Association between anxiolytic or hypnotic drugs and total mortality

First published: 05/04/2013

Last updated: 23/04/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/20236

EU PAS number

EUPAS3772

Study ID

20236

DARWIN EU® study

No

Study countries

- [ ] France
- [ ] United Kingdom

Study description

Benzodiazepines and related drugs are indicated either for the short-term treatment of moderate or severe anxiety or insomnia. They could be involved in a wide range of fatal and non-fatal outcomes. However, the ways by which these drugs can lead to an increased mortality are not entirely elucidated. This study intends to investigate the impact of benzodiazepine and related exposure on all cause and specific mortality among cohorts obtained from a representative sample of French beneficiaries of the national health insurance scheme (EGB) and through a large healthcare database (CPRD) in the United Kingdom. Patients > 18 and exposed to at least one benzodiazepine derivative or related substance will be matched to one to 10 unexposed controls, and followed up from their inclusion to either death or 90 days following the last benzodiazepine exposure. All cause and cause specific mortality will be investigated, together with patients' sociodemographics, medicines use, medical history, and life-style (alcohol, smoking, for CPRD exclusively). Time to death will be analysed using an extended Cox regression model with time-dependent covariates

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Study status

Finalised

Research institutions and networks

Institutions

Pharmacologie En Population cohorteS biobanqueS (PEPSS), Hopitaux de Toulouse

France

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Institution | Educational Institution | Hospital/Clinic/Other health care facility | ENCePP partner

Contact details

Study institution contact

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Primary lead investigator

Maryse Lapeyre-Mestre

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 17/09/2012

Actual: 17/09/2012

Study start date

Planned: 17/04/2013

Actual: 29/04/2013

Date of interim report, if expected

Planned: 17/07/2013

Actual: 23/08/2013

Date of final study report

Planned: 17/09/2013

Actual: 07/10/2013

Sources of funding

- EMA

Study protocol

STUDY_PROTOCOL_2013_0404.pdf(1.14 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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:

The aim of this project will be to investigate mortality associated with benzodiazepine derivatives or related substances exposure in France and in the UK.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(M03BX07) tetrazepam

tetrazepam

(N03AE01) clonazepam

clonazepam

(N05BA) Benzodiazepine derivatives

Benzodiazepine derivatives

(N05CD) Benzodiazepine derivatives

Benzodiazepine derivatives

(N05CF) Benzodiazepine related drugs

Benzodiazepine related drugs

Population studied

Short description of the study population

The French and the UK adult population, including both genders.
Patients aged 18 and more, patients with First Registration Date or Current Registration Date > 12 months, acceptable Patient Flag (patients records meeting sufficient quality standard for research) (for CPRD), patients whose practice consented for linkage scheme (ONS mortality data available) (for CPRD) were included.

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

120000

Study design details

Outcomes

All-cause mortality, Cause-specific mortality

Data analysis plan

The role of potential confounding or explanatory variables will be taken into account by the extended Cox regression model. A univariate analysis will be first performed to select the variables with a p value<0.2, followed by a multivariate approach using the Cox proportional hazard regression model with time dependent covariates, with stratification on the matched pairs. Continuous variables will be tested for linearity. Relevant interactions between covariates will be checked. Proportional hazards assumption will be tested for all covariates. The estimation of the crude and adjusted Hazard Ratio and their 95% confidence interval will be provided.

Documents

Study results

BZD mortality France UK.pdf(1.18 MB)

Summary Deliverable 3a_2013_0822.pdf(139.06 KB)

Study publications

Palmaro A, Dupouy J, Lapeyre-Mestre M. Benzodiazepines and risk of death: Resul...

Data management

ENCePP Seal

This study has been awarded the ENCePP seal

Conflicts of interest of investigators

Declaration of Interests_completed_2013_0226.pdf(81.08 KB)

Composition of steering group and observers

EUPAS3772-3777.pdf(300.02 KB)

Signed code of conduct

2013-0015_DoC ENCePP CoC_SDPP_3772.pdf(31.06 KB)

Signed code of conduct checklist

2013-0015_ENCePP Checklist CoC_SDPP_3772.pdf(376.56 KB)

Signed checklist for study protocols

2013-0015_ENCePP Checklist Study Protocol_SDPP_3772.pdf(165.38 KB)

Data sources

Data source(s)

Clinical Practice Research Datalink

Data source(s), other

CPRD

Data sources (types)

Administrative healthcare records (e.g., claims)

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

Unknown