Long-Term Post-Marketing Observational Study of the Safety of Roflumilast

First published: 22/08/2016

Last updated: 02/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS14852

Study ID

50538

DARWIN EU® study

No

Study countries

- [ ] Germany
- [ ] Norway
- [ ] Sweden
- [ ] United States

Study description

Chronic obstructive pulmonary disease (COPD) is a leading cause of death. Takeda Development Centre (Europe) Ltd (formerly Nycomed) received central marketing authorization in the EU in July 2010 and regulatory approval in Canada in November 2010 for its selective phosphodiesterase-4 (PDE4) inhibitor roflumilast (DAXAS®), which is available as 500µg tablets (once daily) for maintenance treatment of severe COPD associated with chronic bronchitis in adults with a history of frequent exacerbations as add on to bronchodilator treatment. Roflumilast is contraindicated in patients with hypersensitivity to the tablet ingredients and in patients with moderate to severe liver impairment. Since roflumilast is used for maintenance treatment, a long-term safety assessment exceeding 12 months was requested as a condition of approval for marketing in the EU. During the approval process, Takeda as the Marketing Authorisation Holder (MAH) for roflumilast, committed to the European Medicines Agency (EMA) to perform a database study, and proposed that the study be conducted in large, unselected COPD populations, reflecting the use of roflumilast in a real-life setting. Established electronic health care databases in countries where roflumilast is on the market and data on a meaningful number of roflumilast treated patients is captured will be the source on which to base this Post-Authorisation Safety Study (PASS). Due to the sponsorship transfer that occurred in 2015, study is now sponsored by AstraZeneca. The study is conducted by independent investigators qualified in epidemiology. The patient data will remain the properties of the respective database owners, and AstraZeneca will not have direct access to the data but will be co-owner of the results derived from these data, together with the respective investigators. The Lead Investigator will lead the team of investigators, each of whom is responsible for the conduct of the study.

Study status

Finalised

Research institutions and networks

Institutions

Real World Solutions, IQVIA

☐ Netherlands

☐ United Kingdom (Northern Ireland)

First published: 28/04/2011

Last updated: 22/03/2024

Institution **Other** **ENCePP partner**

Leibniz Institute for Prevention Research and Epidemiology - BIPS

☐ Germany

First published: 29/03/2010

Last updated: 26/02/2024

Institution **Not-for-profit** **ENCePP partner**

Epi Research Oy Finland, Quintiles Real World and Late Phase Research (RWLPR), EMR Data and Analytics USA

Contact details

Study institution contact

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Study contact

ClinicalTrialTransparency@astrazeneca.com

Primary lead investigator

Edeltraut Garbe

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 01/07/2010

Study start date

Planned: 13/10/2013

Actual: 30/03/2013

Data analysis start date

Planned: 31/01/2020

Actual: 30/03/2013

Date of interim report, if expected

Planned: 31/10/2017

Actual: 31/10/2017

Date of final study report

Planned: 31/12/2022

Actual: 16/12/2022

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

AstraZeneca

Study protocol

RO-2455-403-RD_ProtocolVersion2.4-31Jul13.pdf (285.69 KB)

D7120R00003_ProtocolVersion3_updated20170207.pdf (443.37 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 1 (imposed as condition of marketing authorisation)

Regulatory procedure number

D7120R00003

Other study registration identification numbers and links

D7120R00003

Methodological aspects

Study topic:

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

The objective of this study is to evaluate the long-term safety of roflumilast in the treatment of COPD, with focus primarily on all-cause mortality.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Observational study

Study drug and medical condition

Medical condition to be studied

Chronic obstructive pulmonary disease

Population studied

Short description of the study population

The study population comprised of patients aged 40 years or older diagnosed with chronic obstructive pulmonary disease (COPD) exposed or unexposed to the treatment of roflumilast identified through the databases in Germany, Sweden, the United States, and Norway.

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

Patients with chronic obstructive pulmonary disease

Estimated number of subjects

21812

Study design details

Outcomes

The primary outcome for this study is all-cause 5 year mortality, Death by suicide or hospitalization due to suicide attempt, hospitalization for any cause, major cardiovascular events leading to hospitalization, hospitalization related to respiratory disease, new diagnosis of depression, new diagnosis of cancer,

hospitalization due to diarrhea of non-infectious origin, abnormal unexplained weight loss, new diagnosis of tuberculosis or hepatitis B or C.

Data analysis plan

The primary outcome (5-year all cause mortality) will be evaluated by a Cox proportional hazards regression model for counting processes, which allow the follow-up time to be divided into several periods and therefore control for baseline and time-dependent covariates, using the full observational period of available data, i.e. up to 9 years of follow up. The Cox proportional hazards regression will take into account the fact that individual matching was performed (based on age, sex and propensity score) by considering the exposed patient and his/her matched controls as one stratum and including this as a stratum in the Cox proportional hazards model. Additional variables will be included in the model if available.

Documents

Study results

DAXAS Final Study Report_Redacted_Reduced.pdf (1.85 MB)

Study report

DAXAS Final Study Report Addendum (NOR)_Redacted.pdf (8.6 MB)

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)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

German Pharmacoepidemiological Research Database

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Other

Data sources (types), other

Discharge registry, death registry, cancer registry, and registries holding socio-demographic data

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