Post-authorisation Safety Study: Risk of Out-of-Hospital Sudden Cardiac Death in Users of Domperidone, Users of Proton Pump Inhibitors, and Users of Metoclopramide

First published: 28/02/2013

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS3590

Study ID

24330

DARWIN EU® study

No

Study countries

☐ United Kingdom

Study description

The overall goal of this research study is to find out whether use of domperidone, a gastrointestinal medication taken for symptoms of nausea and vomiting, may increase the chance of out-of-hospital sudden cardiac death (SCD) compared with the use of two other gastrointestinal medications, the proton pump inhibitor (PPI) medications as a group and metoclopramide, and during periods of non-use of all three types of study medications. Earlier studies have found an increased risk of SCD or a combined outcome of SCD and severe ventricular arrhythmia with current use of domperidone compared with non-use. Evidence from these studies suggested that risk was increased among persons aged older than 60 years and among those receiving a dose of more than 30 mg of domperidone per day orally, but there were not enough exposed individuals for a definitive answer to these questions. The current study will contribute additional information by providing an in-depth analysis of the risk of SCD in relation to domperidone by age and dose. To improve on previous studies it is designed as a nested case control and will include metoclopramide use as a comparator medication in addition to PPI medications, and a case-cross over analysis in which each subject will serve as his/her own control. The study will be performed in the CPRD linkable to Health Episode Statistics data.An important goal of the study is to examine whether higher doses of domperidone are related to higher risk of SCD than lower doses or whether patients using domperidone for longer periods of time are at higher risk. For some patients, the information needed to calculate daily dose of domperidone or length of domperidone use may be missing in the electronic database. For these patients, the researchers plan to conduct a survey of their general practitioners to gather information about dose and duration of exposure.The results of the study will be presented in a study report and in a peer reviewed manuscript.

Study status

Finalised

Research institutions and networks

Institutions

RTI Health Solutions (RTI-HS)

- [ ] France
- [ ] Spain
- [ ] Sweden
- [ ] United Kingdom
- [ ] United Kingdom (Northern Ireland)
- [ ] United States

First published: 21/04/2010

Last updated: 13/03/2025

Institution | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Alejandro Arana

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 24/07/2012

Study start date
Planned: 01/01/2013

Actual: 25/01/2013

Data analysis start date
Planned: 28/01/2013

Actual: 20/02/2013

Date of final study report
Planned: 21/12/2013

Actual: 22/08/2014

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Janssen Research and Development, L.L.C.

Study protocol

0303209 Final Protocol_V1.1_signed.pdf (717.61 KB)

0303209 Final Protocol_V1.1_blackout.pdf (744.28 KB)

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 research goal is to assess the risk of out-of-hospital Sudden cardiac death (SCD) associated with current use of domperidone compared with the risk in periods of non-use of domperidone or use of other gastrointestinal medications.

Of particular interest is the assessment of risk of SCD in relation to estimated daily dose of domperidone and to age.

Study Design

Non-interventional study design

Case-control

Cohort

Other

Non-interventional study design, other

Case-crossover

Study drug and medical condition

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

DOMPERIDONE

Population studied

Short description of the study population

Patients from a single database in the UK, the CPRD, for the years 2005 through 2011 who were at the risk of sudden cardiac death.

Age groups

- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)

- 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

15000

Study design details

Outcomes

The endpoint of the study is SCD that occurs outside a hospital or other institutional setting.

Data analysis plan

The absolute risk of SCD will be estimated as the number of SCD events divided by the person-years of follow-up.Incidence rates of SCD stratified by the following factors (Sex, age group, and diabetes status) will be calculated for current use of domperidone, current use of PPI medications, current use of metoclopramide, and non-use of any of these medications.Incidence rate ratios will be calculated comparing current use of domperidone with current use of PPI medications, current use of metoclopramide, and with non-use time, standardised for age and sex. For domperidone users, incidence rates will also be stratified by dose categories and dose-response trend explored.Multivariable conditional logistic regression will be used to estimate the risk of SCD from current domperidone exposure adjusted by potential confounders. A case-crossover analysis in the cases of SCD will allow further control of confounding

Documents

Study publications

Arana A, Johannes C, Varas C, Rothman KJ, McQuay L, Yang Q. Assessment of daily…

Arana A, Johannes CB, McQuay LJ, Varas-Lorenzo C, Fife D. Risk of Out-of-Hospit…

Varas-Lorenzo C, Arana A, Johannes CB, McQuay LJ, Rothman KJ, Fife D. Improving…

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.

Signed checklist for study protocols

ENCePP Check list for Study Protocols (Revision2)_5Mar2013.pdf (1.58 MB)

Data sources

Data source(s)

Clinical Practice Research Datalink

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

Unknown