

Dose reductions used to manage side effects associated with lorlatinib in the CROWN study

The full title of the scientific abstract is: Impact of lorlatinib dose modifications on adverse event outcomes in the phase 3 CROWN study

VIEW SCIENTIFIC ABSTRACT

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

View Scientific Abstract >



Date of summary:
May 2025

- 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 are the key takeaways from this study?

- In the CROWN study, about one-third of people with a type of lung cancer (called *ALK*-positive NSCLC) who took **lorlatinib** needed to have the dose lowered at least once because of unwanted effects (known as side effects).
- Side effects of **lorlatinib** were managed by lowering the dose, which enabled people to continue to take **lorlatinib** treatment for extended periods of time.

PHONETICS

Find out how to say medical terms used in this summary

Lorlatinib	Crizotinib	Metastatic	ALK gene
< lor-LA-tih-nib >	< krih-ZOH-tih-nib >	< meh-tuh-STA-tik >	< a-ell-kay jeen >

GLOSSARY

Cancer: abnormal cells that grow and divide without control and can 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

1

Introduction

What does this study look at?

[Explore](#) >

2

Study Details

Who took part in this study?

[Explore](#) >

3

Results

What were the results of this study?

[Explore](#) >

4

Conclusions

What were the main conclusions of the study?

[Explore](#) >

5

More Information

Additional information about the study

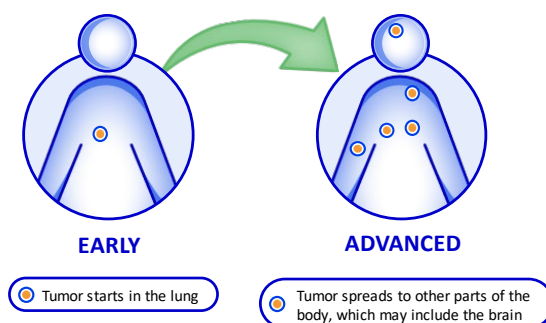
[Explore](#) >



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 the *ALK* protein, which 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 around 3 to 7 of every 100 people (3% to 7%) 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** and **crizotinib** are types of medicines known as *ALK* inhibitors, which are approved to treat *ALK*-positive NSCLC. These medicines stop cancer cells from growing and spreading by blocking the actions of proteins like *ALK*.
- **Crizotinib** is the first *ALK* inhibitor that was used in people with *ALK*-positive NSCLC.
- **Lorlatinib** is a newer type of *ALK* inhibitor.

What is the CROWN study?

- In the CROWN study, researchers are looking at the effects of two *ALK* inhibitors, **lorlatinib** and **crizotinib**. The study is ongoing, which means that people continue to be observed, whether they are still taking the study treatment or have stopped treatment.
- In this study, people were assigned at random to one of two treatment groups to take a specific study medicine. "Random" means by chance, like flipping a coin. The two study medicines were:
 - **Lorlatinib**, taken as tablets by mouth once a day
 - **Lorlatinib** was started at a dose of 100 mg
 - For patients with side effects, the dose could be lowered once to 75 mg or twice to 50 mg
 - **Crizotinib**, taken as capsules by mouth twice a day
- In this study, after being observed for 5 years since starting treatment, people who took **lorlatinib** lived longer without their cancer getting worse than people who took **crizotinib**.
- For patients who took **lorlatinib**, dose reductions during the first 16 weeks of treatment did not affect how well **lorlatinib** worked. These results have been published.

In this study, researchers wanted to find out...

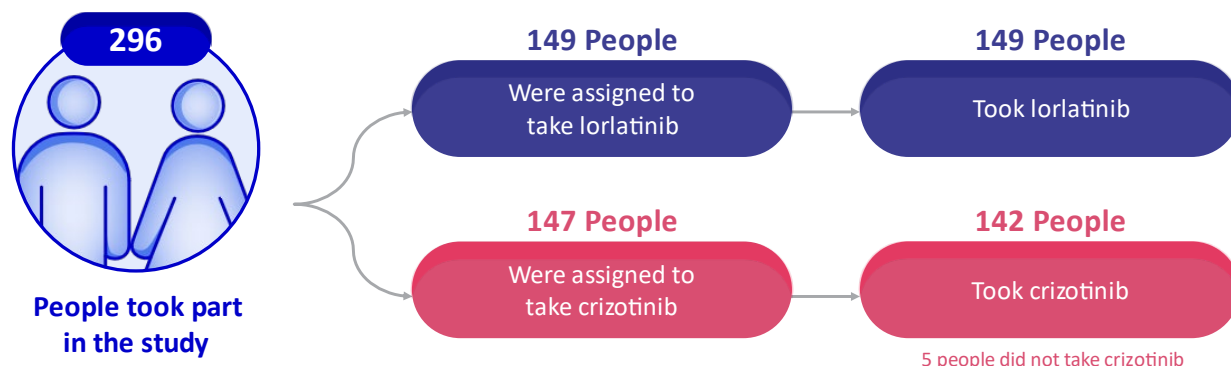
- How many people had their lorlatinib dose lowered to a smaller dose to manage side effects and how well did those dose reductions manage side effects in people with advanced *ALK*-positive NSCLC ?





Who took part in this study?

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



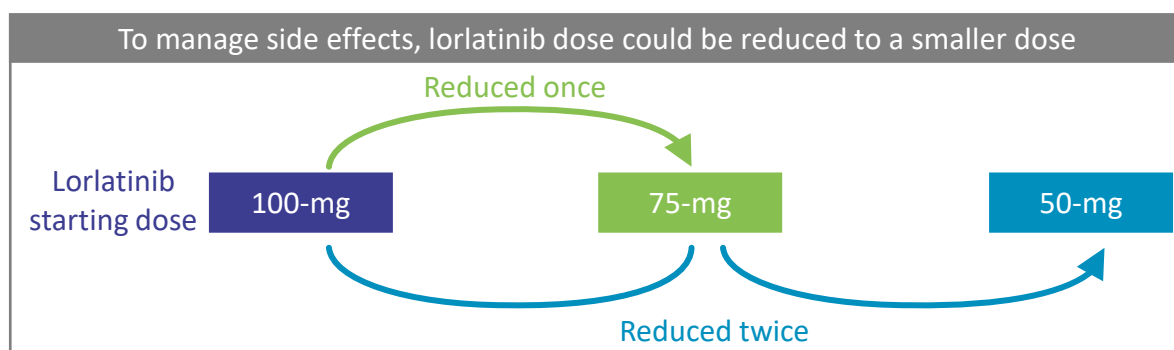
- This summary shows results from the **lorlatinib** group.

RESULTS

What were the results of this study?

After being observed for an average of 5 years, how many people had their lorlatinib dose lowered to a smaller dose at least once because of side effects?

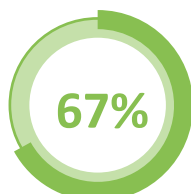
- 49 out of 149 people (33%) treated with **lorlatinib** had their dose lowered at least once
 - 24 people had their **lorlatinib** dose lowered just once to 75 mg once daily
 - 25 people had their **lorlatinib** dose lowered a second time to 50 mg once daily





Among the people who had their lorlatinib dose lowered once to 75 mg daily (n=24):

After being observed for an average of 5 years, how many people were still taking lorlatinib?



Since beginning lorlatinib treatment, how long did it take for at least half of the people to need their lorlatinib dose lowered to 75 mg?

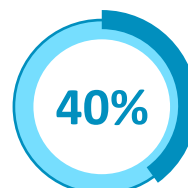


For how long after the dose was lowered did at least half of the people take the 75-mg dose of lorlatinib?



Among the people who had their lorlatinib dose lowered twice to 50 mg daily (n=25):

After being observed for an average of 5 years, how many people were still taking lorlatinib?



Since beginning lorlatinib treatment, how long did it take for at least half of the people to need their lorlatinib dose lowered a second time to 50 mg?



For how long after the dose was lowered for a second time did at least half of the people take the 50-mg dose of lorlatinib?





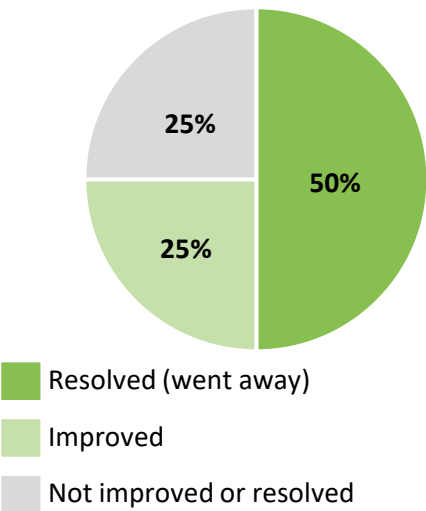
Among the people who had their lorlatinib dose lowered once to 75 mg daily (n=24):

What was the most common side effect leading to dose reduction?



For the side effects that led to lorlatinib being lowered once to 75 mg (n=30), what were the outcomes after dose reduction?

Outcomes of side effects after dose reduction (n=16)



Outcomes of 14 side effects could not be determined because they resolved with a temporary pause in lorlatinib treatment before the lower dose was started

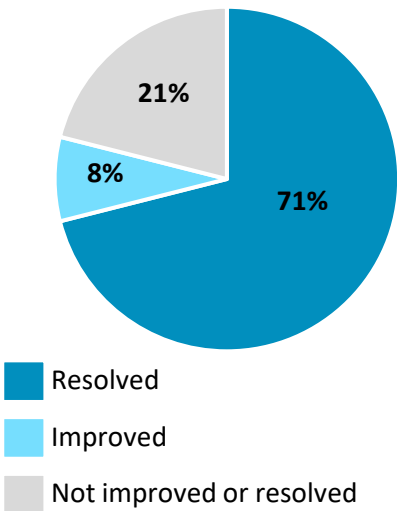
Among the people who had their lorlatinib dose lowered twice to 50 mg daily (n=25):

What was the most common side effect leading to dose reduction?



For the side effects that led to lorlatinib being lowered for a second time to 50 mg (n=59), what were the outcomes after dose reduction?

Outcomes of side effects after dose reduction (n=38)



Outcomes of 21 side effects could not be determined because they resolved with a temporary pause in lorlatinib treatment before the lower dose was started



What were the main conclusions of this study?

- After being observed for 5 years in the CROWN study, about one-third of people who took **lorlatinib** needed the dose lowered at least once because of side effects.
- Side effects of **lorlatinib** were managed by lowering the dose, which enabled people to continue to take lorlatinib for longer times:
 - Of people who had their **lorlatinib** dose lowered to 75 mg, after the dose was lowered, at least half took the 75-mg dose for 42.2 months.
 - Of people who had their **lorlatinib** dose lowered for a second time to 50 mg, after the dose was lowered for a second time, at least half took the 50-mg dose for 20.7 months.
- These findings support the use of dose reductions to manage side effects associated with lorlatinib in patients with *ALK*-positive NSCLC.

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 the condition under study that is discussed in this summary.

MORE INFORMATION

Who sponsored the study?

This study was sponsored by Pfizer Inc.

Pfizer Inc.

66 Hudson Boulevard East

New York, NY 10001

Phone (United States): +1 212-733-2323

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 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.