Comparative effectiveness of triple therapy in COPD: A new-user cohort study

First published: 19/10/2018

Last updated: 05/03/2019

Study Ongoing

Administrative details

EU PAS number

EUPAS26211

Study ID

28740

DARWIN EU® study

No

Study countries

☐ United Kingdom

Study description

The treatment of COPD involves multiple therapies, including long-acting bronchodilators (LAMAs and LABAs) and inhaled corticosteroids (ICS), with dual combinations of these drugs now formulated into single inhalers. Recently,

several single-inhaler triple therapies involving an LABA-LAMA-ICS combination are being developed and being tested for effectiveness in randomized trials. The TRILOGY and TRINITY trials compared a single-inhaler triple therapy with an LABA-ICS and a LAMA respectively and found greater benefit with triple therapy. The TRIBUTE trial and ongoing IMPACT trial also compare triple therapy with a dual long-acting bronchodilator regimen (LABA-LAMA). These trials, however, have methodological issues related to the deleterious effect of withdrawal of maintenance treatment at randomization, the use of run-in periods and the truncated follow-up at treatment discontinuation. Moreover, they represent a limited view of the patients who could potentially use these treatments, so that a real-world study of patients who are representative of clinical practice is of interest.As many of these drugs have been in use in separate inhalers for many years, an observational study of the comparative effectiveness of triple therapy is feasible and would provide useful data on the relative benefits of different combinations in the treatment of COPD. The intended audience is payers and prescribers. The results from the study will be published in the scientific literature.

Study status

Ongoing

Research institutions and networks

Institutions

McGill University

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Institution

Center for Clinical Epidemiology

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: 23/01/2017

Actual: 23/01/2017

Study start date

Planned: 10/11/2018

Actual: 10/11/2018

Data analysis start date
Planned: 12/11/2018

Actual: 12/11/2018

Date of final study report
Planned: 31/05/2019

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Boehringer Ingelheim International GmbH

Study protocol

Suissa_double_triple study.pdf (874.08 KB)

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 type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Main study objective:

To assess the effectiveness of maintenance treatment of COPD with the LABA-LAMA-ICS combination with a LABA-LAMA combination on the risk of COPD exacerbation and the safety on the incidence of community acquired pneumonia.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(R03AC19) olodaterol

olodaterol

(R03AL06) olodaterol and tiotropium bromide

olodaterol and tiotropium bromide

(R03BB04) tiotropium bromide

tiotropium bromide

(R03AL) Adrenergics in combination with anticholinergics incl. triple combinations with corticosteroids

Adrenergics in combination with anticholinergics incl. triple combinations with corticosteroids

Medical condition to be studied

Chronic obstructive pulmonary disease

Population studied

Age groups

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

6000

Study design details

Outcomes

The primary outcome event is the first COPD exacerbation to occur after cohort entry. The event is defined as a hospitalization for COPD (severe exacerbation) or the prescription of an oral corticosteroid, namely prednisolone (moderate exacerbation). The first secondary outcome is the rate of COPD exacerbations over the one-year follow-up. This outcome will be based on the number of hospitalizations and on the number of courses of treatment with an oral corticosteroid. A gap of at least 30 days between treatment courseswill be required to consider the exacerbations as separate

Data analysis plan

For the analysis of the primary objective, the Kaplan-Meier approach will be used with the matched cohort to estimate the crude 1-year cumulative incidence of severe and moderate COPD exacerbations for the two combination treatment groups. The primary comparative analysis will also be based on the matched cohort and a time-dependent Cox proportional hazard regression model to perform an as-treated analysis that assesses the effect of current use of LABA-LAMA-ICS combination versus the LABA-LAMA combination on the risk of a first COPD exacerbation. It will provide an estimate of the hazard ratio (HR) of a COPD exacerbation associated with LABA-LAMA-ICS use relative to LABA-LAMA use, along with 95% confidence intervals (CI). Current use will be defined as prescriptions dispensed within the 60-day period of the date defined by the risk set of the Cox model.

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

No