Post-Authorization Safety Program—Validation of the Danish Data Resources for the Study of Cardiovascular and Neoplasm Events in Users of Treatments for Overactive Bladder

First published: 26/01/2015

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS8441

Study ID

29376

DARWIN EU® study

No

Study countries

Denmark

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, trospium, and fesoterodine. The objectives are: to describe drug-use patterns, to describe the availability of potential confounders, and to calculate background rates of cardiovascular (CV) and cancer outcomes among antimuscarinic drug users in the Danish National Databases, in collaboration with the University of Southern Denmark (SDU). 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 datasources, in the Danish Databases.The study period is January 2004 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: 13/03/2025

Institution | Not-for-profit | ENCePP partner

Pharmacoepi center, University of Southern Denmark

Denmark

First published: 22/04/2010

Last updated: 27/07/2023

Institution | Educational Institution | ENCePP partner

Contact details

Study institution contact

Alejandro Arana aarana@rti.org

Study contact

aarana@rti.org

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: 31/10/2014

Actual: 31/10/2014

Data analysis start date
Planned: 31/01/2015

Actual: 31/01/2015

Date of final study report
Planned: 29/03/2015

Actual: 26/03/2015

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Astellas Pharma Global Development, Inc.

Study protocol

178-cl-119-clp-03-reissue-en-final-v2-02_Redacted.pdf (1.79 MB)

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 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

Drug utilisation

Other

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

Validation of the database Danish National Health Registries 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

(G04BD09) trospium

trospium

(G04BD10) darifenacin

darifenacin

(G04BD11) fesoterodine

fesoterodine

Medical condition to be studied

Urinary incontinence

Population studied

Short description of the study population

New users of individual overactive bladder (OAB) medications: oxybutynin, tolterodine, darifenacin, solifenacin, trospium, and fesoterodine.

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

- Have at least 12 months of continuous residence in Denmark (thereby providing medical and prescription history data) before the first prescription or dispensing of an overactive bladder (OAB) drug of interest.
- Have a first recorded prescription or dispensing for oxybutynin, tolterodine, darifenacin, solifenacin, trospium, or fesoterodine.

 Be aged 18 years or older at the time of first prescription 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

90000

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-119-clrr-03-disc01-en-final-02_redacted.pdf (3.32 MB)

Study publications

Margulis AV, Hallas J, Pottegard A, Kristiansen NS, Atsma WJ, Franks B, D'Silva...

Hallas J, Margulis AV, Pottegard A, Kristiansen NS, Atsma WJ, Appenteng K, de V...

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)

Danish registries (access/analysis)

Data source(s), other

Danish National Registry of Patients, the Danish National Prescription Registry, the Central Person Registry, the Taxation, Registry, the Cause of Death Registry, and the Danish Cancer Registry

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

Unknown