Post-authorization Safety Study Evaluation of Cardiovascular Events in Users of Mirabegron and Other Treatments for Overactive Bladder

First published: 30/11/2016

Last updated: 02/07/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/34999

EU PAS number

EUPAS16282

Study ID

34999

DARWIN EU® study

No

Study countries

- [ ] Denmark
- [ ] Sweden
- [ ] United Kingdom
- [ ] United States

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 post authorization safety study (PASS, or post marketing requirement (PMR) in the US) is designed to generate additional evidence to help evaluate the results observed in the clinical trials. To implement the program, we selected data sources from 5 research centers. The investigators are from RTI Health Solutions, Optum, University of Southern Denmark, Centre for Pharmacoepidemiology at Karolinska Institute, and Comprehensive Health Insights.The study population will include patients observed in each of the 5 databases, providing a wide array of patient characteristics, drug utilization and medical practice patterns, which will enhance the generalizability of the study findings to the population of mirabegron users in real world practice, beyond clinical trials.This will be a cohort study comparing the incidence of commonly occurring cardiovascular events among new users of mirabegron and new users of any comparator antimuscarinic medication (as a group) used in the treatment of OAB. To provide a sufficiently large patient population within which to evaluate the safety of mirabegron, the study will be conducted within multiple databases. Each of these populations will be studied according to the same Core protocol, although operational details will vary across sites due to the specifics of the data environments. In addition to data source-specific analyses, estimates obtained from all data sources will be analyzed using a meta-analysis approach. Overall, the study period includes October 2012 (first observed use of

mirabegron in US data) through June 2019 (submission of final study report).

Study status

Finalised

Research institutions and networks

Institutions

Optum

Germany

First published: 03/01/2012

Last updated: 07/02/2014

Institution | Other | 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

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

University of Southern Denmark Odense C. Denmark, Comprehensive Health Insights Louisville, KY USA

Contact details

Study institution contact

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Study contact

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Primary lead investigator

John Seeger

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 10/08/2015

Actual: 22/09/2015

Study start date
Planned: 09/01/2017

Actual: 06/09/2016

Data analysis start date
Planned: 20/02/2017

Date of interim report, if expected
Planned: 29/06/2018

Date of final study report
Planned: 28/06/2019

Actual: 15/11/2019

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Astellas Pharma Global Development, Inc.

Study protocol

178-CL-114_Protocol Version 9.0_For EnCepp Reg.pdf(1.17 MB)

178-cl-114-clp-10-reissue-v11-en-final-02.pdf(2.09 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:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

Estimate and compare the incidence of CV endpoints within the person-time among users of mirabegron relative to antimuscarinic medication, (a) overall, (b) stratified by naïve user status, (c) restricted to patients 65+ years, (d) restricted to patients at high risk for CV events, (e) by intervals of time since initiation, and (f) by cumulative dose.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(G04BD12) mirabegron

mirabegron

Population studied

Short description of the study population

The study population consisted of patients who contributed episodes of person-time during new use of medications for the treatment of OAB. A new user of any drug of interest was a patient who received a prescription or dispensing for

mirabegron or any antimuscarinic OAB drug during the study period, was at least 18 years of age at the time of the prescription or dispensing, and without a prescription or dispensing for the same specific medication in the previous 12 months. At cohort entry, this definition permitted a person to be either a naïve new user or a non-naïve new user. The predicted probability of starting treatment with mirabegron relative to antimuscarinic medications, conditional on baseline covariates, was estimated to create a propensity score (PS). The cohorts were then formed by PS-matching at a ratio of 1 episode of mirabegron use to 1 comparator episode of antimuscarinic medication use. The PS for each eligible episode was calculated using baseline data for that episode. By updating the covariates included in the PS for each episode contributed by a patient, time-dependent changes in baseline covariates were incorporated into the matching process.

The study included treatment episodes from males and females. The patient episodes in the study will be required to meet all of the following inclusion criteria as ascertained from each of the automated data sources:

1. Have a recorded prescription or dispensing for mirabegron or comparator antimuscarinic medication (oxybutynin, tolterodine, darifenacin, solifenacin, trospium, or fesoterodine), with no dispensing or prescription for that specific medication in the prior 12 months before cohort entry (defined as the index prescription or dispensing). The index prescription will be considered the first treatment episode; once a patient enters the cohort (mirabegron or antimuscarinic medications [as a group]), a patient may switch between individual antimuscarinic medications and mirabegron.
2. Be aged 18 ye

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

100000

Study design details

Outcomes

Acute myocardial infarction, stroke, CV mortality, Major Adverse Cardiovascular Events (MACE) composite outcome, all-cause mortality.

Data analysis plan

Database-specific and meta analyses will be performed. Within each database, mirabegron and antimuscarinic initiators will be 1:1 propensity score matched. Cox proportional hazards regression models will be built for each CV outcome. Models will be developed for: overall study population, stratified by naïve user status, patients 65+ years, patients at high risk for CV events, by intervals of time since initiation, and cumulative dose.

Documents

Study results

178-cl-114-clgr-disc01-en-final-02.pdf(745.17 KB)

Data management

Data sources

Data source(s)

Clinical Practice Research Datalink

Danish registries (access/analysis)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

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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