

# 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

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## 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.

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## 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

Cristina Rebordosa

Study contact

[crebordosa@rti.org](mailto:crebordosa@rti.org)

## Primary lead investigator

Cristina Rebordosa

Primary lead investigator

## ORCID number:

0000-0002-8064-5997

# Study timelines

## Date when funding contract was signed

Planned: 18/08/2015

Actual: 18/08/2015

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## Study start date

Planned: 31/03/2020

Actual: 15/07/2019

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## Data analysis start date

Planned: 01/07/2020

Actual: 03/02/2020

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## 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

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### **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

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**Study type:**

Non-interventional study

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**Scope of the study:**

Safety study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**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

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## **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

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## **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).
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## **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)

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## **Special population of interest**

Other

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## **Special population of interest, other**

Patients with chronic obstructive pulmonary disease

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## **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.

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## **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)

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## Study publications

[Rebordosa C, Farkas DK, Montonen J, Laugesen K, Voss F, Aguado J, Bothner U, Ro...](#)

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# Data management

## Data sources

### Data source(s)

Danish registries (access/analysis)

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### 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

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

Data characterisation

**Data characterisation conducted**

Unknown