Effectiveness and Safety of Maintenance Treatment with Combination of Tiotropium and Olodaterol in comparison to Maintenance Treatment with a Combination of Inhaled Corticosteroids, Long-acting β2 Agonists and Long-acting Muscarinic Antagonists in COPD Patients

First published: 25/10/2019

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Study Finalised

Administrative details

EU PAS number

EUPAS31932

Study ID

31933

DARWIN EU® study

No

Study countries

United States

Study description

The treatment of COPD involves multiple therapies, including long-acting β2 agonists (LABA) (with and without inhaled corticosteroids (ICS) and long-acting muscarinic antagonists (LAMA), with combinations of these drugs now formulated into single inhalers. There are recommendations to restrict triple therapy use further, to only patients who are likely to respond to ICS (such as those with asthma-COPD overlap or patients with high risk of exacerbations and elevated blood eosinophils. There is an increasing body of evidence suggesting that ICS are particularly effective at reducing the incidence of COPD exacerbations in patients only with a very high blood eosinophil concentration, but not in normal levels. Hence there is a clear need for better evidence on specific patient populations upon which to base treatment recommendations. This non-interventional study aims to assess the comparative effectiveness of combination Tiotropium and Olodaterol (Tio+Olo) (FDC) compared to combination LAMA/LABA and ICS (fixed or open).

Study status

Finalised

Research institutions and networks

Institutions

HealthCore

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Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Daina Esposito

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 22/05/2019

Actual: 22/05/2019

Study start date

Planned: 01/11/2019

Date of final study report

Planned: 21/04/2020

Actual: 22/10/2020

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Boehringer ingelheim International GmbH

Study protocol

1237-0094_Prot_SAP_redacted.pdf (441.6 KB)

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Other study registration identification numbers and links

1237-0094; NCT04184297

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Healthcare resource utilisation

Safety study (incl. comparative)

Study design:

A claims-based incident new-user cohort design

Main study objective:

The primary objective is to compare the effectiveness of new use of maintenance therapy initiation with the combination treatment Tiotropium and Olodaterol (Tio+Olo) compared with new use of LABA/LAMA/ICS combination in COPD as the time to the first COPD exacerbation

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

SPIOLTO RESPIMAT

Medicinal product name, other

Stiolto/Spiolto

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

TIOTROPIUM BROMIDE

OLODATEROL

Anatomical Therapeutic Chemical (ATC) code

(R03AL06) olodaterol and tiotropium bromide

olodaterol and tiotropium bromide

(R03AA) Alpha- and beta-adrenoreceptor agonists

Alpha- and beta-adrenoreceptor agonists

(R03B) OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS

OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS

Medical condition to be studied

Chronic obstructive pulmonary disease

Population studied

Short description of the study population

Inclusion Criteria:

1. At least one prescription for Tio+Olo or a LABA/LAMA/ICS combination between 1 January 2013 and 31 March 2019.

a. For Tio+Olo users, the first dispensing of Tio+Olo will be defined as the index date.

b. LABA/LAMA/ICS use can occur either in free or fixed combinations.

The first date when all three medications are used based on either concurrent or overlapping dispensings in the pharmacy claims data will be defined as the

index date.

2. At least one diagnosis of COPD at any time prior to the index date.

3. At least one year of continuous medical and pharmacy health plan eligibility prior to the index date will be required to allow a baseline period for the covariates and identification of new use of the study drugs.

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)

Estimated number of subjects

4.000

Study design details

Setting

The HealthCore Integrated Research DatabaseSM (HIRD)

Outcomes

Severe exacerbation as hospitalization with a principal discharge diagnosis of COPD.Moderate exacerbation defined as ED visit with a discharge diagnosis of COPD and/or dispensing of an antibiotic and an oral corticosteroid on the same day

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Data analysis plan

Patient characteristics at baseline in patients treated with Tio+Olo and patients treated with LABA/LAMA/ICS will be described using standard descriptive statistics. High-dimensional propensity scores including both pre-specified and data-derived variables will then be calculated. We will use fine stratification and reweighting of the exposure propensity score to control for measured covariates. Cox proportional hazard regression model will be used to perform an as-treated analysis that assesses the effect of current use of LABA-LAMA-ICS combination versus the Tio+Olo 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 Tio+Olo use, along with 95% confidence intervals (CI).

Summary results

There were 2,864 Tio+Olo and 24,326 LABA/LAMA/ICS users meeting all study criteria. Users of Tio+Olo were slightly younger (mean age in years 65.4 (SD 10.5) vs 66.8 (SD 10.7)), but no notable difference was seen in gender distribution between the cohorts. They tended to be more often insured commercially rather than through Medicare, and more often resided in the Southern US when compared to LABA/LAMA/ICS users. No Tio+Olo users had index dates prior to 2015. Tio+Olo users had a lower mean number of COPD medications used at baseline, and fewer had baseline COPD exacerbations. Data on race, ethnicity, and lifestyle factors, such as smoking, were not available. In the overall population prior to stratification and reweighting, COPD exacerbations were
observed for 335 Tio+Olo and 6,704 LABA/LAMA/ICS users. This corresponded to an IR per 1,000 person-days of 1.32 (1.18-1.47) for Tio+Olo and 1.86 (1.82-1.90) for LABA/LAMA/ICS. After reweighting, Tio+Olo users had a slightly lower risk of exacerbation than LABA/LAMA/ICS users (aHR 0.85, 0.76-0.96), however risks were similar after excluding patients with exacerbation within 30 days prior to the index date (aHR 1.05, 0.92-1.18).

Community acquired pneumonia was observed in 68 patients in the Tio+Olo cohort and in 1,863 patients in the LABA/LAMA/ICS cohort (IR per 1,000 person-days of 0.25 (0.20-0.32) for Tio+Olo and 0.24 (0.22-0.25) for LABA/LAMA/ICS. Tio+Olo users had a numerically lower aHR of pneumonia than LABA/LAMA/ICS users (aHR 0.83, 0.64-1.07). For both outcomes, stratification by high vs. low exacerbation yielded results that were questionably interpretable given strongly suspected residual confounding by disease severity. Healthcare utilization was lower for Tio+Olo than for LABA/LAMA/ICS users.

Documents

Study results

1237-0094_Abstract (1).pdf (175.48 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 sources (types)

Administrative healthcare records (e.g., claims)

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