Prediction of Early Progression and AEs with 1L Lorlatinib Patient Data Embedded in a Scientific Knowledge Graph

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Study Planned

Administrative details

EU PAS number

EUPAS1000001163

Study ID

1000001163

DARWIN EU® study

No

Study countries

United States

Study description

Lorlatinib is a third-generation ALK tyrosine kinase inhibitor (TKI) approved for the first-line (1L) treatment of ALK-positive advanced or metastatic non-small cell lung cancer (NSCLC). While the majority of patients experience long-duration responses, a subset experience disease progression within the first year. Additionally, lorlatinib is associated with specific adverse events (AEs) requiring monitoring and management, such as central nervous system (CNS) effects, hyperlipidemia, weight gain, edema, and peripheral neuropathy. To better anticipate early progression and AEs, this study will integrate clinical data with the SPOKE biomedical knowledge graph, employing machine learning to generate biologically informed patient health signatures (SPOKEsigs) to predict early progression and incident AEs using baseline characteristics captured around the time of treatment initiation.

The primary objectives are:
1) To identify clinical and SPOKE-based biological predictors of early progression (progression in first 12 months of 1L ALK TKI treatment) and known ALK TKI AEs (CNS effects, hyperlipidemia, weight gain, edema, and peripheral neuropathy) among CROWN pivotal Phase III trial participants, separately in two cohorts: Patients randomized to 1L lorlatinib; and Patients randomized to 1L crizotinib.

2) To predict the risk of early progression and the onset of known AEs (CNS effects, hyperlipidemia, weight gain, edema, and peripheral neuropathy) in patients treated with 1L ALK TKIs in the CROWN trial with and without the inclusion of SPOKE predictors, separately in two cohorts: Patients randomized to 1L lorlatinib; and Patients randomized to 1L crizotinib.

Study status

Planned

Research institutions and networks

Institutions

Pfizer

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Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Diana Garofalo

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 23/06/2026

Actual: 23/06/2026

Study start date

Planned: 23/11/2026

Data analysis start date
Planned: 30/11/2027

Date of final study report
Planned: 30/11/2028

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Other study registration identification numbers and links

B7461065

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Method development or testing

Data collection methods:

Secondary use of data

Study design:

Non-interventional, observational, retrospective cohort study of NSCLC patients

Main study objective:

The primary objectives are:
1) To identify clinical and SPOKE-based biological predictors of early progression (progression in first 12 months of 1L ALK TKI treatment) and known ALK TKI AEs (CNS effects, hyperlipidemia, weight gain, edema, and peripheral neuropathy) among CROWN pivotal Phase III trial participants, separately in two cohorts: Patients randomized to 1L lorlatinib; and Patients randomized to 1L crizotinib.

2) To predict the risk of early progression and the onset of known AEs (CNS effects, hyperlipidemia, weight gain, edema, and peripheral neuropathy) in patients treated with 1L ALK TKIs in the CROWN trial with and without the inclusion of SPOKE predictors, separately in two cohorts: Patients randomized to 1L lorlatinib; and Patients randomized to 1L crizotinib.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

LORVIQUA

Medicinal product name, other

Lorbrena

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

LORLATINIB

Anatomical Therapeutic Chemical (ATC) code

(L01ED05) lorlatinib

lorlatinib

Medical condition to be studied

Non-small cell lung cancer metastatic

Non-small cell lung cancer

Population studied

Short description of the study population

CROWN trial data of ALK-positive advanced or metastatic non-small cell lung cancer (NSCLC)

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Data management

Data sources

Data source(s), other

Flatiron Health

Data sources (types)

Clinical trial

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No