

Plain language summary of the updated results from the CROWN study comparing lorlatinib with crizotinib in people with advanced non-small-cell lung cancer

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First draft submitted: 21 December 2022; Accepted for publication: 19 April 2023; Published online: 12 June 2023

Summary

What is this summary about?

This summary shows the updated results of an ongoing research study called CROWN that was published in *The Lancet Respiratory Medicine* in December 2022. In the CROWN study, researchers looked at the effects of two study medicines called lorlatinib and crizotinib. The study included people with advanced non-small-cell lung cancer (NSCLC) that had not been treated previously. All people in the study had cancer cells with changes (known as alterations) in a gene called *anaplastic lymphoma kinase*, or *ALK*. This *ALK* gene is involved in cancer growth. In this updated study, researchers looked at the continued benefit in people who took lorlatinib compared with people who took crizotinib after 3 years.

How to say (double-click on the icon to play sound)...

- **Crizotinib:** krih-ZOH-tih-nib
- **Lorlatinib:** lor-LA-tih-nib

What did this study find?

After 3 years of being observed, people who took lorlatinib were more likely to be alive without their cancer getting worse than people who took crizotinib. At 3 years, 64% of people who took lorlatinib were alive without their cancer getting worse compared with 19% of people who took crizotinib. The cancer was less likely to have spread within or to the brain in people who took lorlatinib than in people who took crizotinib. After 3 years of being observed, 61% of people were still taking lorlatinib and 8% of people were still taking crizotinib. People who took lorlatinib had more severe **side effects** than people who took crizotinib. However, these side effects were manageable. The most common side effects with lorlatinib were high levels of cholesterol or high levels of triglycerides (a type of fat) in the blood. Life-threatening side effects were seen in 13% of people who took lorlatinib and 8% in crizotinib. Two people who took lorlatinib died because of side effects from lorlatinib.

A **side effect** is an unwanted reaction to the medicine

What do the results of the study mean?

The updated results from the CROWN study showed that a larger percentage of people who took lorlatinib continued to benefit from their treatment after being observed for 3 years compared with those who took crizotinib.

Who should read this article?

This summary was written to help patients, their caregivers and healthcare professionals understand the updated results of the CROWN study.

Who sponsored this study?

The CROWN study was sponsored by Pfizer. 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 *ALK*-positive

What is *ALK*-positive advanced NSCLC?

NSCLC is the most common type of lung cancer. Advanced NSCLC is cancer that has spread to many parts of the lungs or to other parts of the body. Some people with NSCLC have cancer cells with changes in a gene called *ALK*. This type of cancer is known as *ALK*-positive advanced NSCLC.

What are *ALK* inhibitors?





Medicines called *ALK* inhibitors are used to treat people with *ALK*-positive advanced NSCLC. These medicines cause the cancer cells to die and stop the cancer from growing.

Lorlatinib is a new type of *ALK* inhibitor. Lorlatinib is stronger than older *ALK* inhibitors and can get into the brain more easily.

Crizotinib was the first *ALK* inhibitor used in people with *ALK*-positive NSCLC. It was the standard treatment when the CROWN study started.

What did this study look at?

Researchers wanted to find out how well lorlatinib works, compared with crizotinib, in people with *ALK*-positive advanced NSCLC after 3 years of receiving the study medicines. They looked at the following for every person included in their study:

-  **How long they lived without their cancer getting worse**
-  **How many people did not have their tumors spreading within or to the brain**
-  **Side effects they had during the study**
-  **How they felt about their overall health and quality of life**

Who took part in the study?

A total of 296 people with untreated *ALK*-positive advanced NSCLC took part in the CROWN study. This study included people from 23 countries. People included in the study:

- Were 18 years or older
- Had not been treated before
- Did or did not have tumors in their brain when they started the study

What happened in the study?



The CROWN study started in May 2017, and people joined the study through February 2019.

People in the study took either:

Lorlatinib given by mouth as a tablet, once a day

OR

Crizotinib given by mouth as a capsule, twice a day

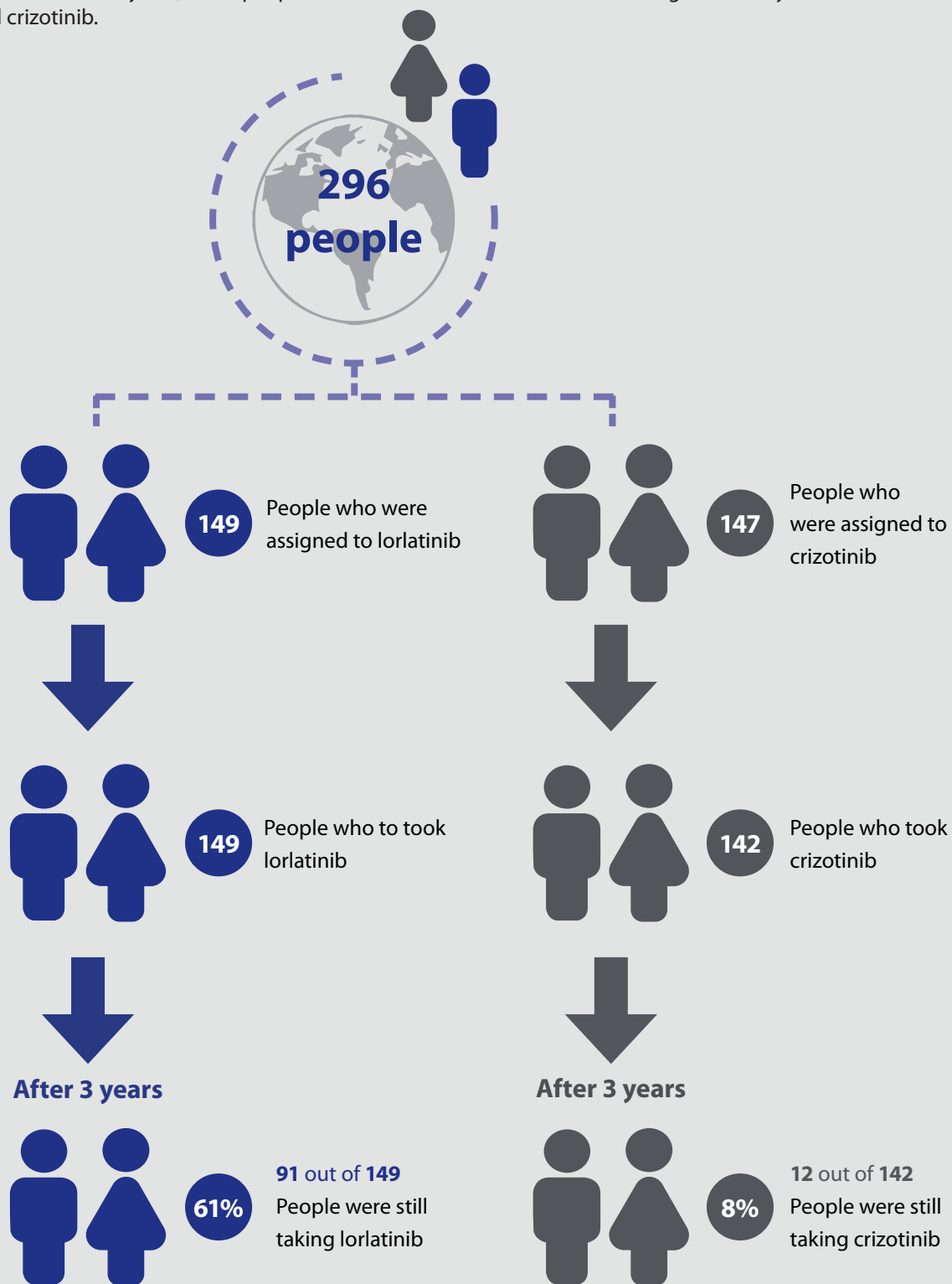
People in the study were not allowed to change from one medicine to another.

People stopped taking the study medicines if:

- Their tumor grew or spread to other parts of their body
- They had side effects that could not be managed
- They no longer wanted to take part in the study
- Their physician decided they were no longer benefitting from their treatment

What were the results of the study?

After being observed for 3 years, more people who received lorlatinib were still taking their study medication than people who received crizotinib.



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

All people:



149

People who were assigned to lorlatinib

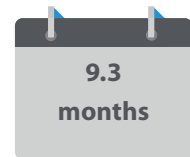


It is too early to tell because more than half of these people are still alive without their cancer getting worse



147

People who were assigned to crizotinib



People with brain tumors at the start of the study:



37

People who were assigned to lorlatinib



It is too early to tell because more than half of these people are still alive without their cancer getting worse



39

People who were assigned to crizotinib



People without brain tumors at the start of the study:



112

People who were assigned to lorlatinib



It is too early to tell because more than half of these people are still alive without their cancer getting worse



108

People who were assigned to crizotinib



How many people lived without their cancer getting worse?



149

People who were assigned to lorlatinib

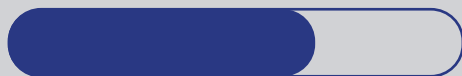


After 3 years



64%

Were alive without their cancer getting worse



147

People who were assigned to crizotinib

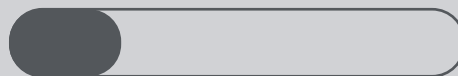


After 3 years



19%

Were alive without their cancer getting worse



How many people did not have their tumors spread within or to the brain?

All people:



Lorlatinib

↑
92%

92% of people who took **lorlatinib** did not have their tumors spread within or to the brain



Crizotinib

↑
38%


38% of people who took **crizotinib** did not have their tumors spread within or to the brain

People with brain tumors at the start of the study:

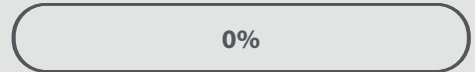
Lorlatinib




↑
73%

 73% of people who took **lorlatinib** did not have their tumors spread within the brain

Crizotinib

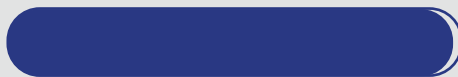


0%


 All patients who took **crizotinib** either had their brain tumors get worse and spread within the brain or were not followed up to 3 years

People without brain tumors at the start of the study:

Lorlatinib




↑
99%

 99% of people who took **lorlatinib** did not have their tumors spread to the brain

Crizotinib

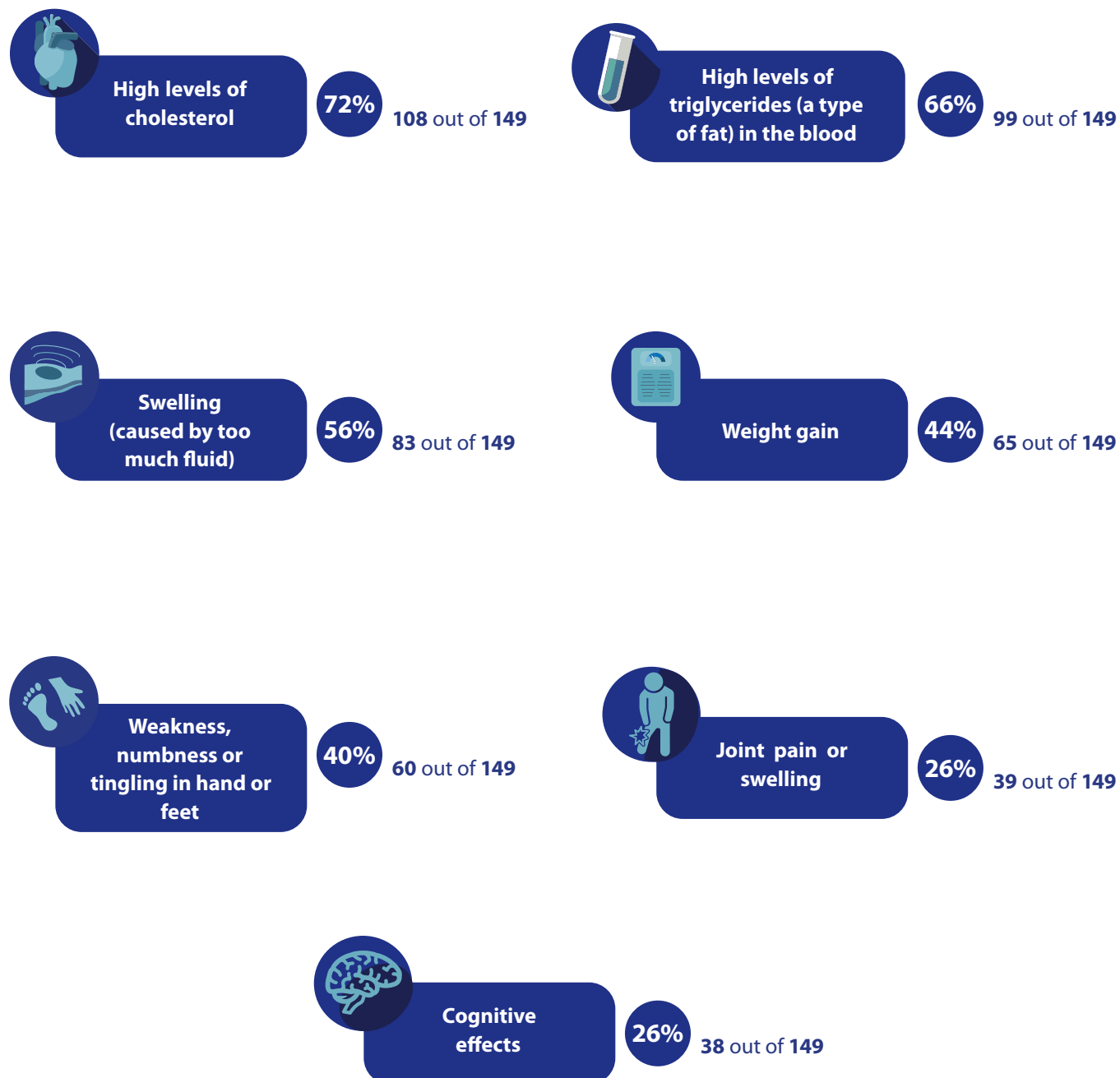


↑
50%

 50% of people who took **crizotinib** did not have their tumors spread to the brain

What were the most common side effects (unwanted reactions to the medicine)?

People who took lorlatinib



People who took crizotinib



Diarrhea (loose or watery stools)

53% 75 out of 142



Nausea (feeling like you want to throw up)

53% 75 out of 142



Swelling (cause by too much fluid)

43% 61 out of 142



Change in vision

39% 56 out of 142



Vomiting

39% 56 out of 142



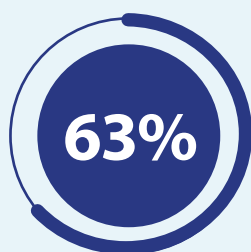
Constipation

30% 43 out of 142

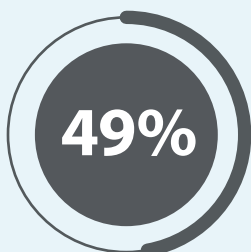
How many people had severe or life-threatening side effects?

Severe side effects

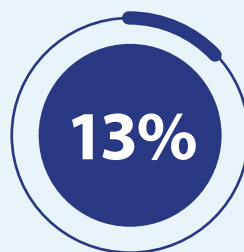
Daily activity is reduced, with some assistance needed; some medical therapy is usually required; a decrease in treatment dose is often required



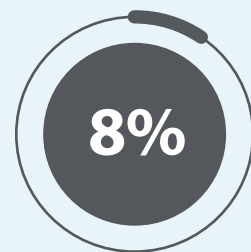
Lorlatinib



Crizotinib



Lorlatinib



Crizotinib

Life-threatening side effects

Daily activity is extremely limited; usually requires hospitalization with a significant number of medical treatments; discontinuation of the treatment drug is often required

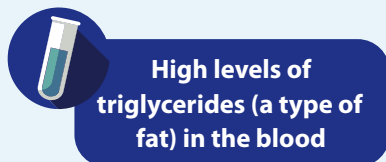
What were the most common severe side effects in people taking lorlatinib?



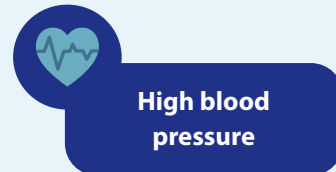
vs 2% with crizotinib



vs 0% with crizotinib

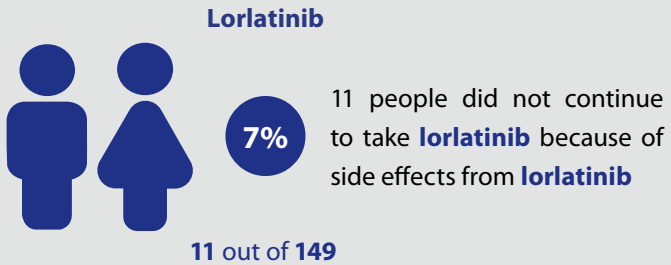


vs 0% with crizotinib

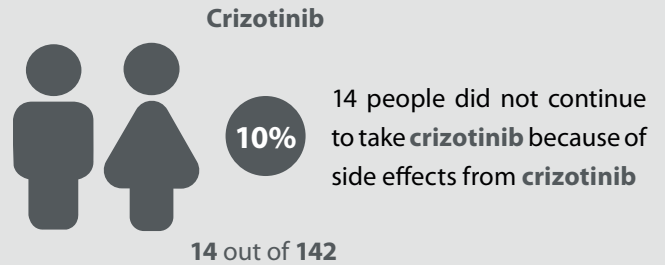


vs less than 1% with crizotinib

How many people stopped treatment because of side effects?



2 people who took **lorlatinib** died because of side effects from **lorlatinib**



There were no people who took **crizotinib** who died because of side effects from **crizotinib**

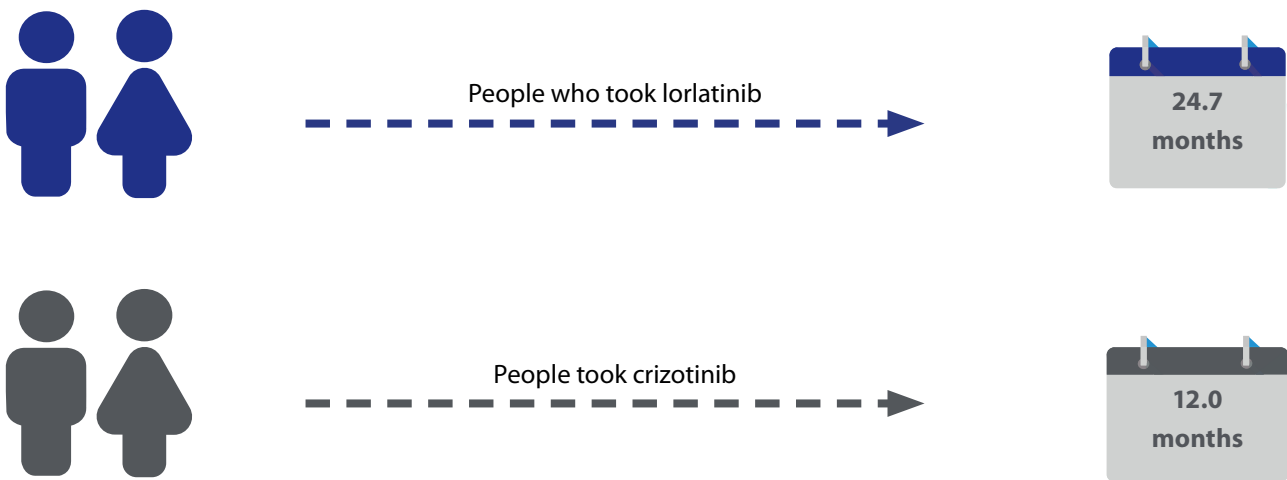
How did people feel about their treatment?

People in the study filled out a survey each month during the study. The survey looked at people's feelings about their overall health, well-being and quality of life.

People who took either **lorlatinib** or **crizotinib** both said that their quality of life improved.

People who took **lorlatinib** had more improvement in quality of life from the start of the study than people who took **crizotinib**.

How long did it take before the quality of life for half of the people got worse?



What are the limitations of the study?

- This study did not provide any data on how long people lived on lorlatinib or crizotinib
- Long-term benefit of lorlatinib was not available at the time of this analysis
- The results from this study may be different in the real-world setting
- The study did not compare how well lorlatinib worked compared with other new medicines that are currently available

What do the results of this study mean?

The CROWN study included people with *ALK*-positive advanced NSCLC who had not been treated previously.

- More people who took lorlatinib lived without their cancer getting worse than people who took crizotinib
- Fewer people who took lorlatinib had their tumors spread to the brain than people who took crizotinib
- The most common side effects with lorlatinib were high levels of triglycerides (a type of fat) in the blood or high cholesterol in the blood. However, these side effects were manageable
- More people taking lorlatinib had a higher improvement in quality of life from the start of the study than people who took crizotinib

Original article

The original article "Efficacy and safety of first-line lorlatinib versus crizotinib in patients with advanced, *ALK*-positive non-small-cell lung cancer: updated analysis of data from the phase 3, randomised, open-label CROWN study" was published in *The Lancet Respiratory Medicine* (Solomon B, *et al. Lancet Respir Med.* 2023;11(4): 354–366.)

You can read the full article at: <https://pubmed.ncbi.nlm.nih.gov/36535300/>

Trial registration sites

You can read more about the phase 3 CROWN study (clinical trial number NCT03052608, Eudra CT number 2016-003315-35) at the following websites:

- <https://www.clinicaltrials.gov/ct2/show/NCT03052608>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-003315-35>

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

- <https://www.clinicaltrials.gov/ct2/about-studies/learn>
- <https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/what-clinical-trials-are>

Educational resources

You can read more about NSCLC on the Cancer.Net website at:

<https://www.cancer.net/cancer-types/lung-cancer-non-small-cell>

Patient guidelines on NSCLC from the National Comprehensive Cancer Network are available at:

<https://www.nccn.org/guidelines/guidelines-detail?category=patients&id=23>

Acknowledgments

Pfizer would like to thank all of the people who took part in this study. The authors of this article thank the people who participated in this trial and their families, as well as the investigators, co-investigators and staff at each of the clinical sites.

Financial & competing interests disclosure

This study was sponsored by Pfizer Inc., 235 East 42nd Street, New York, NY 10017. Phone (United States): +1 212 733 2323.

Full author disclosure information can be found in the original article. Writing support for this summary was provided by Alana Dorfstatter, PharmD, of ClinicalThinking, and was funded by Pfizer.