An Observational Study to Evaluate the Utilisation Patterns and Long-term Effects of Lumacaftor and Ivacaftor Combination Therapy in Patients With Cystic Fibrosis

First published: 21/10/2016

Last updated: 03/03/2025

Study | Finalised

Administrative details

EU PAS number

EUPAS15943

Study ID

39240

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. The lumacaftor/ivacaftor combination therapy (Orkambi) is indicated for treatment of CF in patients 12 years and older who are homozygous for F508del mutation in the CFTR gene. Understanding long term effects in the overall population of patients receiving treatment and in the specified sub-populations will be informative to patients and their parents, prescribers, and payers. Existing CF registries provide an established source to obtain data on long term effects in a real world use for analysis. The primary objectives of this five-year observational cohort study are to evaluate: 1. Safety outcomes in CF patients who are ≥12 years, homozygous for F508del-CFTR mutation, and treated with Orkambi 2. Frequency and outcome of pregnancies in female patients who are ≥14 years, homozygous for F508del-CFTR mutation, and treated with Orkambi 3. CF disease progression in CF patients who are ≥12 years, homozygous for F508del-CFTR mutation, and treated with Orkambi 4. Drug utilisation / potential off-label use of Orkambi The study will use data collected by existing national CF registries in UK and US (all study objectives), as well as Ireland and France (drug utilization objective only). Data will be analysed separately for each registry for 5 years. Annual analyses results will be combined in a single study report for each year. Each annual report will include data collected during the previous calendar year. For the safety analyses, the Orkambi Safety Cohort will include all patients aged ≥12 years who are homozygous for the F508del-CFTR mutation and have received treatment with Orkambi during the analysis year. The Comparator Safety Cohort will include all patients aged ≥12 years who are heterozygous for the F508del-CFTR mutation with a Class I/II mutation on the second allele and who have never received Orkambi or Kalydeco™.

Study status

Finalised

Research institutions and networks

Institutions

Vertex Pharmaceuticals

First published: 01/02/2024

Last updated: 01/02/2024

Institution

UK CF Registry, US CFF Patient Registry, CF Registry of Ireland, CF Registry of France

Contact details

Study institution contact

Vertex Pharmaceuticals Global Medical Information

vertexmedicalinfo@vrtx.com

Study contact

vertexmedicalinfo@vrtx.com

Primary lead investigator

Claire Kim

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 31/01/2017

Actual: 31/01/2017

Study start date
Planned: 31/07/2017

Actual: 31/07/2017

Data analysis start date
Planned: 31/07/2017

Actual: 31/07/2017

Date of interim report, if expected
Planned: 31/12/2017

Actual: 28/11/2017

Date of final study report
Planned: 31/12/2021

Actual: 16/11/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Vertex Pharmaceuticals Incorporated

Study protocol

vx14-809-108_prtl-PASS_v1.2_29Apr2016_Final.pdf (343.34 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

Data collection methods:

Secondary use of data

Main study objective:

To evaluate: 1. Safety outcomes in CF patients ?6 years, homozygous for F508del, and treated with Orkambi, 2. Frequency and outcome of pregnancies in female patients ?14 years, homozygous for F508del, and treated with Orkambi, 3. Disease progression in CF patients ?6 years, homozygous for F508del, and treated with Orkambi, 4. Drug utilisation / potential off-label use of Orkambi

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Observational retrospective study

Study drug and medical condition

Medicinal product name

ORKAMBI

Medical condition to be studied

Cystic fibrosis

Population studied

Short description of the study population

The study population involved cystic fibrosis (CF) patients reported in the US and UK CF registries.

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

Other

Pregnant women

Renal impaired

Special population of interest, other

Patients with cystic fibrosis

Estimated number of subjects

11529

Study design details

Outcomes

Safety analyses: risks of death, organ transplant, hospitalizations, pulmonary exacerbations, CF complications, respiratory microbiology, liver function tests. Pregnancy analyses: pregnancy outcome, gestational age (US and UK), congenital anomalies (UK only). Disease progression analyses: Percent predicted FEV1, clinical signs of CF disease progression. Drug utilization analyses: Orkambi use.

Data analysis plan

Data will be analyzed 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, pregnancy, and CF disease progression endpoints (Objectives 1, 2, and 3, respectively) will be compared between the respective Orkambi and Comparator Cohorts. 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 modeling 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 labeled indications change.

Documents

Study results

Orkambi_VX-14 809-108_CSR_Abstract.pdf (136.11 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