Cohort Study of the Relative Incidence of Major Cardiovascular Events Among Patients Initiating Prucalopride Versus a Matched Comparator Cohort

First published: 08/04/2015

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS9200

Study ID

42866

DARWIN EU® study

No

Study countries

- ☐ Germany
- ☐ Sweden
- ☐ United Kingdom

Study description

The primary objective of this study is to estimate, in real-world settings, the adjusted incidence rate ratio (IRR) and 95% confidence interval (CI) for major adverse cardiovascular events (MACE) in initiators of prucalopride versus initiators of polyethylene glycol 3350 (PEG). Prucalopride and PEG are both used to treat chronic constipation in women for whom laxatives do not work. The primary objective of this study is to estimate, in real-world settings, the adjusted incidence rate ratio (IRR) and 95% confidence interval (CI) for major adverse cardiovascular events (MACE) in initiators of prucalopride versus initiators of polyethylene glycol 3350 (PEG). Prucalopride and PEG are both used to treat chronic constipation in women for whom laxatives do not work. Drugs similar to prucalopride have been associated with adverse cardiovascular events in the past. This study is being done to gain a better understanding of the safety of prucalopride. The study will be implemented in five health care data sources in three countries: in the United Kingdom, the Clinical Practice Research Datalink (CPRD), The Health Improvement Network (THIN), and the Information Services Division of Scotland, in Germany, the German Pharmacoepidemiological Research Database, and in Sweden, the Swedish National Registers. Individuals in the databases will be included in the study if they were 18 years and older, were treated for chronic constipation and meet the criteria of at least 1 year of electronic data before study entry and at least 1 year of enrolment with their GP (for CPRD and THIN). The study period starts January 1, 2010, and will end at the latest available data at each database at the time of analysis. The primary cardiovascular outcome MACE, is a composite of any of the following: (1) hospitalization for nonfatal acute myocardial infarction, (2) hospitalization for nonfatal stroke, and (3) in-hospital cardiovascular death.

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

Fundación Centro Español de Investigación Farmacoepidemiológica (CEIFE)

- [ ] Spain

First published: 15/03/2010

Last updated: 15/02/2024

Institution | Not-for-profit | ENCePP partner

Leibniz Institute for Prevention Research and Epidemiology - BIPS

- [ ] Germany

First published: 29/03/2010

Last updated: 26/02/2024

Institution | Not-for-profit | ENCePP partner

Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

Sweden

First published: 24/03/2010

Last updated: 23/04/2024

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

MEMO Research, University of Dundee

United Kingdom (Northern Ireland)

First published: 12/05/2010

Last updated: 17/05/2024

Institution | Educational Institution | Not-for-profit | ENCePP partner

Contact details

Study institution contact

Alicia Gilsenan agilsenan@rti.org

Study contact

agilsenan@rti.org

Primary lead investigator

Alicia Gilsenan

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 29/08/2014

Actual: 29/08/2014

Study start date

Planned: 28/02/2015

Actual: 09/04/2015

Date of final study report

Planned: 31/12/2017

Actual: 21/12/2017

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Shire Pharmaceuticals

Study protocol

SPD555-802 protocol_ final 30May2014_to Shire .pdf (1.68 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:

Disease /health condition

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:

To estimate the adjusted incidence rate ratio and 95% confidence interval for major adverse cardiovascular events—defined as the composite of hospitalization for acute myocardial infarction, hospitalization for stroke, and in-hospital cardiovascular death—in initiators of prucalopride versus initiators of polyethylene glycol 3350, adjusting for CV risk factors and other confounders.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A06AD15) macrogol

macrogol

(A06AX05) prucalopride

prucalopride

Medical condition to be studied

Acute myocardial infarction

Ischaemic stroke

Haemorrhagic stroke

Cardiac death

Population studied

Short description of the study population

The prucalopride cohort consisted of adult patients who had a dispensing (for claims data sources) or prescription (as recorded in electronic medical record data sources) for prucalopride within the study period with at least 12 months of data coverage in the data source before this first dispensing or prescription, no evidence in the data source of prior use of prucalopride, and no evidence of short use of PEG (i.e., < 5 days) within 12 months before this first prucalopride prescription/dispensing. The first prescription of prucalopride was the index prescription, which determined the index date.

The PEG cohort consisted of patients who had a dispensing or prescription for PEG of at least 5 days within the study period, who had at least 12 months of data coverage in the data source before this first dispensing or prescription, and who had no evidence of prior use of PEG for chronic constipation in the data source. The first prescription for PEG was the index prescription, prescribed or dispensed on the index date. Up to five PEG initiators were selected for each prucalopride initiator, matched by age, sex, and calendar year of first prescription of prucalopride or PEG. (The SNR also matched patients by recent hospitalization and specialty of the prescribing physician to increase comparability between PEG and prucalopride users). At the time of study initiation, PEG was the most commonly prescribed reimbursable medication for chronic constipation in Europe.

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

66900

Study design details

Outcomes

Major adverse cardiovascular events (MACE)—defined as the composite of hospitalization for acute myocardial infarction (AMI), hospitalization for stroke, and in-hospital cardiovascular death, Individual components of MACE – Hospitalization for AMI, hospitalization for stroke, in-hospital cardiovascular death

---

Data analysis plan

For each cohort, the prevalence of baseline risk factors for MACE will be described. Incidence rates of each outcome of interest will be calculated for the prucalopride and PEG cohorts, and IRRs will be estimated. Within each data source, propensity scores will be developed by modeling use of prucalopride against CV risk factors that could be confounders. After stratifying cohort-specific incidence rates by propensity score decile and by data source, the coordinating center will conduct an overall analysis combining the results across all data sources to calculate overall summary incidence rate and IRR estimates. Overall incidence rates will be age- and sex-standardized to the distribution of person-years in the prucalopride cohort across all data sources by age category and sex. Overall IRRs will be standardized to the distribution of propensity score deciles in the prucalopride cohort across all data sources.

Documents

Study results

Study SPD555-802 Final Report Addendum 2.0_24Jan2019_abstract.pdf (160.91 KB)

Study publications

Gilsenan A, Fortuny J, Cainzos-Achirica M, Cantero AF, Flynn RWV, Garcia-Rodrig...

Fortuny J, Gilsenan A, Cainzos-Achirica M, Cantero AF, Flynn RWV, Garcia-Rodrig...

Ruigómez A, Plana E, Gilsenan A, et al. Identification and Validation of Major ...

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®)

Clinical Practice Research Datalink

Sweden National Prescribed Drugs Register / Läkemedelsregistret

German Pharmacoepidemiological Research Database

Data source(s), other

ISD Scotland United Kingdom

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

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