A Randomized, Double-Blind, Placebo-Controlled, Multi-Center Phase 3 Study of Denosumab as Adjuvant Treatment for Women with Early-Stage Breast Cancer at High Risk of Recurrence

Published: 04-06-2010
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The purpose of this research study is to evaluate how safe and effective Denosumab is, compared with placebo, in delaying the time it takes for cancer to spread to the bones in subjects with early-stage breast cancer at high risk of recurrence.The...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON44657

Source
ToetsingOnline

Brief title
D-CARE

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breastcancer, Mamma carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Adjuvant Treatment, Breast Cancer, Denosumab, Placebo-Controlled

Outcome measures

Primary outcome

To compare the treatment effect of denosumab with that of placebo on prolonging

bone metastasis-free survival (BMFS) in subjects with early-stage breast cancer

at high risk of recurrence

Secondary outcome

To compare the treatment effect of denosumab with that of placebo on:

* Disease-free survival (DFS) in the full study population

* DFS in the post-menopausal subset

* Overall survival (OS)

* Distant recurrence-free survival (DRFS)

Study description

Background summary

The purpose of this research study is to evaluate how safe and effective Denosumab is, compared with placebo, in delaying the time it takes for cancer to spread to the bones in subjects with early-stage breast cancer at high risk of recurrence.
The investigational drug that will be tested in this study is called Denosumab. We are testing if Denosumab, a protein, that might stop cancer from getting worse or spreading to bones. It is given as an injection under the skin.
Denosumab is an investigational product, which means that it has not been

approved by an appropriate regulatory agency.
The Patient will have a 1 in 2 (50:50) chance of receiving Denosumab, like flipping a coin. The change of receiving placebo is 1 in 2.
Approximately 250 people will take part in this study in The Netherlands. In total, 4500 people will take part in this study in North and South America, Australia, Europe, and Asia.

Study objective

The purpose of this research study is to evaluate how safe and effective Denosumab is, compared with placebo, in delaying the time it takes for cancer to spread to the bones in subjects with early-stage breast cancer at high risk of recurrence.
The study is also designed to collect more information about the safety of the drug.

Study design

This study exist of a screening period, a treatment period, a follow-up visit and a long-term follow up period.
The treatment visits will occur every 3 to 4 weeks, depending on the treatment which the patient receives.
These visits will take place till the disease progresses or till 5 years of treatment. After that the follow-up visit will take place. The subject will be followed every 3 or 6 months (by visit or by phone) during the long term follow-up period till the study has been completed (about 10 years).
After all participants in this study have finished their 5 years of treatment, the long-term follow up schedule will switch to once every 6 months for everyone, and there will no longer be annual imaging visits. From that moment, study staff will check the patients health status every 6 months and all other assessments for the study will stop. The study staff will let the patient know when this switch occurs.
The subject will be randomly selected to receive Denosumab or placebo.

Intervention

Patients are requested to fill out questionnaires about their general health.
Subcutaneous injections with Denosumab or placebo.
Yearly scans, mammography (after all participants in this study have finished their 5 years of treatment, there will no longer be annual imaging visits.)

Study burden and risks

Review of medical and medication history
Physical examination (including inside of the mouth)
Bone scan, computed tomography (or CT) and/or magnetic resonance imaging (or

MRI), and mammography
Vital signs (temperature, pulse, blood pressure and respiration)
Serum chemistry tests
Health surveys (questionnaires)
Review of current disease and comedications
Subcutaneous injection with Denosumab or placebo

Contacts

Public
Amgen

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Breda 4817 ZK
NL
Scientific
Amgen

Minervum 7061
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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Disease related;* Histologically confirmed, AJCC stage II or III breast cancer;See Appendix D of protocol for breast cancer grading and staging information.;* High risk of breast cancer recurrence, defined as documented evidence of one or more of the following criteria: ;- Biopsy evidence of breast cancer in regional lymph node(s) (LN) (node-positive disease);Nodal micrometastases only are not considered node positive;- Tumor size > 5 cm or locally advanced disease (T4);See Appendix D of protocol for breast cancer grading and staging information.;* Documented pathological evaluation of the breast cancer for hormone receptor (estrogen receptor [ER] and progesterone receptor [PR]) status and HER-2 status;* Subjects must be receiving or be scheduled to receive standard of care systemic adjuvant or neoadjuvant chemotherapy and/or endocrine therapy and/or HER-2 targeted therapy ;* For subjects receiving adjuvant therapy only: ;- Subjects must have undergone complete resection of the primary tumor with clean surgical margins, or;- Subjects must have undergone resection of the primary tumor and be scheduled for further treatment of the primary tumor with curative intent. Definitive treatment must be planned to be completed within approximately 9 months of randomization;- Time between definitive surgery and randomization must be * 12 weeks;Definitive surgery may include secondary interventions (e.g. to clear inadequate surgical margins);- Subjects with node positive disease must have undergone radical treatment of axillary LN with curative intent, or;Subjects must be scheduled for further treatment of regional lymph nodes with curative intent. Definitive treatment must be planned to be completed within approximately 9 months of randomization ;- Subjects must not have received prior neoadjuvant treatment;Endocrine treatment for less than 30 days prior to surgery is not;considered prior neoadjuvant treatment;* For subjects receiving neoadjuvant therapy only: ;- Time between start of neoadjuvant treatment and randomization must be * 8 weeks;- Subjects must be scheduled to undergo definitive treatment (including surgery and/or radiotherapy) with curative intent within approximately 9 months of starting neoadjuvant treatment;Demographic;* Female subjects with age * 18 years ;Laboratory;* Subjects with reproductive potential must have a negative pregnancy test within 14 days before randomization ;* Serum calcium or albumin-adjusted serum calcium * 2.0 mmol/L (8.0 mg/dL) and * 2.9 mmol/L (11.5 mg/dL) ;General;* Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 ;* Written informed consent before any study-specific procedure is performed

Exclusion criteria

Disease related;* Prior or current evidence of any metastatic involvement of any distant site ;* History of breast cancer (other than ductal carcinoma in situ [DCIS] or lobular carcinoma in situ [LCIS]) prior to the current diagnosis ;Medical Conditions;* Osteoporosis requiring treatment at the time of randomization or treatment considered likely to become necessary within the subsequent six months ;* Any prior or synchronous malignancy (other than breast cancer), except:;- Malignancy treated with curative intent and with no evidence of disease for * 5 years prior to enrollment and considered to be at low risk for recurrence by the treating physician;- Adequately treated non-melanoma skin cancer or lentigo maligna without

evidence of disease ;* Active infection with Hepatitis B virus or Hepatitis C virus ;* Known infection with human immunodeficiency virus (HIV) ;Oral/ Dental Conditions;* Prior history or current evidence of osteomyelitis/osteonecrosis of the jaw ;* Active dental or jaw condition which requires oral surgery ;* Planned invasive dental procedure for the course of the study ;* Non-healed dental or oral surgery ;Medications/ Treatments;* Use of oral bisphosphonates within the past 1 year ;* Prior or current IV bisphosphonate administration ;* Prior administration of denosumab ;* Subject currently is enrolled in or has not yet completed at least 30 days since ending other investigational device or investigational drug study(s), or subject is receiving other investigational agent(s) ;General;* Subject is pregnant or breast feeding, or planning to become pregnant within 5 months after the end of treatment. ;* Subject is of child bearing potential and is not willing to use, in combination with her partner, 2 highly effective methods of contraception or abstinence during treatment and for 5 months after the end of treatment ;* Subject has known sensitivity to any of the products to be administered during the study (e.g., mammalian derived products, calcium, or vitamin D) ;* Subject has any kind of disorder that compromises the ability of the subject to give written informed consent and/or to comply with study procedures. ;* Any major medical or psychiatric disorder that in the opinion of the investigator might prevent the subject from completing the study or interfere with the interpretation of the study results

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2011
Enrollment:	75
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	XGEVA
Generic name:	Denosumab

Ethics review

Approved WMO Date:	04-06-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	21-10-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	07-01-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-02-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	01-03-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	29-03-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	01-04-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	16-05-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	14-07-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	19-07-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	28-07-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	09-08-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	15-08-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	26-09-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	06-10-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	11-10-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	17-11-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	12-12-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	13-02-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	21-02-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	13-03-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	06-06-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	12-06-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	22-06-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	29-01-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	21-02-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	06-06-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 07-06-2013

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 12-05-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 19-05-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 31-07-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 08-08-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 06-02-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	20-02-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	06-03-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	26-03-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	13-05-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	19-05-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	20-05-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	26-05-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	01-07-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	09-07-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	23-09-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	11-04-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	26-04-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	12-08-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	18-11-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	17-02-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	13-03-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	12-07-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	04-08-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	23-08-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	25-08-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	04-09-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	13-12-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	08-01-2018
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	EUCTR2009-011299-32-NL
ClinicalTrials.gov	NCT01077154
CCMO	NL32491.098.10