Observational study on the risk of dementia associated with proton pump inhibitor use

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Study Finalised

Administrative details

EU PAS number

EUPAS31571

Study ID

32198

DARWIN EU® study

No

Study countries

Germany

Study description

Proton pump inhibitors (PPIs) are used to suppress the production of gastric acid ingastroesophageal reflux and other acid-related diseases. They are usually tolerated well by patients and thus have been applied widely, inside and

outside the indicated conditions, by prescription and over the counter. However, during the last years, accumulating evidence suggests that the long-term use of PPIs may be associated with numerous adverse outcomes, including dementia. This protocol describes the design and main characteristics of a substudy of the project ‘RiDe-PPI’ (Gesundheitliche Risiken und Determinanten der Dauereinnahme vonProtonenpumpeninhibitoren) planned to be conducted in German claims data and funded by the German governmental Innovarionfonds.The goal of this study is to evaluate whether longterm intake of PPIs increases the risk for dementia. The primary objective will be to compare the risk of dementia in new users of PPIs and PPI-nonusers and the risk of dementia in new users of PPIs with new users of H2-receptor antagonists (H2RAs).The secondary objective will be to investigate the risk of dementia related to high-dose use of PPIs.

Study status

Finalised

Research institutions and networks

Institutions

Chair of Epidemiology of the LMU Munich at UNIKA-T, Augsburg

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Sebastian-Edgar Baumeister

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 11/12/2018

Study start date

Actual: 01/10/2019

Date of final study report

Actual: 06/11/2019

Sources of funding

- Other

More details on funding

Gemeinsamer Bundesausschuss, Innovationsausschuss

Study protocol

RiDe-PPI_Dementia_Studyprotocol_(v1.0).pdf (1.42 MB)

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:

This population-based observational study will investigate whether the long-term use of proton pump inhibitors (PPIs) increases the risk of dementia. The additional study question is the risk of dementia related to different time intervals between PPI exposure and incidence of dementia, and the doseresponse relationship between PPI use and incidence of dementia.

Study Design

Non-interventional study design

Case-control

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A02BC01) omeprazole

omeprazole

(A02BC02) pantoprazole

pantoprazole

(A02BC03) lansoprazole

lansoprazole

(A02BC04) rabeprazole

rabeprazole

(A02BC05) esomeprazole

esomeprazole

(A02BC06) dexlansoprazole

dexlansoprazole

(A02BC07) dexrabeprazole

dexrabeprazole

Population studied

Short description of the study population

All individuals aged 40 years or older with a minimum of two consecutive years of insurance records with the Allgemeine Ortskrankenkasse AOK Bayern (Germany) between 2008 and 2018 and with the Kassenärztliche Vereinigung Bayerns (Association of Statutory Health Insurance Physicians in Bayern, KVB (Germany), between 2010 and 2018.

Age groups

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

Estimated number of subjects

6100000

Study design details

Outcomes

1) The risk of dementia in PPI initiators with two comparator groups:-PPI-nonusers (all PPI-noninitiators among all eligible individuals)- Active comparator users (initiators of an H2RA A02BA, prescribed for a similarindication)2) The dose-response relationship between PPI use and the incidence ofdementia. 1)

The risk of dementia among former, recent and current heavy PPI users2) The risk of dementia by active component of PPI.

Data analysis plan

We plan two different study designs and aim to transfer methodological strategies from clinical studies to our data in order to avoid bias that typically arises in observational studies.This approach is called “target trial emulation” and has been proposed in recent studies. Thus, in the cohort study, an intention-to-treat (ITT) analysis will be conducted, and an as-treated analysis will be performed using dose-response modeling. Cohort studies conducted within computerized big databases such as our claims data can be so large that they are technically unmeasurable for data analysis and thus using sampling designs within the cohort is unavoidable. Therefore, we also plan a nested case-control study as a secondary design to analyze the data based on sampling within the cohort as a more accurate reflection of the underlying cohorts.

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

Unknown