A Phase III Randomized, Placebo-Controlled Clinical Trial to Assess the Safety and Efficacy of Odanacatib (MK-0822) to reduce the Risk of Fracture in Osteoporotic Men Treated with Vitamin D and Calcium

Published: 22-07-2010
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1. To assess the effect of odanacatib 50 mg once weekly versus placebo on lumbar spine BMD over 24 months.2. To assess the safety and tolerability of odanacatib 50 mg once weekly compared to placebo.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine disorders of gonadal function
Study type	Interventional

Summary

ID

NL-OMON38208

Source
ToetsingOnline

Brief title
MK0822-053

Condition

- Endocrine disorders of gonadal function
- Fractures

Synonym
osteoporosis

Research involving
Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: Merck Sharp & Dohme BV

Intervention

Keyword: hypogonadism, idiopathic, men, osteoporosis

Outcome measures

Primary outcome

The primary endpoint in this study is the percent change from baseline in BMD

at the lumbar spine over 24 months.

Secondary outcome

(1) Total hip, femoral neck, and trochanter BMD over 24 months.

(2) Biochemical indices of bone resorption (serum C-Telopeptides of Type 1

collagen [s-CTx] and urine N-Telopeptides of Type 1 collagen [u-NTx]) over 24

months.

(3) Lumbar spine, total hip, femoral neck, and trochanter BMD over 24 months.

Study description

Background summary

Osteoporosis in men is a common and important clinical problem that is associated with significant morbidity, mortality and societal expense. Between 20% and 25% of all osteoporotic patients are men, with number estimates at 2 million in the US (vs. 8 million women), 3 million in the EU and approximately

20 million worldwide (vs. 80 million women). As a result, approximately 20% of all vertebral fractures and up to 30% of all hip fractures occur in men. Men who experience hip fractures are on average 10 years older than their female counterparts, reflecting the higher peak bone mass and relatively lower rate of aging-related bone loss in men. Because of their older age and associated co-morbidities, these men are also at greater risk of death following a hip fracture, with a 1-year mortality rate of 31% vs. 17% in women.
There are different causes of osteoporosis in men, and secondary osteoporosis is much more frequent than in women. Generally, there is evidence of increased osteoclast-mediated bone resorption, although resorption markers are typically not as elevated as in postmenopausal osteoporotic women. However, impaired bone formation is thought to play an important role in idiopathic osteoporosis, and histomorphometry often reveals a predominance of trabecular thinning (evidence of impaired bone formation) over trabecular perforation (resulting from osteoclast activity), which prevails in osteoporotic postmenopausal women. Odanacatib has a high likelihood of being effective in men with osteoporosis due to its bone formation sparing anti-resorptive effects.

Study objective

1. To assess the effect of odanacatib 50 mg once weekly versus placebo on lumbar spine BMD over 24 months.
2. To assess the safety and tolerability of odanacatib 50 mg once weekly compared to placebo.

Study design

This is a randomized, double-blind, placebo-controlled, 24-month study, to assess the effect of treatment with odanacatib 50 mg once weekly on lumbar spine, hip (total and sub-regions), total body, and distal forearm bone mineral density (BMD) as well as on biochemical markers of bone turnover in men with osteoporosis. The primary analysis for these endpoints will occur after 24 months of treatment. Approximately 266 men, between 40 and 95 years of age, who have low BMD (T-score * -2.5 without a prior vertebral fracture or T-score * -1.5 with a prior vertebral fracture) at the lumbar spine or the total hip, or hip subregions (femoral neck or trochanter) will be randomized to receive either odanacatib 50 mg once weekly or placebo for 24 months. All study patients will receive vitamin D3 5600 IU once weekly and daily calcium supplementation as needed, to ensure a total daily calcium intake of at least 1200 mg.

Intervention

Patients will receive either odanacatib 50 mg once weekly or placebo and open label vitamin D3 5600 IU once weekly. Patients will also receive a sufficient supply of open-label daily calcium supplement of 500 mg, supplied as calcium

carbonate, so that their total daily calcium intake (from both dietary and supplemental sources) is at least 1200 mg.

Study burden and risks

See answer to question E9.

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

1) Patient is a man between 40 and 95 years of age on the day of Randomization.
2) Patient has idiopathic osteoporosis or osteoporosis due to hypogonadism and fulfills one of the following criteria:

a) Patient is a candidate for osteoporosis therapy and has BMD T-score * -2.5 at either the lumbar spine or the total hip or any hip subregion (femoral neck or trochanter) and a BMD T-score * -4.0 at all sites, and does not have a prior vertebral fracture (defined as anterior, mid or posterior height loss of >20%).* OR
b) Patient is a candidate for osteoporosis therapy and has BMD T-score * -1.5 at either the lumbar spine or the total hip or any hip subregion (femoral neck or trochanter) and a BMD T-score * -4.0 at all sites, and has one prior vertebral fracture *OR
c) Patient is not a suitable candidate for, or has declined osteoporosis therapy and has BMD T-score * -2.5 at either the lumbar spine or the total hip or any hip subregion (femoral neck or trochanter) and does not have a prior vertebral fracture; or has BMD T-score * -1.5 at either the lumbar spine or the total hip or any hip subregion (femoral neck or trochanter), and has at least one prior vertebral fracture.
Note: For the purpose of study inclusion, a patient may not be a suitable candidate for osteoporosis therapy, due to contraindication, established intolerance, physician*s judgment, or patient*s unwillingness. T-scores should be determined using male normative data. Only the T-scores provided by the central imaging vendor can be used to determine eligibility. Locally determined T-scores can be used to exclude patients, however, scans with borderline exclusionary T-score values should be submitted to the central imaging vendor for analysis.
Note: Eligibility for this criterion is based on the absolute BMD thresholds for male T-scores that are detailed in the central imaging vendor manual.
3) Patient has lumbar spine anatomy suitable for DXA. Specifically, at least 2 vertebral bodies in the L1 to L4 region must be assessable (patient must not have significant sclerosis, degenerative joint disease, bony trauma, and sequelae or hardware from orthopedic procedures). Note, lumbar spine BMD values will be calculated from the average of all evaluable vertebrae, with a minimum requirement for 2. At the hip, at least one femoral neck site must be evaluable by DXA assessment without any sequalae or hardware from orthopedic procedures.
4) Patient understands the study procedures, alternative treatments available, risks involved with the study, and voluntarily agrees to participate by giving written informed consent.
5) Patient is ambulatory.
6) Patient is able to read, understand, and complete questionnaires and diaries.
Note: If a patient who understands the purpose and use of the diary cards and study questionnaires is unable to complete these without assistance, (e.g. due to visual problems, difficulty writing due to arthritis, inability to read, etc.) a family member or care-giver may assist or may complete the diary card on his behalf.

Exclusion criteria

1) Patient has chosen treatment with oral bisphosphonate or other agents for the treatment of osteoporosis.
2) Patient has had a prior clinical fragility hip fracture, and is a suitable candidate for osteoporosis therapy (i.e. bisphosphonates, parathyroid hormone (PTH)).
3) Patient has experienced a clinical fragility fracture (including any vertebral fracture) within 12 months, documented by medical record, or detected on the screening spine radiographs read locally, unless the patient is unwilling to take, or is not a candidate for marketed

osteoporosis therapy.
4) Patient has had more than 1 prior vertebral fracture (defined as anterior, mid, or posterior height loss of > 20%) and he is a suitable candidate for osteoporosis therapy (i.e., bisphosphonates or PTH).
5) Patient has or has had evidence of a metabolic bone disorder other than osteoporosis.
6) Patient has vitamin D deficiency, defined as serum 25-hydroxyvitamin D < 15 ng/ml.
If patients with vitamin D deficiency are otherwise eligible for the study, they may be rescreened once following appropriate vitamin D repletion.
7) Patient has a history of renal stones, and serum calcium, serum 25-hydroxyvitamin D and serum PTH are not all within normal limits as measured by the central lab.
8) Patient has active parathyroid disease. (Note: Serum PTH level should be assessed at screening for patients with a documented history of parathyroid disease. Patients with a history of primary hyperparathyroidism and with curative parathyroidectomy >2 years prior to screening are not excluded.)

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):	29-10-2010
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	(Nog niet beschikbaar)

Generic name:	(Nog niet beschikbaar)

Ethics review

Approved WMO Date:	22-07-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-08-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	20-09-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	14-10-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	02-12-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	17-01-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	26-01-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	24-02-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	15-04-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	22-04-2011
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:	17-02-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	17-04-2012
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:	02-08-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	13-08-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2010-0195454-4-NL
CCMO	NL32582.098.10
Other	Zie sectie J