Plain Language Clinical Study
Summary

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine(s) Studied: Lorbrena® (lorlatinib)

Protocol Number: B7461027

Dates of Study: 29 September 2020 to 23 October 2024

Title of this Study: Study of Lorlatinib in People With ALK-positive Non-small Cell Lung Cancer Whose Disease Progressed After Previous Treatment

[Single-Arm Study of Lorlatinib in Participants With Anaplastic Lymphoma Kinase (ALK)-Positive Non-Small Cell Lung Cancer (NSCLC) Whose Disease Progressed After One Prior Second-Generation ALK Tyrosine Kinase Inhibitor (TKI)]

Date(s) of this Report: 12 August 2025

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– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. Do you have any questions about the study or the results? If so, please contact the doctor or staff at your study site.

Why was this study done?

What is non-small cell lung cancer?

Lung cancer is the name for cancer that starts in the lungs. Non-small cell lung (NSCLC) is the most common type of lung cancer. Some patients have NSCLC that is referred to as "anaplastic lymphoma kinase (ALK)-positive". These patients have changes in a gene that makes a protein called ALK. An abnormal form of ALK is produced that may cause the cancer cells to grow and to spread.

What is Lorbrena® (lorlatinib)?

Lorbrena® (lor-BREH-nuh), also known as lorlatinib is a medicine that works by blocking the activity of ALK. Lorlatinib is also known as an "ALK-inhibitor" medication. As cancer cells grow, they can form into a tumor and spread to other parts of the body, such as the brain. By blocking ALK, lorlatinib may help to slow down the growth or spread of ALK-positive tumors.

Lorlatinib is already approved for use in many countries to treat adults with advanced or recurrent NSCLC that is ALK-positive. Advanced NSCLC means the cancer cells have spread outside the lung where the tumor started. Recurrent cancer is cancer that has come back after treatment. Lorlatinib is approved in the United States under the trade name Lorbrena®, in the European Union under Lorviqua®, and in India under Lorbriqua®. Lorlatinib is taken by mouth, as a tablet.

What was the purpose of this study?

The purpose of this study was to see if lorlatinib could help reduce tumor size and slow growth in people with advanced ALK-positive NSCLC whose disease has worsened despite a first treatment with one of the 2 other medicines named alectinib or ceritinib.

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Alectinib and ceritinib are medicines used to treat specific type of lung cancer called ALK-positive NSCLC.

Researchers wanted to know:

- **Did taking lorlatinib help tumors disappear or shrink?**

What happened during the study?

How was the study done?

First, a study doctor checked each participant to make sure they were able to join the study. This is known as screening.

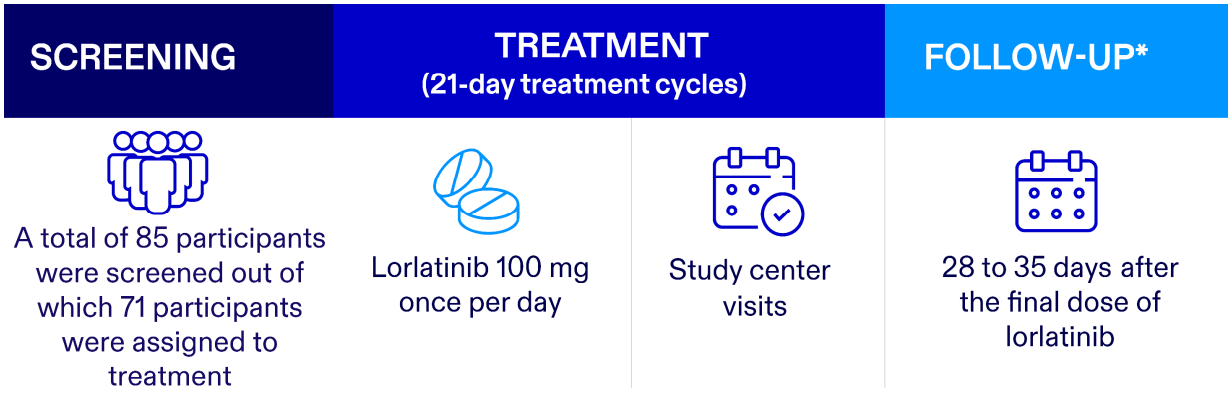
Participants then entered the treatment phase. All participants in this study took lorlatinib 100 milligrams (mg), once per day by mouth. Study treatment was given in continuous blocks of 21 days, called "cycles".

Participants were treated until their cancer got worse, they did not want to continue taking treatment, or they had unacceptable medical problems.

Participants were supposed to have a safety follow-up visit at least 28 days and up to 35 days after they stopped taking their study treatment. Participants who stopped taking treatment for reasons other than their cancer getting worse were supposed to undergo tumor assessments until their cancer got worse up to approximately 24 months.

Both the researchers and participants knew the treatment being given. This is known as an "open-label" study. A summary is shown in Figure 1 below.

Figure 1. Study plan



*Participants who stopped taking treatment for reasons other than their cancer getting worse were supposed to undergo tumor assessments until their cancer got worse up to approximately 24 months.

Where did this study take place?

The Sponsor ran this study at 34 locations in 7 countries in Europe, North America, and South Asia.

When did this study take place?

It began 29 September 2020 and ended 23 October 2024.

Who participated in this study?

The study included participants who had a confirmed diagnosis of advanced ALK-positive NSCLC. Participants' disease had worsened despite a first treatment with either alectinib or ceritinib before joining the study.

- A total of 41 men participated.
- A total of 30 women participated.
- All participants were between the ages of 26 years and 87 years.

All 71 participants who received study treatment, discontinued the study treatment. The most common reason for stopping study treatment was because their cancer eventually got worse. Some participants discontinued the study treatment due to study closure, but they continued taking the same treatment off study.

Other reasons for stopping study treatment were death, participants discontinued treatment by their own choice, a doctor decided it was best for a participant to stop taking the study treatment, participants' health declined, and medical problem.

Thirty-five (35) participants then entered the follow-up. Of these, 31 participants completed the follow-up. Four (4) participants did not finish the follow-up: 2 participants because they died and 2 participants because they stopped the study for other reasons.

How long did the study last?

Study participants were in the study for variable lengths of time. The entire study took about 4 years and 1 month to complete.

When the study ended in October 2024, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

Did taking lorlatinib help tumors disappear or shrink?

To answer this question, the researchers measured the "objective response rate" (ORR), which is the percentage of participants whose cancer got better (their tumor shrank or disappeared on images). Researchers calculated the percentages of participants whose tumor disappeared (called "complete response" [CR]) and/or decreased or shrank under therapy (called "partial response" [PR]) after treatment.

Overall, 30 participants had a tumor that disappeared or shrank (42.3%, or 30 out of the 71 treated participants). Among those, 4 out of 71 participants (5.6%) had no signs of cancer (a CR) and 26 out of 71 participants (36.6%) had their tumor shrinking enough up to an extent (to a certain size) under therapy that qualified for PR.

The percentage of participants whose tumor either stayed the same or had small variations in the size was 19.7% (14 out of 71 participants). These variations in size were because the tumor had got a bit bigger or a bit smaller.

Based on these results, the researchers concluded that participants with ALK-positive advanced NSCLC who were previously treated with either alectinib or ceritinib may have tumors that disappear or shrink after treatment with lorlatinib.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medicine might have on a participant.

Sixty-nine (69) out of 71 participants (97.2%) in this study had at least 1 medical problem. A total of 9 participants left the study treatment because of medical problems. The most common medical problems – those reported by more than 10% of participants – are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 10% of participants are listed. Some medical problems were grouped together because they were the same problem but reported differently. For example, all the medical problems that meant high level of cholesterol were grouped together under the term “high level of cholesterol in the blood (hypercholesterolemia)”. Groups like these are known as clustered medical problems. They are marked with a star (*) in this report.

- The **2nd** column tells how many of the 71 participants who took lorlatinib reported each medical problem. Next to this number is the percentage of the 71 participants who took lorlatinib and reported the medical problem.
- Using these instructions, you can see that 42 out of the 71 participants (59.2%) who took lorlatinib reported high level of cholesterol in the blood (hypercholesterolemia)*.

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Lorlatinib (71 Participants)**
High level of cholesterol in the blood (hypercholesterolemia)*	42 out of 71 participants (59.2%)
High level of triglycerides (a type of fat) in the blood (hypertriglyceridemia)*	40 out of 71 participants (56.3%)
Swelling (edema)*	33 out of 71 participants (46.5%)
Feeling very tired (fatigue)*	19 out of 71 participants (26.8%)
Nerve damage in arms and legs (peripheral neuropathy)*	15 out of 71 participants (21.1%)
Shortness of breath	14 out of 71 participants (19.7%)
Loose stools	13 out of 71 participants (18.3%)
Low red blood cell count	12 out of 71 participants (16.9%)
High level of lipid (fats) in the blood	12 out of 71 participants (16.9%)
Fever	12 out of 71 participants (16.9%)

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Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Lorlatinib (71 Participants)**
Joint pain	9 out of 71 participants (12.7%)
COVID infection	9 out of 71 participants (12.7%)
Mood effects*	9 out of 71 participants (12.7%)
Arm or leg pain	9 out of 71 participants (12.7%)
Cough	8 out of 71 participants (11.3%)

*Clustered (grouped) term

Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

A total of 23 participants (32.4%, or 23 out of 71 participants) had at least 1 serious medical problem. Serious medical problems that were reported in more than 1 participant included:

- Shortness of breath in 3 out of 71 participants (4.2%).
- Clot in a blood vessel in the lungs in 3 out of 71 participants (4.2%).
- Stroke or brain damage caused by disruption of blood supply in 2 out of 71 participants (2.8%).
- Lung infection in 2 out of 71 participants (2.8%).

All other serious medical problems were reported in 1 participant each. Researchers believed that lung infection reported by 1 participant was related to the study treatment.

A total of 20 participants died during the study. For 11 of these participants, this happened within 28 days after their last dose of study treatment. For 3 of these participants, this happened within 30 days after their first dose of study treatment. The most common cause of death was disease under the study (15 participants). These deaths were not believed to be related to study treatment.

Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/ research_clinical_trials/trial_results	Use the protocol number **B7461027**

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT04362072**
https://euclinicaltrials.eu	Use the study identifier **2019-002504-41**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering.
We do research to try to find the best ways to help patients, and you helped us to do that!

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