DARWIN EU® - Co-prescribing of endothelin receptor antagonists (ERAs) and phosphodiesterate-5 inhibitors (PDE-5is) in pulmonary arterial hypertension (PAH)

First published: 07/08/2023

Last updated: 25/09/2024

Study Finalised

Administrative details

EU PAS number

EUPAS106052

Study ID

106394

DARWIN EU® study

Yes

Study countries

- [ ] Estonia
- [ ] France
- [ ] Germany

United Kingdom

Study description

Research question: What is the utilization pattern of endothelin receptor antagonists (ERAs) and phosphodiesterase-5 inhibitors (PDE-5is) in pulmonary arterial hypertension (PAH)?

Study objectives:
Objective 1: To estimate proportions of patients with newly diagnosed pulmonary arterial hypertension (PAH) who initiate treatment with endothelin receptor antagonists (ERAs) or phosphodiesterase-5 inhibitors (PDE-5is), either as monotherapy or in combination, during the period from January 1, 2012, to December 31, 2022.
Objective 2: To estimate the duration of prescription for ERAs and PDE-5is in patients with newly diagnosed PAH between January 1, 2012, and December 31, 2022.
Objective 3: To describe the prescription patterns and sequences of ERAs and PDE-5is in patients with newly diagnosed PAH between January 1, 2012, and December 31, 2022.
Objective 4: To estimate the proportion of patients with newly diagnosed PAH who experience specific events of interest, namely: cardiovascular hospitalization, all-cause hospitalization, and death, after initiating treatment with ERAs and PDE-5isPAH between January 1, 2012, and December 31, 2022.

Study status

Finalised

Research institutions and networks

Institutions

Clinical Practice Research Datalink (CPRD)

United Kingdom

First published: 15/03/2010

Last updated: 17/01/2025

Institution | Laboratory/Research/Testing facility | ENCePP partner

IQVIA NL, Real-World-Evidence

Netherlands

First published: 25/11/2022

Last updated: 21/03/2025

Institution | Other | ENCePP partner

Bordeaux University Hospital (CHU de Bordeaux)

France

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Hospital/Clinic/Other health care facility

Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University

of Oxford

United Kingdom

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility

University of Tartu

Estonia

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Educational Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Johnmary Arinze

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 05/04/2023

Actual: 05/04/2023

Study start date
Planned: 01/01/2012

Actual: 01/01/2012

Date of final study report
Planned: 17/11/2023

Actual: 20/11/2023

Study protocol

Study Protocol P2 C1-003 Version 2.1 final.pdf (1.5 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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:

Disease epidemiology

Drug utilisation

Main study objective:

To describe the patient characteristics, treatment patterns of ERAs/PDE-5is, and the proportion of patients with newly diagnosed PAH who experience the events of interest (cardiovascular hospitalization, all-cause hospitalization, and death) after initiating treatment with ERAs and PDE-5is.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(C02KX01) bosentan

bosentan

(C02KX02) ambrisentan

ambrisentan

(C02KX03) sitaxentan

sitaxentan

(C02KX04) macitentan

macitentan

(G04BE03) sildenafil

sildenafil

(G04BE08) tadalafil

tadalafil

Medical condition to be studied

Pulmonary arterial hypertension

Population studied

Age groups

Infants and toddlers (28 days – 23 months)

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

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

13800000

Study design details

Outcomes

Cardiovascular hospitalisation, all-cause hospitalisation, and death.

Data analysis plan

The number and % of patients receiving each of a pre-specified list of PAH treatments and treatment combinations will be described. A treatment pattern analysis will be conducted to describe the sequence of prescribing of the specific ERAs/PDE-5is following diagnosis. Index date will be the date of diagnosis of PAH. Sunburst plots and Sankey diagrams will be used to describe treatment patterns and sequences over time. Large-scale patient-level characterisation will be conducted to describe age and sex at time of PAH diagnosis. The medical history will include clinical symptoms and signs, comorbidities, and important factors possibly related to PAH diagnosis. We will also report the proportion of patients with outcomes of interest. Patient-level ERAs/PDE-5is use: Patient-level features will be characterized, and the treatment duration of interest will be estimated. For all analyses a minimum cell count of 5 will be used when reporting results, with any smaller counts obscured.

Documents

Study report

DARWIN EU_D2.2.4_Report_P2-C1-003_ERAS & PDE-5is in PAH_v2.1_Clean (1).pdf (2.16 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)

Clinical Data Warehouse of the Bordeaux University Hospital

Clinical Practice Research Datalink (CPRD) GOLD

Estonian Biobank

IQVIA Disease Analyzer Germany

Data sources (types)

Electronic healthcare records (EHR)

Other

Data sources (types), other

Hospital database Biobank

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No