DARWIN EU® - Background rates of serious adverse events to contextualise safety assessments in clinical trials and non-interventional studies in adolescent and adult patients with severe asthma

First published: 14/03/2023

Last updated: 25/09/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/104146

EU PAS number

EUPAS103936

Study ID

104146

DARWIN EU® study

Yes

Study countries

- [ ] Estonia
- [ ] Netherlands
- [ ] Spain
- [ ] United Kingdom

Study description

During the evaluation of the safety results of a clinical trial in patients with severe asthma, differences in rates of serious adverse events were observed in the experimental treatment arm compared to the control arm. In order to contextualize these differences, a non-interventional study was requested to generate background rates of selected health outcomes in patients with severe asthma, with a disease definition that follows recently conducted clinical trials. By means of a retrospective cohort study using routinely-collected health data from 5 databases we will investigate the following: (i) To estimate the rate of mortality due to any cause stratified by calendar year as well as pre-pandemic (2015-2019) and pandemic (2020-2022), sex, age and country/database. (ii) To estimate the rate of mortality due to fatal infections stratified by calendar year as well as pre-pandemic (2015-2019) and pandemic (2020-2022), sex, age and country/database. (iii) To estimate the rate of mortality due to cardiovascular events stratified by calendar year as well as pre-pandemic (2015-2019) and pandemic (2020-2022), sex, age and country/database. (iv) To estimate the incidence rate of serious cardiovascular events (but not necessarily leading to death) stratified by calendar year as well as pre-pandemic (2015-2019) and pandemic (2020-2022), sex, age and country/database.

The study population will consists of all individuals present in the database in the period between 01/01/2015 and 31/12/2022, with at least 1 year of prior history, being diagnosed with severe asthma and fulfilling inclusion and exclusion criteria.

The study period is from 2015-2022. Variables of interest will consist of

outcomes, comorbidity, lifestyle factors, measurements and drug exposure data. Participating databases have their data mapped to the OMOP CDM. Participating databases are SIDIAP, IPCI, CPRD Gold, IMASIS and the Estonian Biobank.

Study status

Finalised

Research institutions and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution **Educational Institution** **ENCePP partner**

Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

Spain

First published: 05/10/2012

Last updated: 23/02/2024

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Parc de Salut Mar Barcelona (PSMAR)

Spain

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Hospital/Clinic/Other health care facility

University of Tartu

Estonia

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Educational Institution

Oxford University, UK

Networks

Data Analysis and Real World Interrogation Network (DARWIN EU®)

- [ ] Belgium
- [ ] Croatia
- [ ] Denmark
- [ ] Estonia
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Greece
- [ ] Hungary
- [ ] Italy
- [ ] Netherlands
- [ ] Norway
- [ ] Portugal
- [ ] Spain
- [ ] Sweden
- [ ] United Kingdom

First published: 01/02/2024

Last updated: 30/04/2025

Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Katia Verhamme

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 19/12/2022

Actual: 19/12/2022

Study start date

Planned: 01/01/2015

Actual: 01/01/2015

Date of final study report

Planned: 01/05/2023

Actual: 17/11/2023

Sources of funding

- EMA
- EU institutional research programme

Study protocol

D2.2.3_DARWIN_EU_Study_Protocol_C3-001_V4.0.pdf(1006.57 KB)

D2.2.3_DARWIN_EU_Study_Protocol_C3-001_V4.1.pdf(1 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

Main study objective:

To estimate the mortality rate (all cause and mortality related to infections or cardiovascular events) and the incidence rate of serious cardiovascular events stratified by calendar year, sex, age and country/database during the study period 2015-2022.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medical condition to be studied

Asthma

Additional medical condition(s)

Severe asthma

Population studied

Age groups

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

80000

Study design details

Outcomes

Mortality and cause specific mortality namely mortality related to cardiovascular events and mortality related to infections. Serious cardiovascular events consisting of: acute myocardial infarction, acute coronary syndrome/ischemic heart disease, stroke and hospitalisation for heart failure.

Data analysis plan

Annual incidence rate of the outcomes of interest were calculated stratified by country/database, calendar year, age and sex, within the cohort of severe asthma patients. For the calculation of the incidence rate, the numerator was the number of patients newly diagnosed with the respective outcomes of interest and the denominator consisted of the number of person-years of the severe asthma patients fulfilling the inclusion and exclusion criteria at risk. In addition, survival time to all-cause mortality was estimated using Kaplan Meier analysis.

Documents

Study report

DARWIN _EU_D2.2.4_Study_report_P1-C3-001_Severe_asthma_v2.1_Public.pdf (1.91 MB)

Data management

Data sources

Data source(s)

The Information System for Research in Primary Care (SIDIAP)

Clinical Practice Research Datalink

Integrated Primary Care Information (IPCI)

Estonian Biobank

Institut Municipal d'Assistència Sanitària Information System

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Data sources (types)

Electronic healthcare records (EHR)

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