A Multi-center, Randomized, Double-blind, Placebo-controlled Study of AMG 785 in Skeletally Mature Adults with a Fresh Unilateral Tibial Diaphyseal Fracture Status Post Definitive Fracture Fixation with an Intramedullary Nail.

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To investigate the effect of AMG 785 compared to placebo on time to radiographic healing of fresh tibial diaphyseal fractures.

Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON32518

Source
ToetsingOnline

Brief title
Study to Assess Healing of Repaired Tibias with Sclerostin Antibody

Condition

- Other condition

Synonym
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, Sclerostin antibody, Tibial Fracture

Outcome measures

Primary outcome

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

radiographic healing of fresh tibial diaphyseal fractures.

Secondary outcome

To evaluate the effect of AMG 785 compared to placebo on

(1) Physical functioning as measured by Short Form (36) Health Survey Physical

Functioning subscale (SF-36 PF)

(2) Incidence of unplanned revision surgery

(3) Time to clinical healing as determined by the ability to bear weight on the

fractured limb and the absence of pain at the fracture site

Study description

Background summary

In this study, the experimental AMG 785 will be investigated in tibial diaphyseal fracture healing time, compared to placebo. AMG 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 fracture healing time, result is less pain at the fracture site and result in

an earlier start of the work the patient did before the accident resulitng in the tibiala fracture. AMG 785 has not been registered by a regulatority authority. The number of patients globally will be 400, in The Netherland 5. About 60 to 80 sites globally will participate in North America, Europe, Africa and Asia-Pacific. There is no registered drug reducing fracture healing time.

Study objective

To investigate the effect of AMG 785 compared to placebo on time to radiographic healing of fresh tibial diaphyseal fractures.

Study design

Randomised, doubl-blind, placebo controlled phase 2a 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 does fulfill all inclusion criteria and does not fulfil any of the exclusion criteria. If the patient does fulfil all criteria, the patient will enter the treatmenet phase with AMG785 and/or placebo. The duration of the treatment phase is 52 weeks. 100 Of the 400 patients globally will receive only placebo. All other patients will receive 4, 3 or 2 AMG 785 administrations and placebo on other days study medication must be administered. One administration does consist 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. See schedule on page 29 of the protocol. 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. Calcium and vitamine D will be dispensed by the investigators and reimbursed by Amgen. There will be 18 visits in total. includng screenig and a long term follow-up visit at 104 weeks. During the long term follow-up visit, only an anteroposterior and lateral X-rays of the tibia will be done.

Intervention

360 Patients globally will receive al least 2 dosis of AMG 785 (see "study design", if the patient will finish the study.

Study burden and risks

During the hospitalization for the tibia diaphyseal fracture, screeing will be done. After screening, the patient should visit the hospital for another 17 times (except if the visit does need to take place on a day the patient is

still hospitalised). The average estimated duration of every visit is 1 hour (week 104 will take less time). 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 study medication and blood collections will only be done by trained and experienced personnell; the involved risks will there fore be minimized. In total, 38 X-rays [(2 X-rays per visit and at screening 2 times 2 X-rays (pre and post fracture fixation)] and 1 DXA scan will be done. The radiation exposure will be minimal; approximately 0.001 mSv per X-ray/DXA scan, this is less then the back ground radiation people recieve on average on one day. 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 a decreased fracture healing time and less pain at the fracture site. In addition, patients receiving AMG 785 may resume earlier their work they did before the accident resulitng in the tibia diaphyseal fracture.

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

-Skeletally mature adults, age <= 18 to >= 85 years at randomization, with radiographically closed growth plates
-Fresh unilateral closed or Gustilo type I or type II open tibia diaphyseal fracture (fracture line must not extend into the ankle or knee joint) as the primary injury
-For closed fractures: Definitive fracture fixation with reamed IM nailing (modern, statically, interlocking nail) performed no later than 14 days after injury
-For Gustilo type I/II open fractures: Definitive fracture fixation with reamed or unreamed IM nailing (modern, statically, interlocking nail) performed no later than 24 hours after injury

Exclusion criteria

-Major polytrauma or significant axial trauma, with injury severity score >16
-Head-injury, as defined by Glasgow Coma Scale <13 at time of randomization
-Use of bone grafts at the time of definitive fracture fixation
-History of pathological fracture or metabolic or bone disease that may interfere with the interpretation of the results, such as Paget*s disease, rheumatoid arthritis, osteomalacia, osteogenesis imperfecta, osteopetrosis, ankylosing spondylitis, Cushing*s disease, hyperprolactinemia
-History of spinal stenosis
-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
-History of solid organ or bone marrow transplants
-Use of the following agents affecting bone metabolism:
•Intravenous bisphosphonates at any time
•Denosumab at any time
•Fluoride (for osteoporosis) within the past 24 months
•Oral bisphosphonates, parathyroid hormone or strontium within the past 12 months
•Calcitonin, selective estrogen receptor modulators, systemic oral or transdermal estrogen within the past three months (estrogen containing contraceptive therapy is permitted)
•Systemic glucocorticosteroids (* 5 mg prednisone equivalent per day for more than 10 days) within the past three months
•Tibolone within the past three months
•BMP-2 or BMP-7 at the time of definitive fracture fixation
-Current use of anticoagulants (doses for deep vein thrombosis prophylaxis are permitted

-•Known intolerance to calcium supplements or vitamin D 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:	Will not start
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine

Ethics review

Approved WMO

Date:	27-11-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Not approved

Date:	11-03-2010
Application type:	First submission
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	EUCTR2008-008392-34-NL
ClinicalTrials.gov	NCT00907296
CCMO	NL30666.100.09