Clinical Trial Protocol
Iranian Registry of Clinical Trials

16 Sep 2026

A Phase III, randomized, two armed, parallel, double blind, active controlled, non-inferiority clinical trial to determine the non-inferior therapeutic efficacy and safety between Denosumab (60 mg, produced by AryoGen Pharmed) compared with Prolia® (60 mg, Denosumab, the reference drug, produced by Amgen Company) in improvement of bone mineral densitometry (BMD) among osteoporotic postmenopausal women

Protocol summary

Study aim

Assessment of non-inferiority effect of Denosumab (AryoGen Pharmed) compared with Prolia® (Denosumab, Amgen) in improvement of bone mineral densitometry (BMD) in lumbar spine (L1-L4), femoral neck and total hip among osteoporotic postmenopausal women during 18 months.

Design

190patients with postmenopausal osteoporosis will be investigated via clinical test, bone densitometry, radiological evaluation, and medical examination, after signing the informed consent form, and if She holds all the inclusion criteria, the patient will be given a randomization code and will be allocated to one of the groups in a random fashion.

Settings and conduct

190 patients who fulfill the inclusion criteria will be given a randomization code and will be allocated to one of the two groups of the study receiving either Denosumab (AryoGen Pharmed) or Prolia (Amgen). During 18 months of follow up, each patient will receive 3 injections and will have 9 visits. Investigators, patients, and data analyzers will be unaware of the patient's grouping.

Participants/Inclusion and exclusion criteria

Postmenopausal women aged between 45 up to 75 with T-score equal to or less than -2.5 and equal to or more than -4 in femoral neck, total hip or Lumbar Spine L1-L4, or patients with high risk of fracture on the basis of FRAX criteria who need medicinal treatment according to osteoporosis treatment guidelines.

Intervention groups

Group I: Denosumab (AryoGen Pharmed ™)prefilled syringe (60 mg/ml), SC injection every 6 months Group II: Prolia (Amgen) prefilled syringe (60 mg/ml), SC injection every 6 months.

Main outcome variables

Assessment of the non-inferiority effect of Denosumab (AryoGen Pharmed) compared with Prolia® (Amgen) in the improvement of BMD in lumbar spines (L1-L4), femoral neck and total hip among osteoporotic postmenopausal women during 18 months.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT2017020521315N9**
Registration date: **2017-03-12, 1395/12/22**
Registration timing: **prospective**

Last update: **2018-10-02, 1397/07/10**
Update count: **2**

Registration date

2017-03-12, 1395/12/22

Registrant information

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Name of organization / entity

Orchid Pharmed

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Recruitment status

Recruitment complete

Funding source

Aryogen Company

Expected recruitment start date

2017-04-21, 1396/02/01

Expected recruitment end date

2018-09-22, 1397/06/31

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

A Phase III, randomized, two armed, parallel, double blind, active controlled, non-inferiority clinical trial to determine the non-inferior therapeutic efficacy and safety between Denosumab (60 mg, produced by AryoGen Pharmed) compared with Prolia® (60 mg, Denosumab, the reference drug, produced by Amgen Company) in improvement of bone mineral densitometry (BMD) among osteoporotic postmenopausal women

Public title

Effect of denosumab administration (produced by Amgen or AryoGen Pharmed) in improvement of bone mineral densitometry (BMD) among osteoporotic postmenopausal women.

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Postmenopausal women aged between 45 up to 75. Bone mineral density T score at the lumbar spine (L1-L4), femoral neck or total hip should be equal or less than -2.5 and equal or more than -4. (-4 ≤T score ≤−2.5); or patients with high risk of fracture on the basis of FRAX criteria which according to osteoporosis treatment guidelines, need medicinal treatment Ability to comprehend and willingness to sign the Informed Consent Form for this study; Signed informed consent with full knowledge and mental health.

Exclusion criteria:

Lack of consent for being in the trial and not complying with an 18-months follow-up. Having hypersensitivity to denosumab or any component in the formulation (excipients include acetic acid, sorbitol, Polysorbate 20, sodium hydroxide, water for injections) Malabsorption syndrome History of thyroid surgery, parathyroid surgery or intestinal resection which has been caused malabsorption Patient with CKD stage 4 and 5 should be excluded (GFR <30cc/min) Level of serum 25-(OH) vitamin D less than 20 ng/ml; (If vitamin deficiency has been corrected, and two tests show the level above 20 ng/ml within a month, the patient can be enrolled.) Pre-existing hypocalcemia (Albumin-adjusted serum calcium level less than 8 mg/dl in fasting specimens) which is uncorrectable Untreated hypercalciuria (>250 mg/24h) and hypocalciuria (<100 mg/24h). If urine calcium level of patient is less than 100 mg per 24 hours and by vitamin D treatment the problem has been solved or if urine calcium level of patient is greater than 250 mg per 24 hours, but PTH is normal, the patient can be enrolled Presence of osteonecrosis of jaw (ONJ) risk factors including a diagnosis of cancer, poor oral hygiene, periodontal and/or dental diseases, having dentures; and comorbid disorders (anemia (hemoglobin level less than 11 g/dl, if it is corrected, patient can enter the study) history of diseases with coagulopathy, oral and dental infection) Malignancy Having severe and active infections; (Severe infection is a difficult treated infection, like diabetic foot infection, but if the infection is treatable, after treatment, the patient can be enrolled.) Being bed rest (for 2 weeks during the past 3 months) A case in which the patient cannot take 1000 mg oral elemental calcium per day; (as supplement) Conditions that influence bone metabolism, including hyperparathyroidism or hypoparathyroidism, hyperthyroidism or hypothyroidism, hypocalcemia, inflammatory rheumatologic diseases such as rheumatoid arthritis, Paget’s disease of bone, osteomalacia that is resistant to therapy (definition of resistant to therapy: not being responder to 1-month administration of vitamin D) Patients will be excluded if they have one severe or more than 2 moderate vertebral fractures. (Severe fracture is defined as more than 50 percent vertebral height loss and moderate fracture is defined as 25-50 percent vertebral height loss). Use of injectable bisphosphonates within the previous 12 months Use of oral bisphosphonates within the previous 3 months History of severe skeletal pain with bisphosphonates Use of parathyroid hormone or its derivatives, systemic hormone-replacement therapy, selective estrogen-receptor modulator, calcitonin, or calcitriol within 6 weeks before study enrollment. Use of corticosteroids (>5 mg/prednisone daily or equivalent for ≥ 3months), in the past 3 months and more Use of heparin (more than 20,000 international units/day for 6 months and longer), in the past 6 months and more. Patient that is possible to be administrated corticosteroids (>5 mg/prednisone daily or equivalent for ≥ 3months) or heparin (more than 20,000 international units/day for 6 months and longer) in the 18 month of the study, because of her chronic disease(s) such as allergy, asthma, coagulation disorders, should be excluded.

Age

From **45 years** old to **75 years** old

Gender

Female

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size

Target sample size: **190**

Randomization (investigator's opinion)

Randomized

Randomization description

The randomization plan of the patients will be carried out centrally using an R-CRAN software version 3.2.3. Using permuted block randomization, blocks (length of each block is 4 or 2) will be made, for a total of 190 patients (with 1:1 allocation ratio). Once the randomization has been made, each patient is given a code with which she will be identified throughout the study. The assigned code will be made up of 3 numbers (corresponding to the randomization number) and by 4 initials (corresponding to the 2 first letter of the first name, the 2 first letter of the first surname) and 2 numbers (center code). The randomization number will be assigned in a consecutive way.

Blinding (investigator's opinion)

Double blinded

Blinding description

To prevent the influence of knowing intervention group on study conclusion, the subjects and those who assess the study outcomes will be unaware of the state of the patient with regard to receiving the active drugs or standard remedy. For this purpose, subjects and administrator of the drug will be blinded by using a similar masked prefilled syringes. All drugs packages will be identified by unique numbers

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Tehran university of medical science

Street address

First floor, NO 21,Dameshgh st, Felestin st.Keshavar Blv

City

Tehran

Province

Tehran

Postal code

411310

Approval date

2017-01-31, 1395/11/12

Ethics committee reference number

IR.TUMS.VCR.REC.1395.1588

2

Ethics committee

Name of ethics committee

Ethics committee of Tabriz university of medical science

Street address

School of medicine, Tabriz university of medical sciences, Tabriz

City

Tabriz

Province

East Azarbaijan

Postal code

1561656

Approval date

2016-10-10, 1395/07/19

Ethics committee reference number

IR.TBZMED.REC.1395.758

Health conditions studied

1

Description of health condition studied

Postmenopausal osteoporosis

ICD-10 code

M80.0

ICD-10 code description

Postmenopausal osteoporosis

Primary outcomes

1

Description

Percentage change in BMD at the lumbar spine (L1-L4), femoral neck, and total hip

Timepoint

Baseline and at 18th month of the study

Method of measurement

BMD by dual-energy x-ray absorptiometry Hologic 4500 or higher

Secondary outcomes

1

Description

adverse events ocurrance

Timepoint

all of the visit (1-9)

Method of measurement

Physical examination, physician Assessment, and laboratory tests

2

Description

Level of biochemical markers of bone metabolism (Serum CTX, Serum NTX, P1NP, OC, BSAP)

Timepoint

Before injection at visit 2, 3, 4, 5, 6, 7, 8 and 9

Method of measurement

ELISA method

3

Description

The incidence of new vertebral fracture

Timepoint

The incidence of new vertebral fracture at baseline and at 18th month of the study

Method of measurement

X-ray radiography

4

Description

Immunogenicity of two products

Timepoint

Before the injections, at visit 2, 5, 7 and 9

Method of measurement

ELISA method

Intervention groups

1

Description

Denosumab (produced by AryoGen Pharmed) prefilled syringe for patients with dose of 60 mg, subcutaneous (S/C) injection every 6 months, at the beginning of the trial, month 6 and 12.

Category

Treatment - Drugs

2

Description

Prolia® (produced by Amgen Company) prefilled syringe for patients with dose of 60 mg, subcutaneous (S/C) injection every 6 months, at the beginning of the trial, month 6 and 12.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Bone marrow Density center of Karaj

Full name of responsible person

Dr. Ahmad Salimzadeh, Dr. Gholam hossein Alishiri

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2

Recruitment center

Name of recruitment center

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Full name of responsible person

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3

Recruitment center

Name of recruitment center

Alzahra Hospital

Full name of responsible person

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4

Recruitment center

Name of recruitment center

Emam Reza hospital

Full name of responsible person

Dr. Mohammad Reza Hatef and Dr. Seyedeh Zahra Mirfeizi

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5

Recruitment center
Name of recruitment center
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Recruitment center
Name of recruitment center
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Recruitment center
Name of recruitment center
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Full name of responsible person
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8

Recruitment center
Name of recruitment center
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Full name of responsible person
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9

Recruitment center
Name of recruitment center
Kasra Clinic
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10

Recruitment center
Name of recruitment center
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11

Recruitment center

Name of recruitment center
Rasool Akram Hospital

Full name of responsible person
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12

Recruitment center

Name of recruitment center
Endocrinology and metabolism research center

Full name of responsible person
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
AryoGen Pharmed company

Full name of responsible person
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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
AryoGen Pharmed company

Proportion provided by this source
100

Public or private sector
Private

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Industry

Person responsible for general inquiries

Contact

Name of organization / entity
Orchid Pharmed company

Full name of responsible person
Ramin Azhdarzadeh

Position
Pharmacist (PhD), Clinical Trial Manager

Latest degree
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Other areas of specialty/work
Medical Pharmacy

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Person responsible for scientific inquiries

Contact

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Full name of responsible person
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Person responsible for updating data

Contact
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
The company have no plan to do this
Study Protocol
No - There is not a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
No - There is not a plan to make this available
Clinical Study Report
No - There is not a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available