An Observational Study to Evaluate the Long-term Safety of Ivacaftor in Patients With Cystic Fibrosis

First published: 22/07/2013

Last updated: 03/03/2025

Study Finalised

Administrative details

EU PAS number

EUPAS4270

Study ID

35683

DARWIN EU® study

No

Study countries

- [ ] France
- [ ] Ireland
- [ ] United Kingdom
- [ ] United States

Study description

Cystic fibrosis (CF) is an autosomal recessive disease with serious, chronically debilitating morbidities and high premature mortality, and at present, there is no cure. Cystic fibrosis affects approximately 70,000 individuals worldwide and is caused by mutations in the CF transmembrane conductance regulator gene (CFTR), which result in absent or deficient function of the CF transmembrane conductance regulator (CFTR) protein at the cell surface.Ivacaftor (Kalydeco™, 150-mg tablets) has been approved in the United States, the European Union (EU), Canada and Australia to date, for the treatment of CF in patients 6 years of age and older who have a G551D mutation in the CFTR gene. Ivacaftor is an orally bioavailable small molecule CFTR potentiator that targets the underlying defect in CF. As such, ivacaftor is a member of a new class of drugs - CFTR modulators - that provide a new therapeutic approach to the treatment of CF. Ivacaftor is the first CFTR modulator to show an improvement in CFTR function and clinical benefit in patients with CF.Ivacaftor is intended for chronic, potentially lifelong use. Understanding of the long term effects will be informative to patients and their parents, prescribers, and payers. Existing CF registries provide an established source to obtain long term safety in a real life use for analysis. The patient registries of the CF Trust in the United Kingdom (UK) and the CF Foundation in the United States (US) provide the ideal source to obtain long term safety information because the data collected are extensive and consistent with one another. In addition, the patients with CF from the CF Trust and the CF Foundation patient registries encompass a majority of the patients in the indicated population.Cystic fibrosis patient registries from France and Ireland were considered for this study and will be used for drug utilization analysis.

Study status

Finalised

Research institutions and networks

Institutions

Vertex Pharmaceuticals

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Contact details

Study institution contact

Vertex Pharmaceuticals Global Medical Information

vertexmedicalinfo@vrtx.com

Study contact

vertexmedicalinfo@vrtx.com

Primary lead investigator

Jennifer Evans

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 31/07/2013

Actual: 17/07/2013

Study start date
Planned: 31/07/2013

Actual: 31/07/2013

Data analysis start date
Planned: 31/07/2013

Actual: 31/07/2013

Date of interim report, if expected
Planned: 31/12/2013

Actual: 10/12/2013

Date of final study report
Planned: 31/12/2017

Actual: 12/12/2017

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Vertex Pharmaceuticals Incorporated

Study protocol

Long-term Safety Study Protocol-v2.2-07may2013.pdf (704.56 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 1 (imposed as condition of marketing authorisation)

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 the long-term safety of ivacaftor in patients with CF,To evaluate outcomes of pregnancy in ivacaftor-treated patients,To evaluate the drug utilisation of ivacaftor,To evaluate CF disease progression in ivacaftor treated patients.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Post-authorisation safety study

Study drug and medical condition

Medicinal product name

KALYDECO

Medical condition to be studied

Cystic fibrosis

Population studied

Short description of the study population

The Ivacaftor Cohort will include all patients who have been treated with ivacaftor and are enrolled in the CF Trust or CF Foundation patient registries.

The Comparator Cohort will include patients who have never been exposed to ivacaftor and are matched on age group, CFTR genotype class, and sex to patients in the Ivacaftor Cohort. The Ivacaftor Pregnancy Study Cohort will include all female patients who have ivacaftor exposure in the analysis year and are enrolled in the CF Trust or CF Foundation patient registries. The Comparator Pregnancy Study Cohort will include female patients who have never been exposed to ivacaftor and are matched on CFTR genotype class to patients in the Ivacaftor Pregnancy Study Cohort. The Comparator and Comparator Pregnancy Study Cohorts will be identified for each registry's Ivacaftor and Ivacaftor Pregnancy Study Cohorts, respectively, at a ratio of m:1, where m is the maximum number of matches available. The Historical Cohort will include patients who have the G551D-CFTR mutation, were enrolled in the patient registries before ivacaftor was available in clinical studies and commercially in the US and the UK (i.e., 2008), and were never exposed to ivacaftor. The Drug Utilisation Cohort will include all patients who have ever been treated with ivacaftor.

Age groups

- Children (2 to < 12 years)
- 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

Pregnant women

Renal impaired

Estimated number of subjects

1654

Study design details

Outcomes

Safety outcomes: death, organ transplant, hospitalisations, CF complications, pulmonary exacerbations and respiratory microbiology and serious safety outcomes.Pregnancy outcomes: pregnancy, live birth, stillbirth, spontaneous abortion, therapeutic abortion, gestational age, congenital anomalies.Drug utilisation: ivacaftor exposure.CF progression: lung disease severity, lung function change.

Data analysis plan

Data for safety-related outcomes will be analysed separately for each registry for 5 years (data "extraction" in 2013 to 2017 of patient data collected at sites in 2012 to 2016, respectively). All enrolled patients exposed to ivacaftor (Ivacaftor Cohort) and matched comparators (Comparator Cohort) will be included in the study analyses at each yearly report. As a reference, a Historical Cohort (patient data from 2008) will be included in the study analyses at the first yearly report.Data analyses will be performed by the CF Trust and CF Foundation to support the study objectives. The results of the annual analyses will be reported by Vertex in the study report.The primary objectives of this study are to evaluate long-term safety, pregnancy outcomes, drug utilisation, and CF disease progression in patients treated with ivacaftor. Descriptive statistics will be presented for all endpoints.

Documents

Study results

Long-term Safety Study Results 13July2018.pdf (170.92 KB)

Study publications

Bessonova L, Volkova N, Higgins M, Bengtsson L, Tian S, Simard C, Konstan MW, S...

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