Cohort study of cardiovascular events in patients with chronic obstructive pulmonary disease initiating olodaterol or other long-acting beta2-agonists

First published: 07/11/2017

Last updated: 18/03/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/49013

EU PAS number

EUPAS21574

Study ID

49013

DARWIN EU® study

No

Study countries

☐ Denmark

Study description

Boehringer Ingelheim GmbH (BI) developed olodaterol, an inhaled long-acting beta2-agonist (LABA), for the indication of chronic obstructive pulmonary disease (COPD). In the Decentralised Procedure for Striverdi Respimat, the health authorities of the European Union/European Economic Area Member States requested the conduct of a post-authorisation safety study (PASS) to gather additional data on safety in long-term use of olodaterol. The PASS will include evaluation of users of olodaterol monotherapy as well as in fixed-dose combination with tiotropium. The results of this study will provide insight into the absolute and relative frequency of cardiac arrhythmias and myocardial ischaemia events of interest in comparison to alternative LABA therapies for COPD. Primary study objectives are to: (1) examine the risk of selected cardiac arrhythmias in patients with COPD exposed to olodaterol compared with the risk in patients exposed to other LABAs, and (2) examine the risk of acute myocardial infarction (AMI) and other serious ischaemic heart disease events, including unstable angina, in patients with COPD exposed to olodaterol compared with the risk in patients exposed to other LABAs. The secondary objective is to examine the risk of overall mortality in patients with COPD exposed to olodaterol compared with the risk in patients exposed to other LABAs. The study population will consist of patients with COPD aged 40 years or older in Denmark, a country where olodaterol is available and where a large proportion of the population is included in health care databases used for pharmacoepidemiologic research. Patients will be new users of olodaterol or other LABA, with no dispensing of any LABA in the 6 months before the first prescription of olodaterol or LABA during the study period (index date) and at least 1 year of enrolment in the database.

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**

Aarhus University & Aarhus University Hospital DEPARTMENT OF CLINICAL EPIDEMIOLOGY

- [ ] Denmark

First published: 20/07/2021

Last updated: 02/04/2024

Institution **Educational Institution** **ENCePP partner**

Contact details

Study institution contact

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Study contact

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Primary lead investigator

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Primary lead investigator

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Study timelines

Date when funding contract was signed

Planned: 18/08/2015

Actual: 18/08/2015

Study start date

Planned: 31/03/2020

Actual: 15/07/2019

Data analysis start date

Planned: 01/07/2020

Actual: 03/02/2020

Date of final study report

Planned: 30/09/2020

Actual: 15/09/2020

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Boehringer Ingelheim International GmbH

Study protocol

1222-0054--protocol_redacted.pdf(667.53 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 2 (specific obligation of marketing authorisation)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To examine the risk of selected cardiac arrhythmias, acute myocardial infarction, and other serious ischemic heart disease events, including unstable angina, in patients with COPD exposed to olodaterol compared with the risk in patients exposed to other LABAs.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine, other

Striverdi Respimat; Stiolto Respimat

Anatomical Therapeutic Chemical (ATC) code

(R03AC12) salmeterol

salmeterol

(R03AC13) formoterol

formoterol

(R03AC18) indacaterol

indacaterol

(R03AC19) olodaterol

olodaterol

(R03AK06) salmeterol and fluticasone

salmeterol and fluticasone

(R03AK08) formoterol and beclometasone

formoterol and beclometasone

(R03AK12) salmeterol and budesonide

salmeterol and budesonide

(R03AL04) indacaterol and glycopyrronium bromide

indacaterol and glycopyrronium bromide

(R03AL05) formoterol and aclidinium bromide

formoterol and aclidinium bromide

(R03AL06) olodaterol and tiotropium bromide

olodaterol and tiotropium bromide

Medical condition to be studied

Chronic obstructive pulmonary disease

Population studied

Short description of the study population

The study focused on chronic obstructive pulmonary disease (COPD) patients aged 40 or older in Denmark, a country where olodaterol is available in a fixed combination with tiotropium. The study population included new users of olodaterol or other LABA, with no dispensing of any LABA within 6 months before the first prescription during the study period and at least 1 year of enrolment in the electronic database.

Eligibility criteria for patients in both exposure cohort:

• Have been diagnosed with COPD

• Be aged 40 years or older (to minimise the likelihood of including individuals who have asthma only)

• Be a new user of olodaterol or a new user of indacaterol, salmeterol, or formoterol (not in fixed-dose combination with an inhaled corticosteroid) and have no dispensing of any LABA in the 6 months before the index date

• Have at least 1 year of enrolment in the electronic database before their first LABA dispensing (defined as the index LABA)

• Have data on sex (i.e., sex must be known).

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

Patients with chronic obstructive pulmonary disease

Estimated number of subjects

150000

Study design details

Outcomes

Incidence of the following: atrial fibrillation or flutter during new use, hospitalisation for ventricular tachycardia, including ventricular fibrillation/flutter and cardiac arrest, supraventricular tachycardia (other than atrial fibrillation/flutter), hospitalisation for acute myocardial infarction, hospitalisation for serious acute coronary heart disease, including unstable angina, Mortality from all causes.

Data analysis plan

The incidence rate ratio (IRR) and incidence rate difference (IRD) for each event of interest in the olodaterol-exposed group relative to that in the comparator group will be derived. The effects of demographics and specified baseline characteristics will be assessed, and adjusted IRR will be calculated by adjusting for each covariate one at a time. A fitted propensity score model will be used to estimate a propensity score for each patient, and the IRRs for each event of interest will be stratified by propensity score deciles. For each endpoint, IRR and IRD will be stratified by propensity score deciles, and the overall adjusted IRR and IRD and associated 95% confidence intervals will be derived by weighting each stratum by the prevalence among the olodaterol cohort.

Documents

Study results

1222-0054_Synopsis_Redacted.pdf(347.32 KB)

Study publications

Rebordosa C, Farkas DK, Montonen J, Laugesen K, Voss F, Aguado J, Bothner U, Ro...

Data management

Data sources

Data source(s)

Danish registries (access/analysis)

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

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