Aclidinium Bromide Post-Authorisation Safety Study to Evaluate the Risk of Cardiovascular Endpoints

First published: 27/05/2016
Last updated: 17/06/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/42316

EU PAS number
EUPAS13616

Study ID
42316

DARWIN EU® study
No

Study countries
United Kingdom

Study description
Aclidinium bromide is a long-acting and potent antagonist of lung M3 receptors indicated as a maintenance bronchodilator treatment to relieve symptoms in adults age 40 or older with chronic obstructive pulmonary disease (COPD). To evaluate potential cardiovascular safety concerns and all-cause mortality identified in the European risk management plan for aclidinium bromide, a PASS will be conducted through sequential studies for the endpoints of interest. Specific aims are:
--To compare the risk of congestive heart failure, acute myocardial infarction, stroke, and all-cause mortality in patients with COPD initiating treatment with aclidinium bromide

(monotherapy or combination therapy with formoterol (not fixed-dose and fixed-dose) and other COPD medications with the risk in patients with COPD initiating treatment with long-acting beta-agonists (LABAs).
--To compare the risk of the study endpoints of interest in patients with COPD initiating treatment with aclidinium bromide (monotherapy or combination with formoterol, not fixed-dose and fixed-dose) with the risk in patients with COPD initiating treatment with other COPD medications.
--To evaluate the effect of dose and duration of each study medication on the risk of each study outcome.
--To compare the risk of cardiac arrhythmias in patients with COPD between:
1) New users of fixed-dose combination of aclidinium and formoterol and other fixed-dose combination COPD medications with new users of LABA,
2) New users of fixed-dose combination of aclidinium and formoterol with new users of each of the other fixed-dose combination COPD medications.
The first and second nested case-control and cohort studies, initiated in March 2016 and February 2017, evaluate the risk of all-cause mortality and congestive heart failure. Sample size considerations will trigger the start of three additional cohort studies evaluating the risk of acute myocardial infarction, stroke, and cardiac arrhythmias.

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
Not-for-profit
ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator
Cristina Rebordosa
Primary lead investigator

Study timelines

Date when funding contract was signed
Planned:
29/02/2016
Actual:
10/03/2016

Study start date
Planned:
31/10/2016
Actual:
27/01/2017

Data analysis start date
Planned:
31/10/2017
Actual:
16/10/2017

Date of interim report, if expected
Planned:
28/06/2019
Actual:
06/06/2019

Date of final study report
Planned:
30/12/2023
Actual:
17/12/2023

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

AstraZeneca

Study protocol

PASS_PROTOCOL_COMBO_2Jun2015_V 2.2_Redacted2.pdf(1.72 MB)

D6560R00004 PASS protocol v4 signed_redacted.pdf(1.87 MB)

Regulatory

Was the study required by a regulatory body?
Yes

Is the study required by a Risk Management Plan (RMP)?
EU RMP category 1 (imposed as condition of marketing authorisation)

Methodological aspects

Study type

Study type list

Study type:
Non-interventional study

Scope of the study:
Drug utilisation
Safety study (incl. comparative)

Main study objective:
To compare the risk of all-cause mortality, congestive heart failure, acute myocardial infarction, stroke, and cardiac arrhythmias in patients with COPD initiating treatment with aclidinium bromide with the risk in patients with COPD initiating other treatments for COPD.

Study Design

Non-interventional study design
Case-control

Study drug and medical condition

Name of medicine
Bretaris
Bretaris Genuair 400 µg - Inhalation powder, pre-dispensed
Brimica
Brimica Genuair 340 µg + 12 µg - Inhalation powder
Duaklir
Duaklir Genuair 340 µg + 12 µg - Inhalation powder
Eklira
Eklira Genuair 322 µg - Inhalation powder, pre-dispensed

Study drug International non-proprietary name (INN) or common name
ACLIDINIUM BROMIDE
FORMOTEROL FUMARATE DIHYDRATE

Anatomical Therapeutic Chemical (ATC) code
(R03AC12) salmeterol
(R03AC13) formoterol
(R03AC18) indacaterol
(R03AC19) olodaterol
(R03AK06) salmeterol and fluticasone
(R03AK07) formoterol and budesonide
(R03AK07) formoterol and budesonide
(R03AL03) vilanterol and umeclidinium bromide
(R03AL04) indacaterol and glycopyrronium bromide
(R03AL05) formoterol and aclidinium bromide
(R03AL06) olodaterol and tiotropium bromide
(R03AL07) formoterol and glycopyrronium bromide
(R03BB04) tiotropium bromide
(R03BB05) aclidinium bromide
(R03BB06) glycopyrronium bromide
(R03BB07) umeclidinium bromide

Medical condition to be studied
Chronic obstructive pulmonary disease

Population studied

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
105000

Study design details

Outcomes
All-cause mortality, congestive heart failure, acute myocardial infarction, stroke, and cardiac arrhythmias.

Data analysis plan
A descriptive analysis of the study cohorts will be performed. Crude and age and sex-standardized incidence rates will be estimated for each study cohort. A cohort analysis will be performed to estimate crude and adjusted relative risks (RRs) and 95% CIs for each study endpoint using conditional multiple logistic regression to compare:--Current, recent, and past use of aclidinium and of each study medication with current use of LABAs--Current single use of aclidinium and of each study medication with current single use of LABAs--Current single use of aclidinium with current single use of each study medication. Analyses will also be performed stratified by specific subgroups of patients (e.g. by COPD severity, age groups, or history of cardiovascular disease) among current users of the study medications. The effect of dose and duration of use will be estimated among current single users of each study medication.

Documents

Study publications
A Cohort Study to Evaluate the Risk of Hospitalisation for Congestive Heart Fai…
Are you really dead? Validation of death and date of death in patients with COP…
Hospitalization for heart failure among patients using aclidinium bromide and o…
Use of aclidinium did not increase the risk of death in a noninterventional coh…
A validation exercise: identifying hospitalizations for heart failure among pat…

Data management

Data sources

Data source(s)
Clinical Practice Research Datalink
Hospital Episode Statistics

Data source(s), other
Hospital Episode Statistics inpatient data, Office of National Statistics data

Data sources (types)
Administrative data (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