

# Utilisation Patterns and Real-World Effects of Tezacaftor and Ivacaftor Combination Therapy (TEZ/IVA) in Patients With Cystic Fibrosis (CF)

**First published:** 18/07/2019

**Last updated:** 03/03/2025

Study

Finalised

## Administrative details

### EU PAS number

EUPAS30550

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### Study ID

39005

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### DARWIN EU® study

No

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### Study countries

☐ France

☐ Germany

☐ Ireland

☐ United Kingdom

☐ United States

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## **Study description**

Cystic fibrosis (CF) is an autosomal recessive disease with serious, chronically debilitating morbidities, and high premature mortality. Tezacaftor (TEZ) and ivacaftor (IVA) combination therapy is currently indicated for treatment of CF in patients 12 and older in the EU and 6 years and older in the US who have specified CFTR mutations and is intended for chronic and potentially lifelong use. In both the EU and the US, the indicated population includes patients who have two copies of the F508del mutation. Additionally in the European Union (EU), TEZ/IVA is indicated for patients heterozygous for the F508del mutation and one of 14 mutations in which the CFTR protein shows residual activity (referred hereafter as residual function RF mutations), in the United States (US) TEZ/IVA is also indicated for patients with at least one copy of 26 RF mutations. Information regarding the safety profile of the therapy under the real-world conditions of use will be informative to patients, caregivers, prescribers, and payers. Existing CF registries provide an established source to obtain these data. The primary objectives of this five-year observational cohort study are to evaluate: 1) safety outcomes in patients with CF who have mutations that are indicated for TEZ/IVA, and are treated with TEZ/IVA, 2) CF disease progression in patients who have mutations that are indicated for TEZ/IVA, and are treated with TEZ/IVA, 3) the frequency and outcome of pregnancies in female patients  $\geq 14$  years, have mutations that are indicated for TEZ/IVA, and are treated with TEZ/IVA, and 4) drug utilisation / potential off-label use of TEZ/IVA. This study will use data collected by CF patient registries in the US, Germany, and UK (all study objectives), as well as Ireland and France (drug utilisation objective only). Within-cohort evaluation of outcomes in the pre- and post-treatment periods will be performed (US, Germany, UK).

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## Study status

Finalised

## Research institutions and networks

### Institutions

[Vertex Pharmaceuticals](#)

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**Institution**

[CF Registry of France, CF Registry of Ireland,  
German CF Register, UK CF Registry, US CFF  
Patient Registry](#)

### Contact details

#### Study institution contact

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**Study contact**

[julie\\_bower@vrtx.com](mailto:julie_bower@vrtx.com)

#### Primary lead investigator

Julie Bower

Primary lead investigator

## Study timelines

### **Date when funding contract was signed**

Planned: 30/06/2019

Actual: 30/06/2019

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### **Study start date**

Planned: 30/06/2019

Actual: 30/06/2019

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### **Date of interim report, if expected**

Planned: 31/12/2019

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### **Date of final study report**

Planned: 31/12/2023

Actual: 02/12/2022

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Vertex Pharmaceuticals Incorporated

## Study protocol

## Regulatory

### **Was the study required by a regulatory body?**

Yes

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

EU RMP category 3 (required)

## Methodological aspects

### Study type

#### Study type list

##### **Study topic:**

Disease /health condition

Human medicinal product

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##### **Study type:**

Non-interventional study

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##### **Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Safety study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**Main study objective:**

To evaluate: 1. Safety outcomes in CF patients with mutations indicated for TEZ/IVA, and treated with TEZ/IVA, 2. Disease progression in CF patients with mutations indicated for TEZ/IVA, and treated with TEZ/IVA, 3. Frequency and outcome of pregnancies in female patients ≥14 years, have mutations indicated for TEZ/IVA, and treated with TEZ/IVA, 4. Drug utilisation/potential off-label use

## Study Design

**Non-interventional study design**

Cohort

Other

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**Non-interventional study design, other**

Observational study

## Study drug and medical condition

**Name of medicine**

SYMKEVI

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**Medical condition to be studied**

Cystic fibrosis

## Population studied

## **Short description of the study population**

The study population included patients with cystic fibrosis (CF), aged 12 years or older, identified from the CF registries of US, UK, Germany, France and Ireland for the period of 2018 to 2022. The study included three cohorts: longitudinal safety and disease progression analyses, pregnancy analyses, and drug utilisation analyses.

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### **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)

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### **Special population of interest**

Hepatic impaired

Immunocompromised

Other

Pregnant women

Renal impaired

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### **Special population of interest, other**

Patients with cystic fibrosis

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### **Estimated number of subjects**

9623

## **Study design details**

## Outcomes

Safety analyses: death, organ transplant, hospitalisations, pulmonary exacerbations, CF complications, respiratory microbiology, liver function tests.

Disease progression analyses: percent predicted FEV1, BMI. Pregnancy analyses: pregnancy outcome, gestational age, congenital anomalies (data availability varies by registry). Drug utilization analyses: TEZ/IVA use outside of labeled indications.

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## Data analysis plan

Data will be analysed separately for each registry for 5 years. The results of the annual analyses will be combined in a single study report for each year. Each annual report will include the patient data collected during the previous calendar year. Descriptive statistics will be presented for all study endpoints. All safety, CF disease progression, and pregnancy endpoints (Objectives 1, 2, and 3, respectively) will be compared within the TEZ/IVA cohort. Risks, as well as crude relative risks with 95% confidence intervals will be calculated for safety outcomes for each of the analyses years. Analyses will be stratified by patient age, percent predicted FEV1, and other variables as appropriate. Multivariate modelling and sensitivity analysis may be performed for outcomes deserving further investigation if sufficient data are available. Off-label use definition will be adjusted for each annual analysis as necessary if labelled indications change and will be region-specific.

## Documents

### Study results

[TEZ\\_IVA\\_PASS\\_Abstract.pdf](#)(144.62 KB)

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## Data management

## Data sources



## **Data sources (types)**

Disease registry

## Use of a Common Data Model (CDM)

### **CDM mapping**

No

## Data quality specifications

### **Check conformance**

Unknown

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### **Check completeness**

Unknown

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### **Check stability**

Unknown

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### **Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

No