Incidence of Cardiovascular and Cerebrovascular Events Among Postmenopausal Women and Men With Osteoporosis Who Initiated Treatment With Denosumab or Zoledronic Acid - A Retrospective Cohort Study (20190038)

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Study Finalised

Administrative details

EU PAS number

EUPAS32133

Study ID

42980

DARWIN EU® study

No

Study countries

United States

Study status

Finalised

Research institutions and networks

Institutions

Amgen

United States

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Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Global Development Leader Amgen Inc.

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 22/10/2019

Actual: 22/10/2019

Study start date
Planned: 27/03/2020

Actual: 27/03/2020

Data analysis start date
Planned: 14/09/2020

Actual: 14/09/2020

Date of final study report
Planned: 14/09/2021

Actual: 24/08/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Amgen Inc.

Study protocol

20190038_01.02.06 Public Redacted Protocol Ver 1.0 2019-09-25 English.pdf (4.53 MB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

Among postmenopausal women and men with osteoporosis, evaluate the risk of cerebrovascular and cardiovascular events in subjects initiating treatment with denosumab relative to those initiating treatment with zoledronic acid.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(M05BX04) denosumab

denosumab

Medical condition to be studied

Osteoporosis

Myocardial infarction

Ischaemic stroke

Haemorrhagic stroke

Population studied

Short description of the study population

Patients with osteoporosis satisfying the following eligibility criteria were included in the study:

Inclusion Criteria

Subjects will be included in the study population if they meet the following criteria:

1. Receipt of one or more administrations (ie, claim containing national drug code (NDC) or Healthcare Common Procedure Coding System (HCPCS) code) for denosumab or zoledronic acid between 01 October 2010 and 31 December 2017.
2. The index date is defined as the first date of administration of study medication (ie, denosumab or zoledronic acid) observable in the data between 01 October 2010 and 31 December 2017.
3. Subjects must be women or men age 55 years or older at index date.
4. At least 455 days of continuous enrollment preceding index date. A 455-day enrollment is included because the dosing interval for zoledronic acid is once a year (365 days). Assessing 455 days (ie, 15 months) of look-back period will permit identification of past use.

Exclusion Criteria

Subjects will be excluded from the study if they meet any of the following criteria during the 455 days preceding the index date (ie, the baseline period)

1. Subjects with any of the following will be excluded to assure that denosumab is given for the osteoporosis indication
- Diagnosis of Paget’s disease of bone
- Diagnosis of cancer (excluding non-melanoma skin cancer)
- Treatment with chemotherapy,
- Treatment with hormonal therapy for cancer,

- Treatment with radiation or radiation therapy for cancer
2. To identify incident events, subjects with a history of stroke or MI events during the 455-day baseline period will be excluded.
3. Previous administration for denosumab or zoledronic acid prior to the index date. Look-back will include all available data (with a minimum required look-back
period of 455 days prior to index date).
- For this exclusion, denosumab use prior to 01 October 2010 will be identified by nonspecific codes (CPT codes: J3490and J3590) in combination with ICD-9 diagnostic codes for osteoporosis prior to 01 October 2010.

Age groups

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

120000

Study design details

Outcomes

Myocardial infarction and stroke (ischemic or hemorrhagic)

Data analysis plan

This study includes a descriptive analysis of the baseline prevalence of cardiovascular risk factors and incidence rates of the following outcomes of interest among post-menopausal women and men with osteoporosis initiating treatment with denosumab or zoledronic acid: MI, stroke, a composite outcome

including MI and stroke, and a composite outcome including MI, stroke, and all-cause mortality (analysis of this last outcome is restricted to the Optum data base that contains information on death). If subjects in the two treatment groups are sufficiently comparable, based on quantitative assessment of balance in propensity scores between groups, the outcomes will be compared between treatment groups under the hypothesis that there exists no difference in rates of outcomes between subjects initiating treatment with denosumab versus those initiating treatment with zoledronic acid.

Documents

Study results

20190038_Observational Research Study Report Published Report _Redacted.pdf(102.93 KB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Administrative healthcare records (e.g., claims)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No