Post-authorization Safety Program Using the Swedish National Registers—A Validation Study of Cardiovascular and Neoplasm Events in Users of PharmacologicalTreatments for Overactive Bladder

First published: 26/01/2015

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS8444

Study ID

29380

DARWIN EU® study

No

Study countries

Sweden

Study description

Mirabegron is a first in class therapeutic agent, with a mechanism of action distinct from that of antimuscarinic agents indicated for the treatment of overactive bladder (OAB). This is a retrospective cohort study of new users of individual antimuscarinic drugs: oxybutynin, tolterodine, darifenacin, solifenacin, and fesoterodine. The objectives are: to describe drug-use patterns, to describe the availability of potential confounders in the Swedish data resources, and to calculate background rates of cardiovascular (CV) and cancer outcomes among antimuscarinic drug users in the Swedish Prescription and Inpatient National Databases, in collaboration with the Karolinska Institutet (KI) Center for Pharmacoepidemiology (CPE). Results will help to refine the study size and statistical power assessment for the post-marketing safety studies of Mirabegron, to be conducted, among other data sources, in the Swedish Databases.The study period is July 1, 2005 through December 2012. The study will calculate incidence rates of the following endpoints : - CV: including acute myocardial infarction, stroke, all-cause mortality, a MACE composite endpoint, and CV mortality.- Neoplasm endpoint: The study will focus on a composite of the 10 most commonly occurring malignancies. For cancer analyses only the first incident targeted cancer is considered.

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: 11/08/2026

Institution | Not-for-profit | ENCePP partner

Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

Sweden

First published: 24/03/2010

Last updated: 02/06/2026

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

RTI Health Solutions (RTI-HS)

France
Spain

Sweden

United Kingdom

United Kingdom (Northern Ireland)

United States

First published: 21/04/2010

Last updated: 11/08/2026

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

Planned: 15/09/2014

Actual: 10/10/2014

Study start date

Planned: 05/01/2015

Actual: 05/01/2015

Date of interim report, if expected

Planned: 06/02/2015

Actual: 26/03/2015

Date of final study report

Planned: 29/02/2016

Actual: 16/02/2016

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Astellas Pharma Global Development, Inc.

Study protocol

178-cl-118-clp-02-reissue-en-v1dot1_Redacted.pdf (969.29 KB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Methodological aspects

Study type

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

Drug utilisation

Other

If ‘other’, further details on the scope of the study

Validation of the database Swedish Prescription and Inpatient National Databases for the study of CV and neoplasm events in users of treatments for overactive bladder

Data collection methods:

Secondary use of data

Main study objective:

Characterize users of OAB drugs.Describe patterns of usage of OAB drugs.Describe the availability of potential confounders in the database, to help in the design of the PASS studies of mirabegron.Estimate IRs of study endpoints in new users of OAB drugs.Estimate the IRRs of CV outcomes in users of OAB drugs compared with tolterodine.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Database validation study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(G04BD04) oxybutynin

oxybutynin

(G04BD07) tolterodine

tolterodine

(G04BD08) solifenacin

solifenacin

(G04BD10) darifenacin

darifenacin

(G04BD11) fesoterodine

fesoterodine

Medical condition to be studied

Urinary incontinence

Population studied

Short description of the study population

New users of any of the following medications for overactive bladder (OAB): oxybutynin, tolterodine, darifenacin, solifenacin, and fesoterodine.

Subjects in the program wiere required to meet all of the following inclusion criteria:

- Be a resident in Sweden for at least 12 months before the first dispensing of an OAB drug of interest (thereby providing medical and prescription history data).
- Have a first recorded dispensing for oxybutynin, tolterodine, darifenacin, solifenacin, or fesoterodine.
- Be aged 18 years or older at the time of first dispensing of a drug of interest.

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)

Special population of interest

Other

Special population of interest, other

Overactive Bladder patients

Estimated number of subjects

78.000

Study design details

Outcomes

CV endpoints: AMI, stroke, CV mortality, all-cause mortality, major adverse cardiac events (MACE).Composite cancer endpoints: lung & bronchus, colon & rectum, melanoma of skin, urinary bladder, non-Hodgkin lymphoma, kidney & renal pelvis, pancreas, prostate (males), breast (females), corpus uteri (females)

Data analysis plan

Summary statistics of the covariates will be generated. Characteristics of the users at cohort entry and the patterns of use of the study medications will be described.Users of OAB medications will be characterized with respect to selected covariates.Patterns of use of OAB drugs including dose, duration of treatment, drug switching, and use of drugs as add-on therapy will be described.The frequency of the different characteristics of the covariates and the degree of missing information will be described.3 types of incidence endpoints will be estimated:-IRs of 4 different CV events+all-cause mortality in new users of antimuscarinic drugs for the treatment of OAB.-IRR of 4 different CV outcomes+all-cause mortality in new users of each of the OAB drugs compared with tolterodine.-IRs of 2 sex-specific, multiple-cancer composite endpoints (1 for men/1 for women), during the first year after start of treatment and during subsequent years, among new users of antimuscarinic drugs

Documents

Study results

178-cl-118-clrr-03-disc01-en-final-02_redacted.pdf (4.17 MB)

Study publications

Linder M, Margulis AV, Anveden-Berglind I, Bahmanyar S, Bui CL, Atsma WJ, Appen...

Margulis AV, Linder M, Arana A, Pottegard A, Anveden-Berglind I, Bui CB, Kristi...

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)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

Data source(s), other

Swedish Cancer Register, National Patient Register, Causes of Death Register

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

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