

# 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)

**First published:** 20/11/2019

**Last updated:** 13/09/2021

Study

Finalised

## Administrative details

### EU PAS number

EUPAS32133

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### Study ID

42980

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### DARWIN EU® study

No

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### Study countries

## Study status

Finalised

## Research institutions and networks

### Institutions

#### Amgen

 United States

**First published:** 01/02/2024

**Last updated:** 27/03/2026

Institution

## Contact details

### Study institution contact

Global Development Leader Amgen Inc.  
medinfo@amgen.com

Study contact

[medinfo@amgen.com](mailto:medinfo@amgen.com)

### 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

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## **Study start date**

Planned: 27/03/2020

Actual: 27/03/2020

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## **Data analysis start date**

Planned: 14/09/2020

Actual: 14/09/2020

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## **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

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**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

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Secondary use of data

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**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

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### **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: J3490 and J3590) in combination with ICD-9 diagnostic codes for osteoporosis prior to 01 October 2010.

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### **Age groups**

- Adults (46 to < 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)
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### **Estimated number of subjects**

120000

## **Study design details**

### **Outcomes**

Myocardial infarction and stroke (ischemic or hemorrhagic)

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### **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)

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## 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

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

No