Combined bronchodilators in COPD and the risk of adverse cardio-pulmonary events: A population-based observational study (Comb Bronchodil in COPD and CardPulm AEs)

First published: 24/03/2014

Last updated: 02/07/2024

Study | Finalised

Administrative details

EU PAS number

EUPAS6134

Study ID

19335

DARWIN EU® study

No

Study countries

Canada

Study description

Background: Recent observational studies have reported possible arrhythmogenic effects with long-acting beta-agonists (LABA), while the long-acting anticholinergic tiotropium has been associated with cardiovascular and cerebrovascular events. Finally, pneumonia was the object of a recent signal in trials of LABAs submitted for marketing approval. Aim: To assess the potential cardio-pulmonary risk arising from the concurrent use of two long-acting bronchodilators as well as from monotherapy use of each of the long-acting bronchodilators. Methods: A series of population-based cohort studies, using both cohort and nested case-control analyses will be conducted using data from the United Kingdom's Clinical Practice Research Datalink (CPRD). The base cohort will consist of new users of long-acting bronchodilators from Jan 2002 until Aug 2012, age >= 55 with chronic obstructive pulmonary disease (COPD) and at least two years of baseline medical history information. The high-dimensional propensity score technique will be used to match new users of each long-acting bronchodilator and new users of two bronchodilators with comparable subjects from the base cohort, with one-year follow-up for outcomes of acute myocardial infarction, stroke, heart failure, arrhythmia and community acquired pneumonia. Data will be analysed using time-dependent Cox proportional hazard regression models and conditional logistic regression models.

Study status

Finalised

Research institutions and networks

Institutions

McGill University

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Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Samy Suissa

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 10/05/2013

Actual: 10/05/2013

Study start date

Planned: 01/11/2013

Actual: 24/03/2014

Data analysis start date
Planned: 01/02/2014

Actual: 25/03/2014

Date of interim report, if expected
Planned: 30/09/2014

Date of final study report
Planned: 31/05/2016

Actual: 31/05/2016

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Boehringer Ingelheim GmbH

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

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

Disease epidemiology

Data collection methods:

Secondary use of data

Main study objective:

Assess (1) the risk of acute myocardial infarction (AMI), stroke, heart failure, arrhythmia or pneumonia in combined LABA+tiotropium compared to mono treatment (2) incidence of those outcomes in LABA vs. tiotropium mono users (3) whether the risk increases for LABA or tiotropium use compared to non-use.'

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Nested case-control analysis

Study drug and medical condition

Medicinal product name, other

Spririva

Study drug International non-proprietary name (INN) or common name

TIOTROPIUM BROMIDE

Anatomical Therapeutic Chemical (ATC) code

(R03BB) Anticholinergics

Anticholinergics

Medical condition to be studied

Chronic obstructive pulmonary disease

Population studied

Short description of the study population

Chronic obstructive pulmonary disease patients who were new users of tiotropium or a a long-acting beta2-agonist (LABA) between September 25, 2003, and August 31, 2013, aged 55 years or older.

Age groups

- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

Special population of interest

Hepatic impaired

Immunocompromised

Renal impaired

Estimated number of subjects

160000

Study design details

Data analysis plan

Time-dependent Cox proportional hazard regression models will be used to estimate hazard ratios of the outcomes for the exposures of interest in both as-treated and intention-to-treat analyses. Conditional logistic regression models will be used to perform the nested case-control analyses assessing the effects of each long-acting bronchodilator, relative to non-use.

Documents

Study results

0205-0526--main-part-report-nis-existing-data_redacted.pdf (105.99 KB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

Clinical Practice Research Datalink

Data sources (types)

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