A multinational active safety surveillance study of crizotinib in Europe and the United States

First published: 02/12/2014

Last updated: 02/07/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/24869

EU PAS number

EUPAS8097

Study ID

24869

DARWIN EU® study

No

Study countries

☐ Denmark

- [ ] Finland
- [ ] Netherlands
- [ ] Sweden
- [ ] United States

Study description

Crizotinib (XALKORI®), an orally administered selective ATP competitive small molecule inhibitor of the anaplastic lymphoma kinase (ALK), has been approved multinational, including in Europe, for the treatment of patients with previously treated locally advanced ALK-positive non small cell lung cancer (NSCLC). This non interventional Post-Authorization Safety Study (PASS) examines the safety and effectiveness of crizotinib among ALK-positive NSCLC patients using existing healthcare databases in Denmark, Sweden, Finland, the Netherlands and the United States. The primary objective of this study is to estimate the incidence of adverse events that were observed in crizotinib clinical trials including 1) hepatotoxicity, 2) pneumonitis/ interstitial lung disease, 3) QT interval prolongation, 4) bradycardia, and 5) vision disorder. Less frequently observed adverse events, i.e. renal cysts, edema, leukopenia, neuropathy, and photosensitivity as well as patient survival will also be examined. To contextualize the incidence of the adverse event in crizotinib treated patients, the incidence of these adverse events in patients prescribed three other orally administered tyrosine kinase inhibitors, ceritinib, erlotinib and gefitinib, will be estimated.The international classification of diseases (ICD) diagnostic codes and procedural codes will be used to capture the safety endpoints in the healthcare databases. Additionally, a validation sub study among all crizotinib patients and the same number of ceritinib, erlotinib or gefitinib patients will evaluate the accuracy of the ICD-based endpoint classifications. The validation study will compare ICD-based classification of primary endpoints to endpoints adjudicated by a panel of experts using data abstracted from patient medical records.

Study status

Finalised

Research institutions and networks

Institutions

Aarhus University & Aarhus University Hospital DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Denmark

First published: 20/07/2021

Last updated: 02/04/2024

Institution | **Educational Institution** | **ENCePP partner**

Aarhus University & Aarhus University Hospital DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Denmark

First published: 20/07/2021

Last updated: 02/04/2024

Institution | **Educational Institution** | **ENCePP partner**

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

☐ Netherlands

First published: 07/01/2022

Last updated: 24/07/2024

Institution | **Laboratory/Research/Testing facility** | **ENCePP partner**

Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

☐ Sweden

First published: 24/03/2010

Last updated: 23/04/2024

Institution | **Educational Institution** | **Laboratory/Research/Testing facility** | **Not-for-profit** | **ENCePP partner**

Global Database Studies, IQVIA

☐ Czechia

☐ Finland

☐ Germany

☐ Slovakia

☐ Spain

First published: 17/01/2011

Last updated: 31/07/2024

Institution | **Other** | **ENCePP partner**

Contact details

Study institution contact

Kui Huang

Study contact

kui.a.huang@pfizer.com

Primary lead investigator

Henrik Toft Sørensen

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 19/03/2014

Actual: 09/07/2014

Study start date

Planned: 30/12/2014

Actual: 30/12/2014

Date of interim report, if expected

Planned: 30/06/2016

Actual: 30/06/2016

Date of final study report

Planned: 30/06/2018

Actual: 12/06/2018

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer Inc

Study protocol

A8081038 Final Crizotinib Protocol 02 April 2013.pdf(1.63 MB)

A8081038 Final Protocol Amendment 2, 19 February 2015 register.pdf(486.25 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

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

The main objective of this study is to evaluate the safety and effectiveness of crizotinib among ALK positive NSCLC patients in the real world setting. Safety and effectiveness will be measured with data from pre-existing European and US databases, and these data will be validated with information extracted from medical records.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Active surveillance of existing databases

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

CRIZOTINIB

ERLOTINIB

GEFITINIB

CERITINIB

Medical condition to be studied

Non-small cell lung cancer

Population studied

Short description of the study population

Patients who were diagnosed with primary lung cancer and receive dispensation/prescription for crizotinib, ceritinib, erlotinib, or gefitinib as recorded in national or regional health care databases in Denmark, Finland, the Netherlands, Sweden, and the US from September 1st , 2011 to June 30th, 2017. In addition, all other cancer patients receiving crizotinib dispensation/prescription were included.

Age groups

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

Renal impaired

Estimated number of subjects

2683

Study design details

Outcomes

To estimate the incidence rate and incidence proportion over a 3-year period of observation for hepatotoxicity, pneumonitis/ILD, QTc prolongation related events, bradycardia, and visual disorders among lung cancer patients receiving crizotinib dispensation. To estimate the incidence of the primary endpoints for lung cancer patients receiving ceritinib/erlotinib/gefitinib dispensation, To estimate the incidence of renal cysts, edema, leukopenia, neuropathy, and photosensitivity among lung cancer patients receiving crizotinib, ceritinib, erlotinib, or gefitinib dispensation,To estimate Kaplan-Meier survival probabilities for patients in the study.

Data analysis plan

This study will link existing national or regional databases within Sweden, Denmark, the Netherlands, Finland, and the United States. Demographics, tumor characteristics, pertinent medical history, comorbidities, safety outcomes of interest, and overall patient survival will be examined.All statistical analyses will be descriptive. Incidence rates and incidence proportions for all study endpoints will be calculated. Subgroup analyses by age, presence or absence of brain metastases, and pre-existing renal or hepatic impairments at baseline will be conducted for all primary study endpoints. Kaplan-Meier survival probability will be estimated for all patients. In addition, sensitivity, specificity and positive predictive value (PPV) of primary study endpoints captured using ICD codes (compared to patient medical records) will be calculated.

Documents

Study report

A8081038 NI Study Report.pdf(3.23 MB)

Crizotinib A8081038 Second Interim Report Synopsis_21 Sept 2016.pdf(151.16 KB)

Study, other information

Crizotinib A8081038 Second Interim Report Synopsis_21 Sept 2016.pdf(151.16 KB)

Data management

Data sources

Data source(s)

Danish registries (access/analysis)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

PHARMO Data Network

Data source(s), other

Finnish healthcare registries Finland

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

Electronic healthcare records (EHR)

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

Unknown