

# 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

### EU PAS number

EUPAS8097

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### Study ID

24869

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### DARWIN EU® study

No

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### Study countries

- Denmark
- Finland
- Netherlands
- Sweden

United States

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### **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.

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### **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:** 19/12/2025

**Institution**

**Non-Pharmaceutical company**

**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

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**Study contact**

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**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

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**Study start date**

Planned: 30/12/2014

Actual: 30/12/2014

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**Date of interim report, if expected**

Planned: 30/06/2016

Actual: 30/06/2016

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**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

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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

Effectiveness study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**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

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**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

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### **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.

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### **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)
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### **Special population of interest**

Hepatic impaired

Renal impaired

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### **Estimated number of subjects**

## 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.

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### **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

### 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 source(s)

Danish registries (access/analysis)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

PHARMO Data Network

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### Data source(s), other

Finnish healthcare registries Finland

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### 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

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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**

Unknown