

## Summary of Clinical Trial Results

### A study to compare alectinib with chemotherapy in previously treated people with a type of lung cancer called 'ALK-positive non-small cell lung cancer'

See the end of the summary for the full title of the study.

#### About this summary

This is an updated summary of the results of a clinical trial (called a 'study' in this document) – written for:

- members of the public and
- people who took part in the study.

This summary is based on information known at the time of writing.

The study started in November 2015 and finished in August 2018. This summary is an update of a previous version which summarised the information known up until 26<sup>th</sup> January 2017 (and can be found by clicking on 'Intermediate Results' on the ALUR ForPatients webpage).

This summary was written after the study had ended and includes the results from the start of the study until 28<sup>th</sup> September 2018, the final time point of the study.

No single study can tell us all we need to know about the risks and benefits of a medicine. The results from this study may be different from other studies with the same medicine in lung cancer.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

#### Contents of the summary

1. General information about this study
2. Who took part in this study?
3. What happened during the study?
4. What were the results of the study?
5. What were the side effects?
6. How has this study helped research?
7. Are there plans for other studies?
8. Where can I find more information?

#### Thank you to the people who took part in this study

The people who took part in this study have helped researchers to answer important questions about anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC), written as 'ALK-positive lung cancer' in this summary, and the medicine being looked at (alectinib).

## Key information about this study

- This study was done to compare alectinib to chemotherapy in people with ‘late stage’ *ALK*-positive lung cancer. The people who took part had been previously treated with chemotherapy and another medicine, called crizotinib.
- It was decided by chance whether people in the study would be given alectinib or chemotherapy.
- This study included 119 people in 13 countries.
- The main finding was that, on average, people received alectinib for 10.9 months before their *ALK*-positive lung cancer got worse (i.e., until their cancer grew bigger or spread to other parts of the body) compared with 1.4 months for people who received chemotherapy.
- People took alectinib for about 10.2 months, and 26% of people (20 out of 77) had at least one serious side effect.
- People received chemotherapy for a shorter period of around 1.4 months, and 19% of people (7 out of 37) had at least one serious side effect.

## 1. General information about this study

### Why was this study done?

*ALK*-positive NSCLC is specific type of lung cancer. It is caused by an overactive ‘enzyme’ in the body called *ALK* (‘anaplastic lymphoma kinase’), which is genetically altered and causes lung cells to grow abnormally. When this study began, treatment options for people with *ALK*-positive lung cancer included ‘platinum-based’ chemotherapy or crizotinib. Crizotinib was the first treatment designed to reduce the effects of overactive *ALK*.

*ALK*-positive lung cancer usually gets worse within a year of crizotinib treatment, which is often due to the cancer spreading to the brain (called a ‘brain metastasis’). This is because crizotinib can’t reach the brain very well and doesn’t tend to work for very long if the cancer has spread there.

‘Standard’ chemotherapy was often given to people whose *ALK*-positive lung cancer got worse (grew or spread) with crizotinib. However, chemotherapy may not be as effective as medicines that are designed to target *ALK* directly. Chemotherapy is also associated with various side effects that can impact people’s day-to-day lives.

This study was done to see if an alternative medicine, alectinib, may prolong the time until their *ALK*-positive lung cancer got worse compared with ‘standard’ chemotherapy, after they have had previous treatment with ‘platinum-based’ chemotherapy and crizotinib.

## What were the treatments being studied?

---

This study looked at two different medicines:

- **Standard chemotherapy** – an existing treatment option for people whose *ALK*-positive lung cancer gets worse while receiving crizotinib. It works by damaging or ‘killing’ tumour cells, but can also damage healthy cells.
- **Alectinib** – the medicine that was studied here. Alectinib directly targets *ALK* – an ‘enzyme’ that is overactive in *ALK*-positive lung cancer. Alectinib slows down how quickly cancer cells multiply and can help to stop tumours from growing.

## What did researchers want to find out?

---

- Researchers did this study to compare chemotherapy with alectinib – to see how well alectinib worked in treating previously treated people with ‘late-stage’ *ALK*-positive lung cancer (see section 4, “What were the results of the study?”).
- They also wanted to find out how safe the medicine was – by checking how many people had side effects and seeing how serious they were, when taking each of the medicines during this study (see section 5, “What were the side effects?”). Side effects (also known as ‘adverse reactions’) are unwanted medical problems (such as a headache) that happen during a study.

### The main question that researchers wanted to answer was:

1. How long did it take (in months) for a tumour to get worse (grow or spread) for people receiving alectinib compared with people receiving chemotherapy?

### Other questions that researchers wanted to answer included:

2. What proportion of people had tumours that got smaller or shrunk completely, after receiving alectinib or chemotherapy?
3. What proportion of people had tumours in the brain that got smaller or shrunk completely, after receiving alectinib or chemotherapy?

## What kind of study was this?

---

This was a ‘Phase 3’ study that followed earlier studies in animals (‘pre-clinical’), healthy individuals (‘Phase 1’) and people with *ALK*-positive lung cancer who were previously treated with alectinib only (‘Phase 2’).

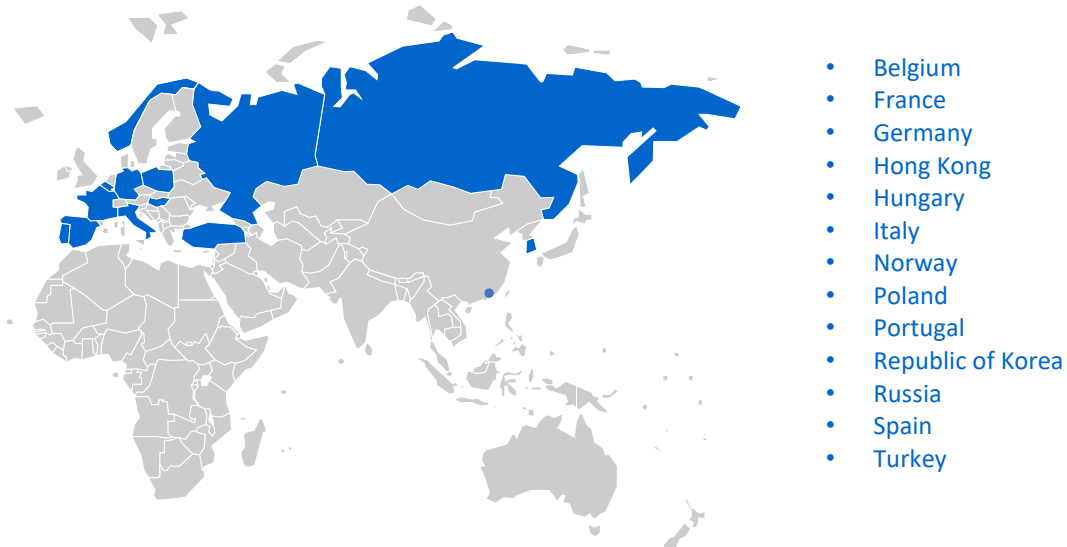
In this study, people with *ALK*-positive lung cancer received either alectinib or chemotherapy (pemetrexed or docetaxel). This was to find out if alectinib gave people more time before their *ALK*-positive lung cancer got worse (grew or spread), and to find out more about the possible side effects of alectinib.

This was an ‘open label’ study, meaning that patients, doctors and study staff knew which medicines people were taking.

## When and where did the study take place?

A total of 43 study centres, across 14 countries around the world were involved in forming the study and were on standby to recruit people with *ALK*-positive lung cancer to take part.

At 40 study centres across 13 countries in Europe and Asia, 119 adults were then selected to receive one of the study medicines (see section 3, “What happened during the study?”). The following map shows the countries where people were involved in this study:



## 2. Who took part in this study?

In this study, 119 adults with previously treated, confirmed *ALK*-positive lung cancer took part.

People who took part in the study were between 21 and 82 years of age.  
66 of the 119 people (55%) were male and 53 of the 119 people (45%) were female.

Before the study medicines were given, 49 out of 79 people (62%) who would receive alectinib in the study and 28 out of 40 people (70%) who would receive chemotherapy had *ALK*-positive lung cancer, which had already spread to the brain.

People could take part in the study if they had:

- *ALK*-positive lung cancer that had spread to other parts of the lung or body (called ‘late-stage’, ‘advanced’ or ‘metastatic’ disease).
- Healthy enough lives such that they could carry out their usual activities and were out of bed for more than 50% of waking hours.
- Experienced worsening of their *ALK*-positive lung cancer (grew or spread) while being treated with crizotinib and had also been treated with chemotherapy.

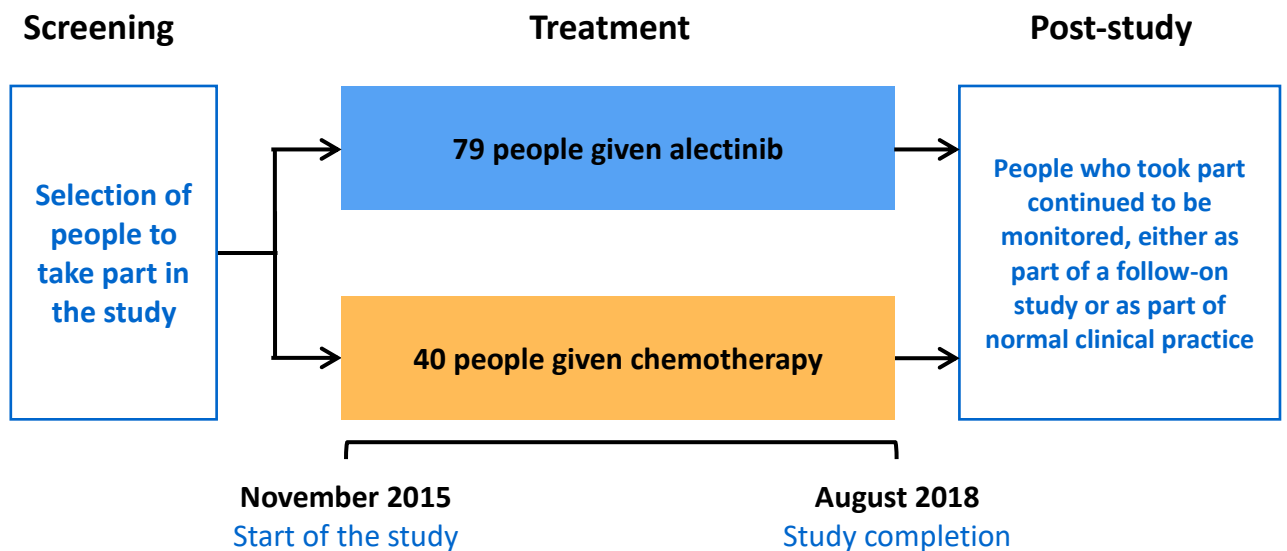
People could not take part in the study if they had:

- Any other cancers in the last three years.
- Any stomach, gut or liver problems that could affect how well the body takes up (or 'absorbs') medicines.
- Received any other medicine which targets *ALK* directly, other than crizotinib.

### 3. What happened during the study?

During the study, people were selected by chance, to get one of the two study medicines below. The study medicines given to people were selected at random by a computer:

- **Standard chemotherapy** – people could receive one of two types of standard chemotherapy, either 'pemetrexed' (500mg/m<sup>2</sup> dose) or 'docetaxel' (75mg/m<sup>2</sup> dose) – both taken via an injection into the vein every three weeks.
- **Alectinib** – given in capsule form (600mg dose) and taken by mouth twice daily.



People were treated with alectinib or chemotherapy until their cancer got worse, they (or their doctor) decided they should not continue in the study, they experienced undesirable effects from the treatment that caused them to withdraw from the study, or they died. People who were being treated with chemotherapy were allowed to change from chemotherapy to alectinib if their cancer got worse.

When the study finished, all people still receiving alectinib were invited to join a follow-on study or received alectinib and regular health checks as part of normal clinical practice.

Look below to see more information about what happened in the study.

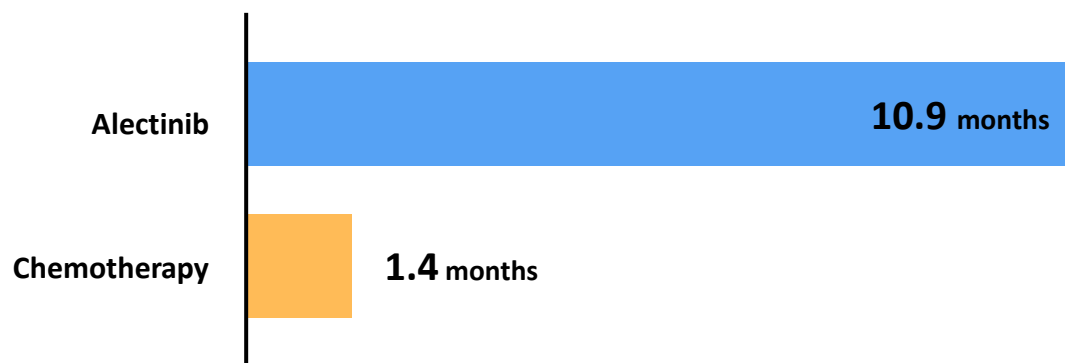
## 4. What were the results of the study?

### Question 1: How long did it take (in months) for a tumour to get worse (grow or spread) for people receiving alectinib compared with people receiving chemotherapy?

Researchers looked at the length of time between the date when each person entered the study and when their *ALK*-positive lung cancer got worse.

People who were given alectinib had **10.9 months** on average before their *ALK*-positive lung cancer got worse. This compares with **1.4 months**, on average, for people who were given chemotherapy.

**How long, on average, people in each group lived without worsening of their *ALK*-positive lung cancer:**



### Question 2: What proportion of people had tumours that got smaller or shrunk completely, after receiving alectinib or chemotherapy?

Researchers also looked at how many people responded to the study medicine. In other words, how many people had tumours that got smaller or shrunk completely.

A total of 40 out of 79 (**51%**) people responded to treatment with alectinib:

- 2 out of 79 people (3%) who were receiving alectinib had their *ALK*-positive lung cancer shrink completely (called a 'complete response').
- 38 out of 79 people (48%) who were receiving alectinib had their *ALK*-positive lung cancer shrink partly (called a 'partial response').

One out of 40 people (**3%**) responded to treatment with chemotherapy. This person had their *ALK*-positive lung cancer shrink partly (called a 'partial response').

### Question 3: What proportion of people had tumours in the brain that got smaller or shrunk completely, after receiving alectinib or chemotherapy?

---

Another piece of information that researchers collected was how many people responded to the study medicine in the brain. In other words, whether their *ALK*-positive lung cancer, which had already spread to the brain (i.e. a 'brain metastasis'), got smaller or shrunk completely.

This analysis included people who had 'measurable' brain metastases, i.e. at least 10mm in size using a 'CT' or 'MRI' scan.

A total of 16 out of 24 (**67%**) people responded to treatment with alectinib in the brain:

- 2 out of 24 people (8%) who were receiving alectinib had their 'brain metastases' shrink completely in the brain (called a 'complete response').
- 14 out of 24 people (58%) who were receiving alectinib had their 'brain metastasis' shrink partly (called a 'partial response').

No one out of the 16 people whose *ALK*-positive lung cancer had already spread to the brain responded to treatment with chemotherapy.

## 5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Side effects can vary from mild to very serious and may vary from person to person.

Serious and common side effects are listed in the following sections.

### Serious side effects

---

A side effect is considered 'serious' if it is life-threatening, needs hospital care, causes lasting problems or death.

People took alectinib for a period of 10.2 months and 26% of people (20 out of 77) had at least one serious side effect in this time. In comparison, people received chemotherapy for a shorter period of 1.4 months and 19% of people (7 out of 37) had at least one serious side effect in this time.

A small number of people experienced side effects that indicated that they may need to stop taking the study medicine. After speaking to the study doctors, a total of 4 people in the alectinib group (5%) and 4 people in the chemotherapy group (11%) stopped taking their study medicine because of a side effect (serious or non-serious).

### Most common side effects

---

The most common side effects are shown in the following table – these are the 10 most common side effects that occurred in either of the treatment groups.

	People taking alectinib	People taking chemotherapy
Average time on treatment	10.2 months	1.4 months
<b>Most common side effects reported in this study</b>		
Constipation	21% (16 out of 77)	11% (4 out of 37)
Low level of red blood cells (anaemia)	16% (12 out of 77)	16% (6 out of 37)
Muscular pains (myalgia)	14% (11 out of 77)	11% (4 out of 37)
Fluid retention in the limbs (peripheral oedema)	14% (11 out of 77)	5% (2 out of 37)
Back pain	13% (10 out of 77)	5% (2 out of 37)
Physical weakness or lack of energy (asthenia)	12% (9 out of 77)	16% (6 out of 37)
Feeling tired (fatigue)	7% (5 out of 77)	24% (9 out of 37)
Feeling sick (nausea)	4% (3 out of 77)	19% (7 out of 37)
Hair loss (alopecia)	1% (1 out of 77)	22% (8 out of 37)
Low level of white blood cells (neutropenia)	0% (0 out of 77)	14% (5 out of 37)

### Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

## 6. How has this study helped research?

The information presented here is from a single study of 119 people with *ALK*-positive lung cancer. These results are helping researchers learn more about *ALK*-positive lung cancer and alectinib, including how effective alectinib is and what the common side effects are.

The results from this study show that alectinib is more effective than chemotherapy in treating ‘late-stage’ *ALK*-positive lung cancer in people who have previously received crizotinib and chemotherapy. On average, people taking alectinib had **10.9 months** on average without worsening of their *ALK*-positive lung cancer (grew or spread) compared with **1.4 months** on average for people taking chemotherapy.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**



## 7. Are there plans for other studies?

Other studies looking at the safety and effectiveness of alectinib are taking place. These studies are looking at the use of alectinib in different situations, for example:

- In people with untreated, 'late-stage' *ALK*-positive lung cancer.
- In people with 'early stage' *ALK*-positive lung cancer, rather than 'late stage' *ALK*-positive lung cancer that is described in this summary.

## 8. Where can I find more information?

You can find more information about this study on the websites listed below:

- <https://clinicaltrials.gov/ct2/show/NCT02604342>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-000634-29/results>
- <https://forpatients.roche.com/en/trials/cancer/lung-cancer/alectinib-compared-with-chemotherapy-in-previously-treated-patie.html>

If you would like to find out more about the results of this study, the full title of the latest scientific paper is, "Final efficacy and safety data, and exploratory molecular profiling from the phase III ALUR study of alectinib versus chemotherapy in crizotinib-pretreated *ALK*-positive non-small cell lung cancer". The authors of the scientific paper are: J. Wolf, Å. Helland, I-J. Oh, MR. Migliorino, R. Dziadziuszko, J. de Castro, J. Mazières, F. Griesinger, M. Chlistalla, A. Cardona, T. Ruf, K. Trunzer, V. Smoljanovic & S. Novello.

The paper is published in the journal 'ESMO Open' and is available online:

<https://doi.org/10.1016/j.esmoop.2021.100333>

### Who can I contact if I have questions about this study?

---

If you have any further questions after reading this summary:

- Contact a representative at your local Roche office.
- Visit the ForPatients platform and fill out the contact form – <https://forpatients.roche.com/>.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

### Who organised and paid for this study?

---

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

## **Full title of the study and other identifying information**

---

The full title of this study is, “Randomized, Multicenter, Phase III, Open-Label Study Of Alectinib Versus Pemetrexed Or Docetaxel In Anaplastic Lymphoma Kinase-Positive Advanced Non-Small Cell Lung Cancer Patients Previously Treated With Platinum-Based Chemotherapy And Crizotinib”.

The study is known by the acronym ‘ALUR’.

- The ClinicalTrials.gov identifier for this study is: NCT02604342.
- The EudraCT number for this study is: 2015-000634-29.
- The protocol number for this study is: MO29750.