Delayed Denosumab Injections and Fractures Risk Among Subjects with Osteoporosis

First published: 19/11/2019

Last updated: 22/02/2024

Study Finalised

Administrative details

EU PAS number

EUPAS32386

Study ID

35405

DARWIN EU® study

No

Study countries

- ☐ China
- ☐ United Kingdom
- ☐ United States

Study description

The overall research question of the proposed study is to examine the fracture risk of delayed denosumab injections among patients who used this medication for long-term osteoporosis management using observational methods in large healthcare databases. The primary exposure delay of subsequent denosumab injections. The primary outcome of interest is composite fracture including all types of fracture. Secondary outcomes include major osteoporotic fracture, vertebral fracture, and hip fracture. The primary analysis strategy is emulating a sequential randomized controlled trials(RCT) comparing the three different strategies (on time, short delay and long delay) using observational data. This study will use an electronic medical record database from general practitioners in the United Kingdom (UK). The analysis will take advantage of naturally occurring variations in the timing of denosumab administration, and examine variation in administration schedule's impact on fracture risk in routine clinical settings.

Study status

Finalised

Research institutions and networks

Institutions

Brigham and Women's Hospital

First published: 01/02/2024

Last updated: 01/02/2024

Institution

National Clinical Research Center for Musculoskeletal Diseases Beijing, China, Xiangya Hospital Changsha, Hunan, China, University of Liverpool Liverpool, UK

Contact details

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Primary lead investigator

Daniel Solomon

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 12/03/2019

Study start date

Planned: 07/11/2019

Actual: 14/11/2019

Data analysis start date
Planned: 14/11/2019

Actual: 14/11/2019

Date of final study report
Planned: 31/01/2020

Actual: 18/02/2020

Sources of funding

- Other

More details on funding

Xiangya Hospital, National Clinical Research Center for Musculoskeletal Diseases

Study protocol

a20191006_THIN Proposal-DMAb Delay and Fracture_V1.pdf (187.41 KB)

a20200521_THIN Proposal-DMAb Delay and Fracture_V3.pdf (256.14 KB)

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

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

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

The proposed analyses aim to examine the fracture risk of delayed denosumab injections among patients who used this medication for long-term osteoporosis management.

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

Population studied

Short description of the study population

Our study population will include individuals aged ≥45 years who used denosumab for the management of osteoporosis between 2010 and 2018.

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

3000

Study design details

Outcomes

The primary outcome of interest is composite fracture including all types of fracture. Secondary outcomes include major fracture (hip fracture, vertebral fracture, wrist fracture, humerus fracture, pelvis fracture and rib fracture), vertebral fracture, and hip fracture.

Data analysis plan

We will emulate sequential randomized controlled trials (RCT) comparing the three different strategies (no delay, short delay, and long delay) using observational data. To avoid fatal bias, we will use the "clone and censor" method and results from sequential emulated studies will be combined. We will fit a pooled logistic regression model for each fracture outcome. Because the outcome of the models is rare at all times, the odds ratio from this model approximates the hazard ratio (HR). We will compare the HR across groups, with a specific interest in the trend. Inverse probability weighting will be used to ameliorate the selection bias issue introduced by censoring. Non-linear relationships between denosumab injection delay and fracture risk will be examined exploratorily.

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 source(s)

THIN® (The Health Improvement Network®)

Data source(s), other

THIN

Data sources (types)

Electronic healthcare records (EHR)

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