DARWIN EU® - Drug utilisation study in individuals with cystic fibrosis in Europe

First published: 14/08/2025

Last updated: 26/09/2025

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000708

Study ID

1000000708

DARWIN EU® study

Yes

Study countries

- [ ] France
- [ ] Germany
- [ ] Italy
- [ ] Norway
- [ ] Spain
- [ ] United Kingdom

Study description

Cystic fibrosis (CF) is a rare, life-limiting genetic disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, resulting in multi-organ dysfunction primarily affecting the respiratory and gastrointestinal systems. While symptomatic treatments remain essential, recent advances in CFTR modulators represent a shift toward targeted therapies addressing the underlying protein defect.

Emerging evidence highlights both clinical benefits and potential safety concerns, including psychiatric adverse effects.

This study aims to generate real-world evidence on treatment utilisation and safety outcomes among individuals with a CF diagnosis across Europe.

Study status

Ongoing

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**

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

Ellen Gerritsen

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 09/04/2025

Actual: 09/04/2025

Study start date

Planned: 25/07/2025

Actual: 25/07/2025

Date of final study report

Planned: 28/11/2025

Sources of funding

- EMA

Study protocol

DARWIN EU_Protocol_P4-C1-008_DUS CF_V3.0.pdf (1.2 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 topic:

Herbal medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Data collection methods:

Secondary use of data

Study design:

A cohort study will be conducted using routinely collected health data from 7 data sources.

Main study objective:

1. To describe treatment patterns of CFTR modulators at the active ingredient level, from the first recorded CFTR modulator treatment after CF diagnosis until end of follow up, including the proportion of individuals switching between CFTR modulators, overall and stratified by paediatric and adult populations.
2. To characterise individuals initiating CFTR modulator therapy, overall (any CFTR modulator) and by active ingredient, in terms of demographics, and use of other CF related therapies, overall and stratified by paediatric and adult populations.
3. To characterise CFTR modulator use, overall (any CFTR modulator) and by active ingredient, including treatment duration, cumulative dose, number of repeated prescriptions, overall and stratified by paediatric and adult populations.
4. To estimate the background incidence rates of pre-specified adverse events of special interest (cataract, depression, anxiety, and haemoptysis) in the CFTR modulator treated individuals, overall (any CFTR modulator) and by active ingredient level, presented overall and stratified by paediatric and adult populations and by calendar year.
5. To measure the incidence of pulmonary exacerbation following CFTR modulator initiation, overall (any CFTR modulator) and by active ingredient, presented overall and stratified by paediatric and adult populations, and time since CFTR modulator initiation (one- and two-years post-initiation).

Study Design

Non-interventional study design
Cohort

Study drug and medical condition

Medicinal product name, other

Ivacaftor

Ivacaftor and lumacaftor

Ivacaftor and tezacaftor

Ivacaftor, tezacaftor and elexacaftor

Ursodeoxycholic acid

Multienzymes (lipase, protease etc.)

Dornase alfa (desoxyribonuclease)

Mannitol, acetylcysteine, ambroxol

Salbutamol

Tobramycin

Proton pomp inhibitors

Medical condition to be studied

Cystic fibrosis

Population studied

Short description of the study population

The study population (objectives 1 - 5) will include individuals with first recorded CFTR modulator treatment in the period between 1st of January 2015 and 31st of December 2024 (or latest date available) after CF diagnosis. Only individuals with first recorded CFTR modulator treatment at least 180 days prior to the end of data availability in each database will be included. Eligible individuals must have at least one year of data visibility prior to the first recorded CFTR modulator treatment and no use of CFTR modulator treatment before the index date. This requirement of one year of prior data history will not hold for children below 1 year of age.

For objectives 4 and 5, additional exclusion criteria will be applied on an event-specific basis. Individuals will be excluded from the analysis of a specific adverse event if they have a record of that condition within one year before the index date (objective 4). This includes:
• A SNOMED disease code for depression (for exclusion from the depression outcome), a SNOMED disease code for anxiety (for exclusion from the anxiety outcome), a SNOMED disease code for cataract (for exclusion from the cataract outcome), a SNOMED disease code for haemoptysis (for exclusion from the haemoptysis outcome).
Additionally, individuals with a SNOMED disease code of upper or lower respiratory tract infection, requiring treatment with antibiotics or antiviral medications within 30 days prior to the start of follow-up, will be excluded from the analysis of pulmonary exacerbation (objective 5).

Age groups

- **In utero**
- **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)

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)

IATROS

Clinical Data Warehouse of the Bordeaux University Hospital

Clinical Practice Research Datalink (CPRD) GOLD

IQVIA Disease Analyzer Germany

Norwegian Linked Health registry at University of Oslo

Research Repository @Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico

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Data source(s), other

Hospital Universitario 12 de Octubre

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