An Observational Multi-Country Post-Authorisation Safety Study to Evaluate the Risk of Serious Adverse Cardiovascular Events in Adolescent and Adult Patients with Severe Asthma taking Tezepelumab (TRESPASS)

First published: 24/05/2024

Last updated: 11/12/2025

Study Planned

Administrative details

EU PAS number

EUPAS1000000169

Study ID

1000000169

DARWIN EU® study

No

Study countries

Denmark

France

Germany

United States

Study description

The study is a non-interventional, longitudinal, population-based, cohort design using multiple secondary data sources from Denmark, France, Germany, and the United States of America (USA). The study will describe and compare the risk of adverse cardiovascular outcomes in adolescent and adult patients with severe asthma who initiated tezepelumab and in matched patients unexposed to tezepelumab (treated with standard of care for severe asthma).

Study status

Planned

Research institutions and networks

Institutions

IQVIA

United Kingdom

First published: 12/11/2021

Last updated: 22/04/2024

Institution | **Non-Pharmaceutical company** | **ENCePP partner**

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Efe Eworuke

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/07/2023

Actual: 13/07/2023

Study start date

Planned: 01/05/2025

Data analysis start date

Planned: 01/09/2025

Date of interim report, if expected

Planned: 30/04/2026

Date of final study report

Planned: 31/05/2030

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

ASTRAZENECA PHARMACEUTICALS LP

Study protocol

TRESPASS - Protocol Redacted.pdf (2.11 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Non-interventional, longitudinal, population-based, cohort design using secondary data sources. It will use a descriptive and a prevalent new-user design for comparative analyses of serious cardiovascular events outcomes in patients with severe asthma exposed and unexposed to tezepelumab.

Main study objective:

To estimate and compare the risk of a composite of major adverse cardiovascular events (MACE) in adolescent and adult patients with severe asthma who initiated tezepelumab vs. matched patients unexposed to tezepelumab (treated with standard of care for severe asthma).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

TEZSPIRE

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

TEZEPELUMAB

Anatomical Therapeutic Chemical (ATC) code

(R03DX11) tezepelumab

tezepelumab

Medical condition to be studied

Asthma

Population studied

Short description of the study population

The source population will consist of patients with a diagnosis of asthma receiving tezepelumab or high-intensity SOC treatment for severe asthma at any point during the study inclusion period. From this source population, the exposed study population (i.e. patients who initiate tezepelumab treatment) and the unexposed study population (i.e. comparable patients who are unexposed to tezepelumab) will be identified. Inclusion of patients who are unexposed to tezepelumab will be based on the presence of a trigger exposure designed to mirror the start of tezepelumab in exposed patients (i.e. augmentation or change of the non-biologic high-intensity treatment that does not represent treatment de-escalation). Unexposed patients are required to have matching clinical and treatment characteristics to the exposed patients, including a similar baseline risk of cardiovascular events.

Age groups

- Adolescents (12 to < 18 years)
- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Estimated number of subjects

95574

Study design details

Setting

A total of four large longitudinal patient-level data sources have been selected for this study, representing four countries: Denmark, France, Germany, and USA.

The included data sources are:

1. Danish National Registries (Denmark)
2. French National Health Data System (SNDS) (France)
3. Statutory Health Insurance (SHI) (Germany)
4. Carelon (USA)

The start of the study period corresponds to tezepelumab market launch date in each country of interest (i.e. between 2022 – 2023). An approximately five-year study period is planned in each country, with an anticipated last date of study

period in 2029.

Comparators

Patients with severe asthma on Standard of Care, i.e., on high-intensity treatment, defined as: concomitant use of high dose ICS + LABA; concomitant use of medium to high dose ICS + low dose OCS at least 50% of the past year; concomitant use of medium to high dose ICS + LABA + low dose OCS at least 50% of the past year; concomitant use of medium to high dose ICS + LABA + third controller other than low dose OCS; biologics.
Comparators must additionally present a trigger exposure, defined as change of the non-biologic high-intensity treatment that does not represent treatment de-escalation. For the comparative analyses, patients exposed to non-tezepelumab biologics will be excluded from the comparator group.

Outcomes

The primary outcome of interest is the composite outcome MACE, consisting of non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death.
The secondary outcomes of interest are a composite of four serious adverse cardiovascular events, including arrhythmias, coronary artery disease, heart failure and myocardial disorders, and the individual components of the primary and secondary composite outcomes.

Data analysis plan

A full description of the analytical approach will be developed and described in the SAP. Details on data derivations, category definitions, analyses, handling of missing data, and presentation of the study results will be provided in SAP. SAP will be finalised prior to the conduct of the study analyses. All study results will be presented separately for each country in the study reports, as appropriate when data become available. The final study report will include all descriptive, comparative, exploratory and sensitivity analyses as well as the meta-analysis

for all the data sources.

Documents

Study report

d5180r00024-pass-study-progress-report_10Sep2025_Redacted.pdf (5.77 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)

Système National des Données de Santé (French national health system main database)

The Information System for Research in Primary Care (SIDIAP)

Data source(s), other

- National Registers and Register of Selected Chronic Diseases and Severe Mental Disorders (RUKS), Denmark
- Statutory Health Insurance Claims (SHI), Germany
- Carelon, USA

- PharMetrics Plus, USA
- National Registers, Finland

Data sources (types)

Administrative healthcare records (e.g., claims)

Non-interventional study

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name (other)

TRESPASS CDM

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No