A Multi-center, Randomized, Double-blind, Placebo-controlled Study to Determine the Efficacy, Safety, and Tolerability of AMG 785 in Adults with Fresh Unilateral Hip Fracture, Status Post Surgical Fixation

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To investigate the effect of AMG 785 compared to placebo on functionalhealing as measured by the timed-up-and-go test (TUG) over Weeks 6 through 20 in subjectswith fresh unilateral low energetic hip (intertrochanteric or femoral neck) fracture

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

Summary

ID

NL-OMON36359

Source
ToetsingOnline

Brief title
Assessing healing itc hip fractures w Sclerostin Antibody

Condition

- Other condition

Synonym
bone growth stimulation, Fracture healing

Health condition

Fractuurgenezing

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AMG 785, Fracture healing, Hip Fracture, Sclerostin antibody

Outcome measures

Primary outcome

To investigate the effect of AMG 785 compared to placebo on functional healing

as

measured by the timed-up-and-go test (TUG) over Weeks 6 through 20 in subjects

with

fresh unilateral low energetic hip (intertrochanteric or femoral neck) fracture

(refer to

Appendix F for description of TUG procedure).

Secondary outcome

To investigate the effect of AMG 785 compared to placebo on:

• TUG by visit

• Time to radiographic healing

• Harris Hip Score

• Pain as a result of the hip fracture as assessed by the Visual Analog Scale

(VAS)

Study description

Background summary

In this study, the effect will be investigated of the experimental AMG-785 compared to placebo on functional healing as measured by the timed-up-and-go test (TUG) over Weeks 6 through 20 in subjects with a fresh unilateral low energetic hip (intertrochanteric or femoral neck) fracture. AMG 785 is a humanized monoclonal antibody that binds and inhibits sclerostin, thereby promoting osteoblast differentiation and activity leading to an increase in bone formation, bone mineral density and bone strength. AMG 785 might reduce the time needed to stand up out of an armchair and sit down again (measured by the TUD test). Stimulation of bone growth may also reduce complications such as femur shortening, which is common after both intertrochanteric and subtrochanteric fractures. Fracture healing time may be shorter and patients may experience less pain by the hip fracture. AMG 785 has not been registered by a regulatority authority. The number of patients globally will be 330, in The Netherland 60. About 50 to 55 sites globally will participate. There is no registered drug reducing fracture healing time.

Study objective

To investigate the effect of AMG 785 compared to placebo on functional healing as measured by the timed-up-and-go test (TUG) over Weeks 6 through 20 in subjects
with fresh unilateral low energetic hip (intertrochanteric or femoral neck) fracture

Study design

Randomised, doubl-blind, placebo controlled phase 2 study.
The study does consist of 3 phases:
The first phase is the screening phase. At screening, the patient is informed about the study. If the patient does want to participate and the ICF has been signed, it will be verified whether the patient is eligible. If the patient is eligible, the patient will enter the treatmenet phase with AMG785 and/or placebo. The duration of the treatment phase is 52 weeks. 90 Of the 330 patients globally will receive only placebo. One administration consists of 3 sc injections. Each injection is 1 mL. The concentration of AMG 785 in every vial containing AMG 785 is 70 mg/mL. This means only placebo can be administered, 70 mg AMG 785, 140 mg AMG 785 or 210 mg AMG 785. Study medication will be administered on day 1 (within 96 hours after surgery), 2 weeks after

the first injection, 6 weeks after the first injection and 12 weeks after the first injection. Patients must take calcium (at least 1000 mg) and vitamine D (at least 800 IU) daily (until week 36). After surgery and siging the ICF (because this is not a standard proceduere in NL), a vitamine D boost will be administered of at least 50,000 IU (oral or systemic). Calcium and vitamine D will be dispensed by the investigators and reimbursed by Amgen. There will be 11 visits and 3 phone calls in total, includng screenig and a long term follow-up visit at 104 weeks. The first 2 visits will take place during hospitalisation (9 additional visits after discharge). During the long term follow-up visit, only an anteroposterior and lateral X-rays of the proximale femur will be done. During the phone conversations, only the Parker Mobility Score will be assessed.

Intervention

240 Patients globally will receive 3 dosis of either 70 mg AMG 785, 140 mg AMG 785 or 210 mg AMG 785, if the patient will finish the study.

Study burden and risks

During the hospitalization for the hip (intertrochanteric or femoral neck) fracture, screeing and day 1 will be done. After screening, the patient should visit the hospital for another 9 times. The average estimated duration of every visit is 1-2 hours (week 104 will take less time). During weeks 8,10 and 14 the patient will be called to assess the Parker Mobility Score. The riscs for the participating patient are minimal. The sc injections with AMG 785 or placebo and the blood collections may involve some risks. But, administration of medication and blood collections will only be done by trained and experienced personnel; the involved risks will there fore be minimized. In total, 22 X-rays [(2 X-rays per visit and at screening 2 times 2 X-rays (pre and post fracture fixation)] will be done. In addition, only for the participants in the participating in the PK/PD and DXA sub study, 3 DXA scans of the lumbal spine and proximal femur (wk 8, 16 and 52) will be done. The subpopulation will consist of 40 patients per treatment arm (160 patients in total). The radiation exposure will be minimal; approximately 1.6 and 0.4 mSv per X-ray and DXA scan, respectively. AMG 785 is an experimental drug. The patient could may experience side effects as mentioned in the answer to question E9; in addition, the patient also may experience side effects which are unknow at this moment. The patients recieving AMG 785 may benefit from the treatment, which may result in reduced time needed to stand up out of an armchair and sit down again (measured by the TUG test). Stimulation of bone growth may also reduce complications such as femur shortening, which is common after both intertrochanteric and subtrochanteric fractures. Fracture healing time may be shorter and patient may experience less pain by the hip fracture.

Contacts

Public
Amgen

Minervum 7061
4817 ZK Breda
NL
Scientific
Amgen

Minervum 7061
4817 ZK Breda
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Adult women or men, age >= 55 to <= 95 years at randomization
-Fresh unilateral low energy intertrochanteric or femoral neck fractures as the primary injury, confirmed by X-ray and in the opinion of the treating surgeon amenable to repair by internal fixation
-Intertrochanteric fractures eligible for this study must have at least two displaced fractures
-Internal fixation of the fracture with devices approved by local regulatory agency, performed no later than 7 days after injury for intertrochanteric or undisplaced femoral neck fractures and no later than 2 days after injury for displaced femoral neck fractures
•ntertrochanteric fracture: sliding hip screw or intermedullary nail
•femoral neck fracture: sliding hip screw or at least three cancellous screws
-Pre- and postoperative care performed as defined in Appendix J in the protocol

-Subject or subject's legally acceptable representative has provided informed consent

Exclusion criteria

Conditions that may affect the ability to perform functional or clinical assessments required by the protocol, such as:
• Severe symptomatic osteoarthritis of the lower extremity
• Inability to independently rise from armchair or walk 200 meters before hip fracture (use of unilateral assistive device or rolling walker is acceptable)
• Cognitive deficit, as defined by Mini-Mental Status Examination score < 22 at time of randomization
• Symptomatic neurological conditions such as Parkinson*s disease or persistent gross motor or sensory deficits such as hemiparesis or hemiplegia
• Presence of concomitant injuries such as rib fractures, wrist fractures, or acute symptomatic vertebral fractures which severely impair the ability to rise from a chair
• Associated extremity injuries including ipsilateral or contralateral fractures of the foot, tibia or fibula, wrist, humerus, femoral shaft, femoral head or hip dislocation, that may delay weight-bearing beyond one week after surgery
-Use of bone grafts or bone substitutes at the time of fracture fixation
-Head-injury, as defined by Glasgow Coma Scale <13 prior to randomization
-Major polytrauma or significant axial trauma, with Injury Severity Score > 16
-Pathological fracture or history of metabolic or bone disease that may interfere with the interpretation of the results, such as Paget*s disease, rheumatoid arthritis, osteomalacia, osteopetrosis, ankylosing spondylitis, Cushing*s disease, hyperprolactinemia
-History of symptomatic spinal stenosis that has not been surgically corrected. If surgically corrected, the subject must be asymtomatic to be eligible for the study
-History of facial nerve paralysis
-Malignancy (except fully resected cutaneous basal cell or squamous cell carcinoma, cervical carcinoma in situ) within the last 5 years
-Severe asthma or severe chronic obstructive pulmonary disease or recent exacerbation
-Myocardial infarction or unstable angina pectoris within the last 12 months
-Current alcohol dependence-
-History of solid organ or bone marrow transplants
-hypocalcemia or hypercalcemia, outside of 1.1 x the normal range set by the local laboratory
-Use of the following agents affecting bone metabolism
•Within the past 12 months: parathyroid hormone, strontium, fluoride (for osteoporosis)
•Within the past 6 months: IV bisphosphonates, denosumab, odanacatib (MK-0822)
•WIthin the past 3 months: calcitonin, tibolone, cinacalcet, systemic glucocorticosteroids (>=5 mg prednisone equivalent per day for more than 10 days)
-BMP-2 or BMP-7 at the time of definitive fracture fixation
-Subjects to be enrolled in DXA sub-study may not have had previous instrumentation with implants (ie, nails, screws, pins, plates) to either hip or lower spine

-Subject has known sensitivity to any of the products to be administered (calcium supplements, vitamin D products, or mammalian cell derived products)

Study design

Design

Study phase:	2
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):	08-02-2011
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AMG 785
Generic name:	Nog niet beschikbaar

Ethics review

Approved WMO

Date:	18-05-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	02-12-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-07-2011
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-11-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-12-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-07-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-08-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-04-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	09-04-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2009-015939-33-NL
ClinicalTrials.gov	NCT01081678
CCMO	NL31032.100.09