Comparing the Incidence between Tiotropium and ICS/LABA in Real world Use in South Korea (CITRUS study)

First published: 15/11/2019

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Study Ongoing

Administrative details

EU PAS number

EUPAS32329

Study ID

40660

DARWIN EU® study

No

Study countries

Korea, Republic of

Study description

Non-interventional study to compare effectiveness of LAMA to fixed dose combination of inhaled corticosteroid and long-acting beta agonists (ICS/LABA) in patients with chronic obstructive pulmonary disease (COPD) based on existing data

Study status

Ongoing

Research institutions and networks

Institutions

Soeun Lee

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Soeun Lee Lee

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 20/12/2019

Actual: 08/06/2020

Study start date
Planned: 24/12/2019

Actual: 03/03/2020

Data analysis start date
Planned: 07/01/2020

Actual: 06/04/2021

Date of interim report, if expected
Planned: 02/06/2020

Date of final study report
Planned: 30/06/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Boehringer-ingelheim

Study protocol

0205-0542_CTP_final-rule_Proposal_new_Redacted.pdf (819.97 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

0205-0542

NCT04172701

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)

Data collection methods:

Secondary use of data

Study design:

Retrospective cohort study

Main study objective:

To see the effectiveness of tiotropium compare to ICS/LABA in terms of prevention of COPD acute exacerbation and reducing incidence of pneumonia. The study will be conducted in a general practice setting, Korea National Health Insurance claim data & mortality data from the Bureau of Statistics, which includes computerized medical records of more than half million patients in South Korea

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Prescription event monitoring

Study drug and medical condition

Medicinal product name, other

Spiriva

Medical condition to be studied

Pneumonia

Death

Tuberculosis

Additional medical condition(s)

COPD exacerbations, lung cancer, non-tuberculosis mycobacteria (NTM) lung disease

Population studied

Short description of the study population

COPD patient aged ≥55 years with a prescription of LAMA or ICS/LABA during the selection period and received LAMA or ICS/LABA more than twice within 12 months from the index date were identified for the study.

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

10.000

Study design details

Setting

Korean national health insurance claims data

Outcomes

The primary outcomes were pneumonia, COPD exacerbations, and time to initiating triple combination therapy from the index date, and the secondary outcomes were the healthcare utilization (HCRU), all-cause mortality, lung cancer, tuberculosis (TB), and non-tuberculosis mycobacteria (NTM).

Data analysis plan

All analyses will be performed with SAS and R . All variables will be summarized descriptively through displays of mean(± standard deviations), median, and ranges for continuous variables, and frequency distributions of categorical variables. To address the imbalance of potential confounders between LAMA ICS/LABA groups, we matched treatment groups using propensity scores estimated as by multiple logistic regression analysis based on as age, sex, socioeconomics status, Charlson Comorbidity Index, and asthma, and history of COPD exacerbation. Cox proportional hazards regression analyses will be used to estimate hazard ratios (HRs) HRs and 95% confidence intervals (95% CIs) for all outcomes. For (possibly) repeating events (such as exacerbation event) additionally a Poisson regression model will be fitted for the number of events (taking into account the matching). Detailed methodology for summary and statistical analyses of data in this study will be documented in an SAP.

Summary results

After matching with propensity scores, a total of 4,888 patients were selected for this study. The mean (SD) age of LAMA group (N=2,444) was 69.57 (7.85) whereas ICS/LABA group (N=2,444) was 69.73 (7.91) after matching. Among LAMA group, 1,854 (75.86%) was male and 590 (24.14%) was female. Similarly, 1,822 (74.55%) was male and 622 (25.45%) was female in ICS/LABA group. ICS/LABA group showed significantly higher risks for pneumonia events (overall

hazard ratio [HR] 1.475, 95% confidence interval [CI] 1.308-1.663; inpatient HR 1.517, 95% CI 1.314-1.751; outpatient HR 1.358, 95% CI 1.187-1.554) , COPD exacerbations (overall HR 1.145, 95% CI 1.059-1.237; moderate exacerbations HR 1.151, 95% CI 1.057-1.253; severe exacerbations HR 1.166, 95% CI 1.022-1.330) , and escalation to triple combination (HR 1.601, 95% CI 1.404-1.826) compared to LAMA group, whereas no significant difference between study groups were observed for lung cancer, pneumonia-related or all-cause mortality, TB, and NTM. LAMA significantly delayed the time to initiation of triple combination therapy (LAMA 450.44±510.56; ICS/LABA 358.12±418.70), and patients of LAMA group spent less on medical care on average than those on ICS/LABA group.

Documents

Abstract of study report

0205-0542_Synopsis.pdf (278.98 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), other

Korea National Health Insurance Claim Database (NHID) from National Health Insurance Service (NHIS) and mortality data from the Bureau of Statistics

Data sources (types)

Administrative healthcare records (e.g., claims)

Death registry

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