Comparing the Estimated Risk of Hip Fracture Among Subjects Exposed to Tramadol as Compared to Subjects Exposed to Codeine (Tramadol vs Codeine)

First published: 27/06/2020

Last updated: 30/01/2025

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/48348

EU PAS number

EUPAS36038

Study ID

48348

DARWIN EU® study

No

Study countries

United States

Study description

Hip fractures greatly impact an individual’s quality of life and carry a high risk of death within 1 year. Tramadol is a commonly used weak opioid for treatment of pain. A recent study by Wei et al. found that risk for hip fractures was higher for new users of tramadol than for new users of codeine or NSAIDs. We were concerned of that study’s design choices because of several limitations such as: A less-than-optimal propensity score adjustment strategy, the absence of negative controls, the failure to address possible differences in the initial doses of tramadol versus codeine, and the fact that the study was done in only one data source limited to one countries data. We propose to do a study to assess hip fracture incidence among users of tramadol versus codeine that will reassess the relationship and address the Wei et al. study limitations. Wei, J., et al., Association of Tramadol Use With Risk of Hip Fracture. J Bone Miner Res, 2020.

Study status

Finalised

Research institutions and networks

Institutions

Johnson & Johnson

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Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Erica Voss

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 19/02/2020

Actual: 19/02/2020

Study start date

Planned: 19/02/2020

Actual: 19/02/2020

Data analysis start date

Planned: 19/02/2020

Actual: 19/02/2020

Date of final study report

Planned: 24/09/2021

Actual: 09/07/2022

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Janssen Research & Development, LLC.

Study protocol

Protocol - Tramadol vs Codeine and Risk of Hip Fracture.pdf(1.45 MB)

Protocol - Tramadol vs Codeine and Risk of Hip Fracture - Admendment.pdf
(633.46 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 type list

Study topic:

Human medicinal product

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:

Does exposure to tramadol have a different risk of experiencing hip fracture within 1 year, relative to codeine?

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Retrospective, observational, comparative

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

CODEINE

TRAMADOL

Population studied

Short description of the study population

The study used two variants of the target (tramadol) and comparator (codeine) cohorts among 50-89-year-olds with 365 days of continuous observable time prior to the index date. The first cohort variants (T1, C1) excluded subjects who had been exposed to tramadol, codeine, or other opioids within 365 days prior to the index date, hip fracture, cancer, or opioid abuse diagnoses. The second cohort variants (T2, C2) aimed to make the target and comparator cohorts more comparable by excluding subjects diagnosed with cough or cold within 30 days of initial exposure to the opioids of interest and those prescribed cold or cough medications, antibiotics, or antihistamines within 30 days.

Age groups

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Special population of interest

Frail population

Estimated number of subjects

1000000

Study design details

Outcomes

Hip fracture

Data analysis plan

This study will follow a retrospective, observational, comparative cohort design . The target cohort is new users of tramadol, the comparator cohort are new users of codeine, and the outcome hip fracture. A Cox proportional hazards regression model will be used to model the time to the first outcome occurrence for the target group relative to the comparator group while accounting for the propensity score (PS) matching. Estimates of risk will be generated as the empirically calibrated hazard ratios (HR), 95% confidence intervals (CI), and p-values. This will be done across four observational datasets.

Documents

Study publications

Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, Van Staa T, Smeeth L…

Voss EA, Makadia R, Matcho A, Ma Q, Knoll C, Schuemie M, DeFalco FJ, Londhe A, …

Voss EA, Ma Q, Ryan PB. The impact of standardizing the definition of visits on…

Data management

Data sources

Data source(s)

Clinical Practice Research Datalink

Data sources (types)

Electronic healthcare records (EHR)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

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