# A Multicenter, International, Randomized, Double-blind, Alendronate-controlled Study to Determine the Efficacy and Safety of Romosozumab in the Treatment of Postmenopausal Women With Osteoporosis

Published: 13-06-2012
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To assess the effect of AMG785 treatment for 12 months followed by alendronate treatment compared with alendronate on the incidence of clinical fracture and new vertebral fracture.

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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-OMON43694

**Source**
ToetsingOnline

**Brief title**
ARCH - 20110142 / AMG785 / Romosozumab

### 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:** Alendronate, AMG785/Romosozumab, Osteoporosis, Postmenopausal

## Outcome measures

### Primary outcome

For the primary analysis periode:

- To assess the effect of AMG 785 treatment for 12 months followed by ALN treatment compared with ALN treatment alone on the subject incidence of clinical fracture (nonvertebral fracture and clinical vertebral fracture) in women with PMO;

- To assess the effect of AMG 785 treatment for 12 months followed by ALN treatment compared with ALN treatment alone on the subject incidence of new vertebral fracture in women with PMO.

### Secondary outcome

For the primary analysis periode:

To assess the effect of AMG 785 treatment for 12 months followed by ALN treatment compared with ALN treatment alone on:

- Subject incidence of fractures (all fractures [nonvertebral fractures and new vertebral fractures], new or worsening vertebral fracture, nonvertebral fracture, major nonvertebral fracture [pelvis, distal femur, proximal tibia, ribs, proximal humerus, forearm, and hip], hip fracture, multiple new or worsening vertebral fracture and clinical vertebral fracture)

- Percent changes in Dual energy X-ray Absorptiometry (DXA) bone mineral density (BMD) at the lumbar spine, total hip, and femoral neck

2) For the 12-month double-blind ALN-controlled study period

To assess the effect of AMG 785 treatment for 12 months compared with ALN treatment on:

- Subject incidence of fractures (clinical fracture [nonvertebral fracture and clinical vertebral fracture], new vertebral fracture, all fractures [nonvertebral fractures and new vertebral fractures], nonvertebral fracture, hip fracture, clinical vertebral fracture, and major osteoporotic fracture [hip, forearm, humerus, and clinical vertebral])
- Percent changes in DXA BMD at the lumbar spine, total hip, and femoral neck

3) For the overall study (randomization to end of study):

- To assess the effect of AMG 785 treatment for 12 months followed by ALN treatment compared with ALN treatment alone on subject incidence of hip fracture, major nonvertebral fracture [pelvis, distal femur, proximal tibia, ribs, proximal humerus, forearm, and hip], and nonvertebral fractures

# Study description

**Background summary**

Osteoporosis is a chronic disease and despite long-term administration of bisphosphonates, patients with severe PMO remain at increased risk of fracture and are in need of therapies with strong efficacy and the potential to reverse their disease condition by increasing bone formation and improving bone

structure. Approved treatments for PMO include inhibitors of bone resorption such as selective estrogen receptor modulators (SERMs, eg, raloxifene), bisphosphonates (eg, ALN, risedronate, ibandronate, and zoledronate), calcitonin, denosumab, or agents that stimulate bone formation like teriparatide. A novel bone forming agent for the treatment of PMO, with a different mechanism of action and the potential to reverse the features of PMO by increasing bone volume and BMD and by improving bone architecture, ultimately resulting in increased bone strength and reduced risk for fracture, would be a welcome new therapeutic option particularly for subjects with significantly compromised bone strength at high risk of fracture. AMG 785 is a humanized monoclonal antibody that is designed to bind and inhibit sclerostin, thereby promoting osteoblast differentiation and activity, leading to an increase in bone formation, BMD, and bone strength.

**Study objective**

To assess the effect of AMG785 treatment for 12 months followed by alendronate treatment compared with alendronate on the incidence of clinical fracture and new vertebral fracture.

**Study design**

The study consists of three parts. The first part will be acrried out to define if the patient is eligible for the study (screening). The second part is the research/study phase which will take 12 months. During this phase (and after a positive screening outcome), patients will be randomzied (ratio 1:1) into one of the two study arms:

1. AMG785, subcutane injection, 210 mg, every month + placebo for oral alendronate, 70 mg, every week
2. Alendronate, oral, 70 mg, every week + placebo for AMG785, subcutane injection, 210 mg, every month

During the study phase, patients receive daily calcium- and vitamin D supplements.

the third part is the open label phase in which patients recieve alendronate for at least 12 months. During this phase patients will visit the hospital but will also be followed up by phone calls. The complete study will take 25-71 months.

In total, 4095 patients in 325 hospitals wordwide were randomized. None of the sites in the Netherlands will participate in the PK/BTM substudy.

**Intervention**

Patients will receive AMG785, subcutane injection, 210 mg, every month +

placebo for oral alendronate, 70 mg, every week or alendronate, oral, 70 mg, every week + placebo for AMG785, subcutane injection, 210 mg, every month.

**Study burden and risks**

The following procedures will be performed according to appendix A (schedule of assessments) of the protocol: physical examination, vital signs, blood sampling. DXA scans (femur and spine) will be performed at 7 visits and X-rays of the spine will be carried out at 8 visits. Questionnaires need to be completed at 7 visits.

Patients need to come to the hospital for 14 times during the first 12 months , every 3 months during the next half year and every 6 months therafter untill the end of the study. There will be phone call visits during the study duration.

For adverse events of AMG785, please see question E9.

# Contacts

**Public**
Amgen

Minervum 7061
Breda 4800DH
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

- Ambulatory postmenopausal women, age * 55 to * 90 years
- Subject meets at least one of the following BMD and fracture criteria
* BMD T-score * -2.50 at the total hip or femoral neck (as assessed by the central imaging vendor based on DXA scans and using data for Caucasian women from the National Health and Nutritional Examination Survey (NHANES) 1998) AND EITHER at least one moderate (SQ2) or severe (SQ3) vertebral fracture OR at least 2 mild (SQ1) vertebral fractures
OR
* BMD T-score * -2.00 at the total hip or femoral neck AND EITHER at least 2 moderate (SQ2) or severe (SQ3) vertebral fractures OR a fracture of the proximal femur.
Refer to Sections 7.13 and 7.14 for details.
- At least one hip is evaluable by DXA, as assessed by the principal investigator
- Subject has provided informed consent

## Exclusion criteria

- Use of the following agents affecting bone metabolism (4.2.1 through 4.2.9):
* Strontium ranelate, or fluoride (for osteoporosis): more than 1 month of cumulative use within 5 years prior to randomization
* Intravenous (IV) bisphosphonates
o Zoledronic acid: any dose received within 3 years prior to randomization
o more than 1 dose received within 5 years prior to randomization
* IV ibandronate or IV pamidronate:
o any dose received within 12 months prior to randomization
o more than 3 years of cumulative use, unless last dose received * 5 years prior to randomization
* Oral bisphosphonates:
o any dose received within 3 months prior to randomization
o more than 1 month of cumulative use between 3 and 12 months prior to randomization
o more than 3 years of cumulative use, unless last dose received * 5 years prior to randomization
* Denosumab or any cathepsin K inhibitor, such as odanacatib (MK-0822): any dose received within 18 months prior to randomization
* Teriparatide or any PTH analogs:
o any dose received within 3 months prior to randomization
o more than 1 month of cumulative use between 3 and 12 months prior to randomization
* Systemic oral or transdermal estrogen or SERMs: more than 1 month of cumulative use within 6 months prior to randomization
* Hormonal ablation therapy: more than 1 month of cumulative use within 6 months prior to

randomization
* Tibolone, cinacalcet, or calcitonin: any dose received within 3 months prior to randomization
* Systemic glucocorticosteroids: * 5 mg prednisone equivalent per day for more than 14 days within 3 months prior to randomization;- History of metabolic or bone disease (except osteoporosis) that may interfere with the interpretation of the results, such as sclerosteosis, Paget*s disease, osteomalacia, osteogenesis imperfecta, osteopetrosis, ankylosing spondylitis, Cushing*s disease, hyperprolactinemia, and malabsorption syndrome;
- History of solid organ or bone marrow transplants;
- Current hyper- or hypocalcemia, defined as albumin-adjusted serum calcium outside the normal range, as assessed by the central laboratory;
- Current, uncontrolled hyper- or hypothyroidism, per subject report or chart review. Uncontrolled hyperthyroidism is defined as TSH and T4 outside the normal range. Uncontrolled hypothyroidism is defined as TSH > 10;
- Current, uncontrolled hyperparathyroidism or history of hypoparathyroidism, per subject report or chart review. Uncontrolled hyperparathyroidism is defined as: PTH outside the normal range in subjects with concurrent hypercalcemia; or PTH values > 20% above the upper limit of normal in normocalcemic subjects;
- Possible diagnosis of multiple myeloma or related lymphoproliferative disorder, as assessed by serum protein electrophoresis performed by the local laboratory (electrophoresis results within 6 months prior to signing consent will be acceptable);
- Exclusion criteria related to contraindications or possible signs of intolerance to ALN (see protocol section 4.2.17)
- General exclusion criteria as described in protocol section 4.2.18

# Study design

## Design

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

## Recruitment

NL
Recruitment status: Recruitment stopped

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|---|---|
| Start date (anticipated): | 06-11-2012 |
| Enrollment: | 25 |
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Fosamax |
| Generic name: | Alendronate |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Onbekend |
| Generic name: | Romosozumab |

## Ethics review

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| Approved WMO Date: | 13-06-2012 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 08-08-2012 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 26-02-2013 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 08-03-2013 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO | |

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| Date: | 09-07-2013 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 22-08-2013 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 30-08-2013 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 16-12-2013 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 17-01-2014 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 25-02-2014 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 13-03-2014 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 31-07-2014 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek |

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| | (Assen) |
| Approved WMO Date: | 14-11-2014 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 06-03-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 27-05-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 28-10-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 12-11-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 25-02-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 06-04-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 13-12-2016 |

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| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 22-12-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |

# 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 | EUCTR2011-003142-41-NL |
| ClinicalTrials.gov | NCT01631214 |
| CCMO | NL39710.056.12 |