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

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Study | Finalised

Administrative details

Contact details

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PURI
https://redirect.ema.europa.eu/resource/29376

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 institution 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 19/02/2024

Institution | ENCePP partner | Not-for-profit

Pharmacoepi center, University of Southern Denmark

Denmark
First published: 22/04/2010
Last updated
27/07/2023

Institution

Educational Institution

ENCePP partner

Study timelines

Date when funding contract was signed
Planned:
15/09/2014
Actual:
10/10/2014

Data collection
Planned:
31/10/2014
Actual:
31/10/2014

Start date of data analysis
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 data collection

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 O

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
100000095934
oxybutynin
100000095937
tolterodine
100000095938
solifenacin
100000095939
trospium
100000095940
darifenacin
100000095941
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

Results tables
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

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 data (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