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

Study ID

39005

DARWIN EU® study

No

Study countries

- ☐ France
- ☐ Germany
- ☐ Ireland

☐ United Kingdom

☐ United States

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 Stated (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 ≥ 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).

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

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Primary lead investigator

Julie Bower

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 30/06/2019

Actual: 30/06/2019

Study start date
Planned: 30/06/2019

Actual: 30/06/2019

Date of interim report, if expected
Planned: 31/12/2019

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

TEZ IVA PASS Protocol.pdf (483.72 KB)

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:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

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

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

Non-interventional study design, other

Observational study

Study drug and medical condition

Medicinal product name

SYMKEVI

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.

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)

Special population of interest

Hepatic impaired

Immunocompromised

Other

Pregnant women

Renal impaired

Special population of interest, other

Patients with cystic fibrosis

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.

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)

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 sources (types)

Disease registry

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No