# Rates and management of side effects with lorlatinib in the CROWN study: 5-year results

**The full title of this abstract is:** Kinetics and management of adverse events associated with lorlatinib after 5 years of follow-up in the CROWN study

## VIEW ABSTRACT

**Please note this summary only contains information from the scientific abstract:**

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**Date of summary:**
September 2024

**Study number:** NCT03052608

**Study start date:**
April 2017

**Study end date:**
December 2028

For more information on this study, go to:
**https://clinicaltrials.gov/study/NCT03052608**

## KEY TAKEAWAY

### What is the key takeaway from this study?

- In this 5-year update of the CROWN study, people with a type of lung cancer (called ALK-positive NSCLC) who took lorlatinib had low rates of stopping treatment due to unwanted effects (known as side effects).
- Side effects of lorlatinib were well managed by using a smaller dose or taking a break from treatment (known as dose modifications).
- Taking a smaller dose of lorlatinib did not change the benefit observed with lorlatinib.

## PHONETICS

### Find out how to say medical terms used in this summary

**Crizotinib**
< krih-ZOH-tih-nib >

**Lorlatinib**
< lor-LA-tih-nib >

**Metastatic**
< meh-tuh-STA-tik >

## GLOSSARY

**Cancer:** abnormal cells that grow and divide without control and spread to other parts of the body

**Gene:** a part of our genetic material (DNA) that contains information for making a specific protein. Proteins are substances that help the body to function

**Metastatic:** cancer that has spread from the place where it started to another part of the body

**Side effect:** an effect of a medicine that is unwanted and can be harmful

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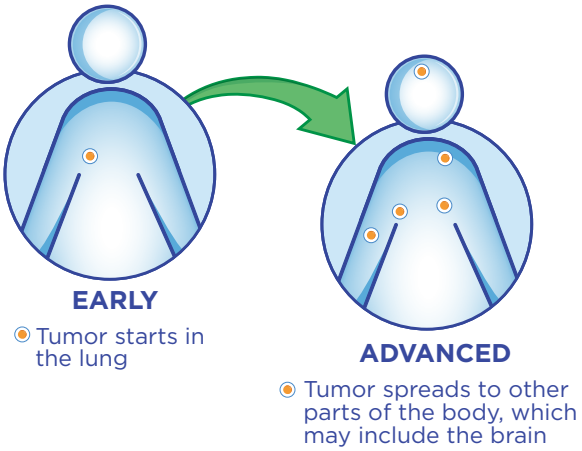
# What does this study look at?

## What is advanced *ALK*-positive NSCLC?

- Non-small cell lung cancer or NSCLC is the most common type of lung cancer.
- NSCLC that has spread to other parts of the lungs or body is called advanced or metastatic NSCLC.
- Some people with NSCLC have changes in a gene called anaplastic lymphoma kinase or *ALK* in their cancer cells.
- The *ALK* gene makes a protein that controls how cells grow. If there is a change in the *ALK* gene, the ALK protein does not work properly. This leads to problems with cell growth that can cause cancer.




- Changes in the *ALK* gene are found in about 3% to 7% of people with NSCLC. This type of cancer is called *ALK*-positive NSCLC.
- People with advanced *ALK*-positive NSCLC have a high chance of the cancer spreading to the brain.

## What are lorlatinib and crizotinib?

- **Lorlatinib** is a type of medicine known as an ALK inhibitor. It is a third-generation ALK inhibitor, meaning that it is a newer type of ALK inhibitor. It stops cancer cells from growing and spreading by blocking the actions of proteins like ALK.
- **Crizotinib** is the first-generation ALK inhibitor that was used in people with *ALK*-positive NSCLC. "First generation" means that it is the first ALK inhibitor.

## What is the CROWN study?

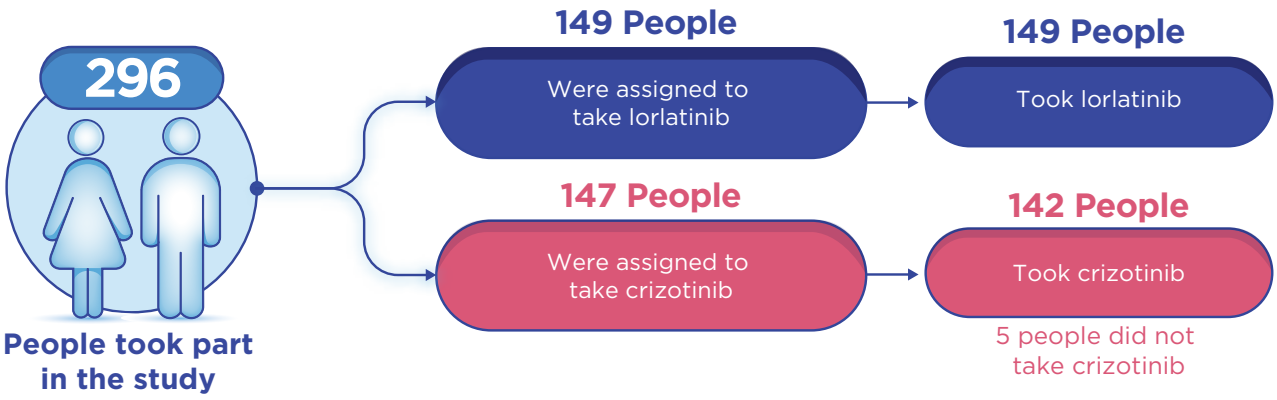
- In the CROWN study, researchers are looking at the effects of two ALK inhibitors, **lorlatinib** and **crizotinib**. People were assigned at random to one of two treatment groups. "Random" means by chance, like flipping a coin. The two treatments were:
  - **Lorlatinib**, taken as tablets by mouth once a day
  - **Crizotinib**, taken as capsules by mouth twice a day
- People who took **lorlatinib** lived longer without their cancer getting worse than people who took **crizotinib**. **Lorlatinib** also reduced or delayed the chance of cancer from spreading to the brain or from getting worse if it was already in the brain.

### Researchers wanted to find out...

- How common are side effects and how well are they managed in people with advanced *ALK*-positive NSCLC who were treated with lorlatinib for 5 years?

# Who took part in this study?

- A total of 296 people with advanced *ALK*-positive NSCLC who had not been treated for lung cancer took part in the CROWN study.




- This summary shows results from the **lorlatinib** group.



# What were the results of this study?

## How long did at least half of the people live without their cancer getting worse?

- After people treated with **lorlatinib** were observed for an average of 5 years, more than half of them are still alive without their cancer getting worse. This means that it is too early to tell how long people lived without their cancer getting worse.

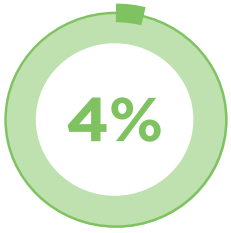
# What were the results of this study?

## After 5 years, how many people had a lorlatinib dose modification because of side effects? What were the most common side effects leading to lorlatinib dose modification?

**Used a smaller dose**

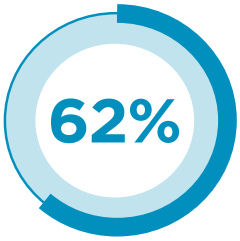

**Edema**


**Hypertriglyceridemia**




**Cognitive effects, mood effects, and peripheral neuropathy (each)**


**Stopped lorlatinib and then restarted**



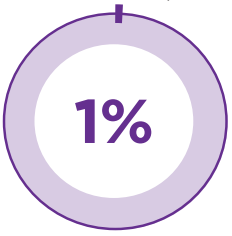

**Hypertriglyceridemia and pneumonia (each)**


**Cognitive effects and positive COVID test (each)**


**Edema, peripheral neuropathy, and mood effects (each)**


**Stopped lorlatinib and did not restart**


**Cognitive effects and heart failure (each)**

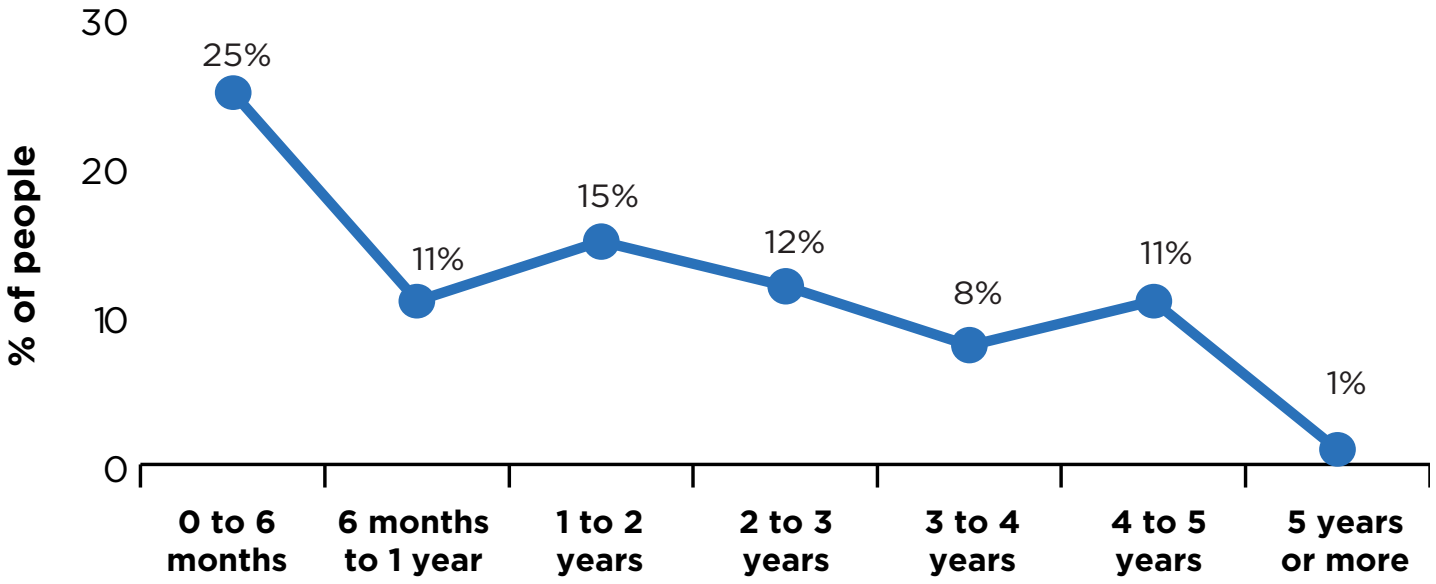



- **Cognitive effects:** problems with memory, speaking, or thinking
- **Edema:** swelling
- **Hypertriglyceridemia:** high levels of triglycerides, which is a type of fat
- **Peripheral neuropathy:** a nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body

- Taking a smaller dose of lorlatinib did not change:
  - How long people lived without their cancer getting worse.
  - The chance of cancer that had spread to the brain to get worse or new tumors to spread to the brain.

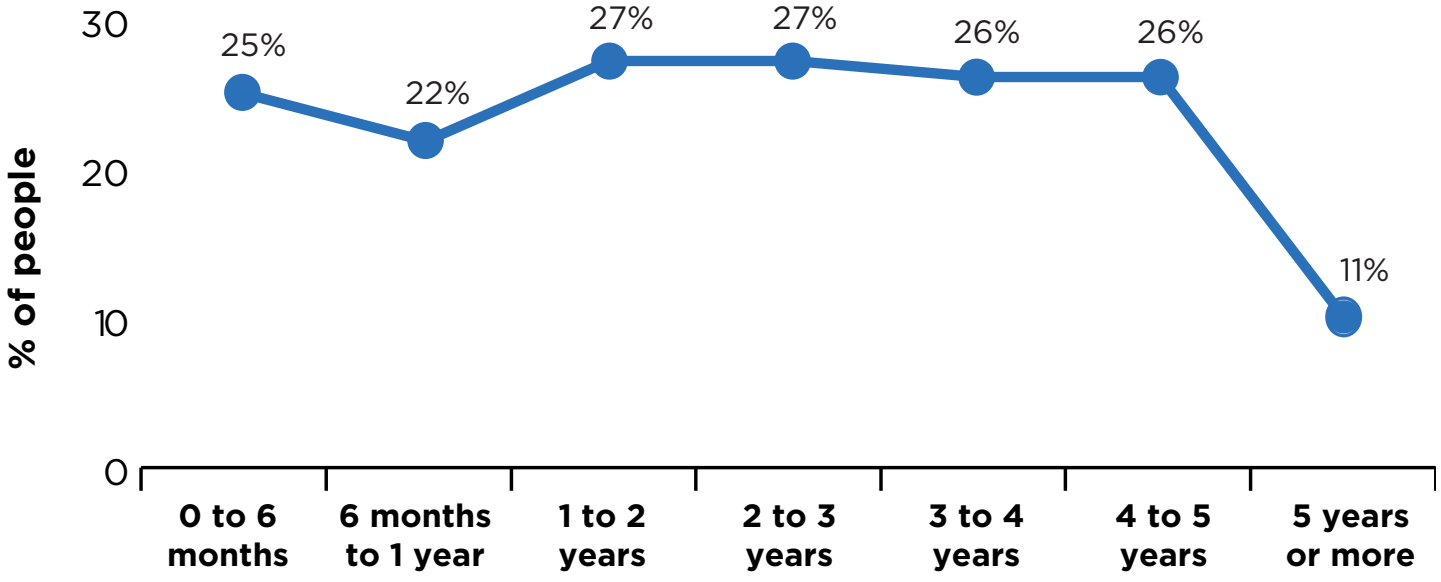
## How many new side effects in the central nervous system (the brain and the nerves in the spine) were reported over 5 years?

- The new side effects in the central nervous system did not increase over time.




## How many total side effects in the central nervous system were reported over 5 years?

- The total number of side effects in the central nervous system did not increase over time.




- Central nervous system side effects include cognitive effects, mood effects, speech effects, and psychotic effects.

## When do the most common side effects start in at least half of the people? How long do the side effects last in at least half of the people?

| | Start time of side affect after treatment started | How long the side effect lasts |
|---|---|---|
| **Hypercholesterolemia** (high levels of cholesterol) | 0.5 MONTHS | 36 MONTHS |
| **Hypertriglyceridemia** | 0.5 MONTHS | 38 MONTHS |
| **Edema** | 2 MONTHS | 12 MONTHS |
| **Peripheral neuropathy** | 4 MONTHS | 18 MONTHS |
| **Central nervous system effects** | 4 MONTHS | 8 MONTHS |

## What were the main conclusions of this study?

- In this 5-year update of the CROWN study, people who took **lorlatinib** had low rates of stopping treatment due to side effects.
- The most common side effects that led to dose modification of **lorlatinib** were high levels of triglycerides, edema, and central nervous system side effects.
- New and total central nervous system side effects did not increase over time with **lorlatinib**.
- Cholesterol and triglyceride levels increased within 0.5 months after starting **lorlatinib** and lasted for 36 to 38 months.
- Edema, peripheral neuropathy, and central nervous system side effects started within 2 to 4 months after starting lorlatinib and lasted for 8 to 18 months.

This summary reports the results of a single study. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study.

This study described is still ongoing; therefore, the final outcomes of this study may differ from the outcomes described in this summary.

Lorlatinib and crizotinib are approved to treat people with advanced *ALK*-positive NSCLC.



## Who sponsored this study?

### This study was sponsored by Pfizer Inc.

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### The sponsor thanks everyone who took part in this study.

## Where can I find more information?

For more information on this study, please visit:

View Scientific Abstract ›

https://clinicaltrials.gov/study/NCT03052608

For more information on clinical trials in general, please visit:

https://www.clinicaltrials.gov/study-basics/learn-about-studies
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/what-clinical-trials-are

Pfizer's generative artificial intelligence (AI) assisted technology, MAIA (Medical Artificial Intelligence Assistant) was used in the production of this abstract plain language summary to prepare the first draft. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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