10-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-01-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2009-010587-42-NL
ClinicalTrials.gov	NCTnummernognietbekend
CCMO	NL28193.068.09