A multi-centre randomised double blind, placebo and active controlled parallel group study to investigate efficacy and safety of ONO-5334 in post menopausal women with osteopenia or osteoporosis.

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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-OMON35369

Source
ToetsingOnline

Brief title
OCEAN

Condition

- Bone disorders (excl congenital and fractures)

Synonym
bone weakness, osteoporosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ONO-5334, osteopenia, osteoporosis, post-menopausal

Outcome measures

Primary outcome

The primary objective of this clinical study is to compare the percentual change in bone density of the lumbar spine between baseline and 12 months following treatment with ONO-5334 or placebo. The objective of the extension study is to investigate the efficacy of ONO-5334 over a longer period.

Secondary outcome

- To compare the effect of ONO-5334 or once weekly Alendronate versus placebo on DXA BMD and BMC and biochemical markers of bone turnover.

- To compare the proportions of responders to ONO-5334 or Alendronate therapy versus placebo.

- To compare the safety and tolerability of ONO-5334 or Alendronate versus placebo.

- To compare compliance with treatment with ONO-5334 or Alendronate versus placebo.

- To compare the efficacy and safety of ONO-5334 versus Alendronate.

- To investigate the efficacy and safety of three different doses of ONO-5334.

Study description

Background summary

Osteoporosis is a systemic disease characterized by a progressive decrease in bone mass due to an imbalance between bone resorption (involving the protein cathepsin K) and bone formation. Bisphosphonates are commonly used for prevention and treatment of osteoporosis, but inhibit not only bone resorption, but also bone formation. If a cathepsin K inhibitor that inhibits bone resorption without affecting bone formation would be available, there is a possibility this would strongly improve bone mass and bone strength. ONO-5334 is a potent and selective cathepsin K inhibitor and has shown suppressive effects on bone resorption, and may have a clinical role in treatment of osteoporosis. The hypothesis of this study is that one or more of the investigational doses of ONO-5334 will result in a relative increase of bone density in the lumbar spine of at least 4% compared with baseline levels.

Study objective

The objective of this study is to investigate if use of ONO-5334 has a more positive effect on bone density and biochemical markers of bone turnover than Alendronate (a bisphosphonate) and placebo.

Study design

This is a double blind, placebo controlled trial, in which patients will receive one out of three dosages of ONO-5334, placebo or Alendronate once weekly after randomisation, for a treatment period of 12 months. During the trial, bone density will be assessed using X-rays of the lumbar spine, DXA BMD and QCT BMD. Additionally, biochemical bone turnover markers will be assessed from blood and urine samples. The extension study reflects an extension of the study with 12 months, to determine long term efficacy of ONO-5334.

Intervention

During the treatment period, the subjects will receive:
either 50 mg ONO-5334, twice daily,
either 100 mg ONO-5334 once daily,
either 300 mg ONO-5334 once daily,
either a weekly dose of Alendronate (Fosamax 70mg Once Weekly)
or placebo, and additionally (for all groups) daily 1000mg Calcium and 800IU Vitamin D as a supplement.

Study burden and risks

- The patients will need to keep a weekly telephone diary
- Patients need to have fasted overnight before the second screening visit and all following study visits (except visits 7 and 9)
- Physical examination at screening, visits 4, 6, 10, Follow Up 1
- ECG at screening, visits 3, 4, 5, 6, 8, 10, Follow Up 1
- Spine X-ray at screening, visit 6, and visit 10
- CT scan of spine and femur at visit 1, 6 and 10 (optional)
- DXA BMD at screening, and visits 3,4, 6, 8, 10
- Drawing of blood samples at screening and all treatment visits except 7 and 9
- Urine sample at screening and all treatment visits except 7 and 9
- Measuring blood pressure and heart rate at screening and visits 3, 4, 5, 6, 8, 10, Follow Up 1

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

- Post-menopausal women aged between 55 and 75 years old
- Osteoporosis defined as a value of DXA BMD 2.5 standard deviations or more below the young adult mean at the lumbar spine or total hip in the absence of any fragility fractures OR
- Osteopenia defined as a value of DXA BMD more than 1 standard deviation below the young adult mean, but less that 2.5 standard deviations below this value at the lumbar spine or total hip with the presence of one or more fragility fractures
- Written informed consent

Exclusion criteria

- Patients with a value of DXA BMD more than 3.5 standard deviation below the young adult mean at the lumbar spine or total hip,
- Patients who have abnormalities of the lumbar spine or femoral neck or internal organs around them precluding the assessment of BMD,
- Patients who have experienced clinical fractures one year prior to the Randomisation visit (visit 1)
- Patients who have secondary causes of osteoporosis
- Patients who have other disorders of bone and mineral metabolism
- Patients for whom once weekly Alendronate treatment is contraindicated
- Patients with a low bone turnover defined as urinary CTX-I below 200 microgramme/mmolCr at the Screening visit
- Patients who have history or presence of other significant disease, which in the opinion of the investigator, might compromise the patient*s safety or the evaluation of the study results
- A history of drug or alcohol abuse
- Patients who have history of malignancy within the past 5 years of the Screening visit.
- Patients with impaired hepatic function
- Patients with impaired renal function
- Any previous use of PTH and its derivatives, Strontium or Fluoride including ones in development before screening visit
- Use of bisphosphonates in the three years preceding screening visit
- Use of HRT, SERMs, Calcitonin, Anabolic Steroid, Thiazides, Vitamin K or any medication that may in the opinion of the investigator have an effect on bone metabolism in the preceding one year or the screening visit
- Use of Antacids, Systemic oral glucocorticiods, high daily dose of inhaled glucocorticoids, Methotrexate, Systemic heparin or Anti-convulsant in the preceding one year of the Screening visit
- Poor medication compliance (<80%)

Patients who have sed any investigational drug and/or participated in any clinical trial within 3 months of the Screening visit

- Patients who have previously received ONO-5334
- In the opinion of the invastigator, the patient may not be able to cooperate fully with the study staff, may have difficulty following some requirements, or is otherwise not qualified for

the study.

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:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2007
Enrollment:	80
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Dronal®
Generic name:	Alendronate

Ethics review

Approved WMO

Date:	17-08-2007
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)

Approved WMO

Date:	21-08-2007
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	20-09-2007
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	18-10-2007
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	22-01-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	26-02-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	29-03-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	31-03-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	14-08-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam

	(Amsterdam)
Approved WMO Date:	24-09-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	04-11-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	06-03-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	10-03-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	02-06-2010
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	17-06-2010
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)

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	EUCTR2007-002417-39-NL
CCMO	NL18017.003.07