Comparative effectiveness of combination therapies in COPD

First published: 21/11/2017

Last updated: 01/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS21699

Study ID

28232

DARWIN EU® study

No

Study countries

United Kingdom

Study description

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

of ICS has increased disproportionately with respect to COPD treatment guidelines and may be inappropriate in a subset of these users. New evidence suggests that patients can be safely weaned off ICS, including the WISDOM trial that observed no difference in the risk of moderate or severe exacerbations between patients who discontinued ICS and those who continued receiving ICS. Moreover, discontinuation of ICS has been associated with a reduction in the risk of pneumonia. While most trials of the combination treatments have been conducted against the respective mono components or placebo, very few head-to-head trials versus other combinations have been performed to date. For example, the recent FLAME randomized trial reported that patients receiving the LABA-LAMA combination had fewer exacerbations than those receiving the LABA-ICS combination over a one-year follow-up period. Also, the ENERGITO trial reported significant improvements in lung function with a LAMA/LABA combination versus LABA/ICS in GOLD 2-3 patients after 6 weeks of treatment. These trials, however, represent a limited view of the patients who could potentially use these treatments, with many exclusion criteria based on for example stage of disease, lung function and exacerbation history, as well as exclusions of many patients during the screening and run-in periods. Thus, a real-world study of patients who are representative of clinical practice is of interest.

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: 23/01/2017

Actual: 23/01/2017

Study start date

Planned: 01/12/2017

Actual: 01/12/2017

Date of final study report

Planned: 31/08/2018

Actual: 01/10/2018

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Boehringer Ingelheim International 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:

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To assess the effectiveness of maintenance treatment of COPD with the combination of a LABA and the LAMA tiotropium (LABA-TIO) compared with the combination of a LABA and an ICS (LABA-ICS) on the time to COPD exacerbation.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(R03AC) Selective beta-2-adrenoreceptor agonists

Selective beta-2-adrenoreceptor agonists

(R03BA) Glucocorticoids

Glucocorticoids

(R03BB) Anticholinergics

Anticholinergics

Medical condition to be studied

Chronic obstructive pulmonary disease

Population studied

Short description of the study population

Patients with COPD aged 55 years or older who were new users of tiotropium, LABA or ICS between 1 January 2002 and 31 December 2015.

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

Other

Special population of interest, other

Chronic obstructive pulmonary disease (COPD) patients

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 courses will be required to consider the exacerbations as separate

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Data analysis plan

For the analysis of the primary objective, the matched cohort will be used to estimate the crude 1-year cumulative incidence of severe and moderate COPD exacerbations for the two combination treatment groups. The main 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-TIO combination versus the LABA-ICS 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-TIO use relative to LABA-ICS use, along with 95% confidence intervals (CI). Current use will be defined as a prescription dispensed within the 60-day period of the date defined by the risk set of the Cox model. This approach allows consideration of exposure as time-dependent, accounting for the changes in exposure during the follow-up.

Documents

Study results

Double-double Full Report 2018-10-01 Final_Abstract (Page 5-7)_Redacted.pdf (361.63 KB)

Data management

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