Summary of Clinical Trial Results

A clinical study to determine the effect of alectinib as a treatment for people with *ALK*-positive lung cancer after their type of lung cancer was diagnosed using a blood test (BFAST: Blood First Assay Screening Trial)

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

About this summary

This is a 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 overall study started in September 2017 and is expected to end in 2024. This summary includes the results from one part of the study looking at people with anaplastic lymphoma kinase (*ALK*)-positive lung cancer which started in November 2017 and is based on information known up until June 2019. At the time of writing this summary, the study is still happening – study doctors are still collecting information.

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.**

Contents of the summary

Glossary

- BFAST = Blood First Assay Screening Trial

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about the use of a blood test to diagnose *ALK*-positive non-small cell lung cancer, written as '*ALK*-positive lung cancer' in this summary, and the medicine being looked at (alectinib).

Key information about this study

- This part of the study was done to see if using a blood test to detect alterations in certain genes could predict the people with lung cancer who will respond well to certain treatments. This summary will focus on results in people whose blood test found an alteration in the *ALK* gene (*ALK*-positive lung cancer).
- In this study, people were given a medicine called 'alectinib'.
- This study included 87 people in 15 countries.
- So far, the study has shown that 87% of people (76 out of 87) responded to treatment with alectinib, according to the doctors who were treating them.
- At the time of this analysis, on average, people took alectinib for a period of 11.1 months and 6% of people (5 out of 87) had at least one serious side effect related to alectinib.
- At the time of writing this summary, the study is still happening and is anticipated to end in 2024.

1. General information about this study

Why was this study done?

Changes in genetic material, known as genetic alterations, can cause cancer. There are lots of different types of genetic alterations and knowing which gene has been altered can help the doctor to identify the best treatment. In lung cancer, the type of genetic alteration that a person has is usually identified by a 'biopsy' – this is where a doctor removes cancer cells or tissue to examine underneath a microscope or to perform other types of tests on. However, some people's cancer may be difficult to get to or the doctor may not get enough cancer cells or tissue to test.

A blood test is a newer way of finding out what type of genetic alteration a person's cancer has, and it doesn't involve cutting out any of the cancer. As tumours grow and die, the dead tumour cells get broken down and they release fragments of their DNA into the blood. Doctors can take a sample of blood and find out what type of genetic alteration a person has by testing the DNA from the tumour in their blood.

This study is called the 'Blood First Assay Screening Trial' or 'BFAST'. It is one of the first studies to see if you could use only a blood test to identify genetic alterations in the blood of people with a specific type of lung cancer and then see how well specific medicines for these types of lung cancer work.

Everyone who joins this study will be split into groups based on what type of genetic alteration has been found from their blood test:

- ***ALK* group** – these people will receive a medicine called 'alectinib'.
- ***RET* group** – these people will also receive alectinib.
- **bTMB group** (known as blood tumour mutational burden) – these people will be split into groups to receive either a medicine called 'atezolizumab' or chemotherapy.
- ***ROS1* group** – these people will receive a medicine called 'entrectinib'.
- ***BRAF* group** – these people will receive a combination of medicines called 'cobimetinib' and 'vemurafenib', and after 4 weeks will also receive atezolizumab.
- ***EGFR* exon 20 group** – these people will receive a combination of atezolizumab, a medicine called 'bevacizumab' and chemotherapy.

This summary will focus on the group of people with lung cancer with an alteration in the *ALK* gene. *ALK*-positive lung cancer is a 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. This part of the study was done to see if you could use a blood test to identify people with *ALK*-positive lung cancer and then see how well the study medicine, alectinib, works.

What is the study medicine?

A medicine called 'alectinib' (ALECENSA™) is looked at in this study.

- 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?

- This study aimed to test how well alectinib works when it is used to treat people with *ALK*-positive lung cancer that have been diagnosed using a blood test (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the medicine is – by checking how many people had side effects, and seeing how serious they were, when taking alectinib during this study (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:

1. What proportion of people had tumours that got smaller or shrank completely, after receiving alectinib?

Other questions that researchers wanted to answer included:

2. How long did people live with their *ALK*-positive lung cancer after receiving alectinib, without it getting worse?
3. How long did people live overall with their *ALK*-positive lung cancer after receiving alectinib?

What kind of study was this?

This study was a Phase 2 study. A Phase 2 study involves treating a medium-sized group of people to find out if a drug works and is safe. In this study, people with *ALK*-positive lung cancer received alectinib – this was to find out if alectinib works after their *ALK*-positive lung cancer was diagnosed using a blood test.

When and where did the study take place?

This part of the BFAST study started in November 2017. This summary includes the results up until June 2019. At the time of writing this summary, the study is still happening – study doctors are still collecting information.

The study took place at 36 study centres, across 15 countries around the world. The following map shows the countries where this study took place:

- Belgium
- Brazil
- Canada
- Chile
- France
- Hong Kong
- Israel
- Italy
- Mexico
- Poland
- Republic of Korea
- Singapore
- Spain
- Thailand
- United States of America

2. Who took part in this study?

In this study, 87 people with untreated, confirmed *ALK*-positive lung cancer took part.

People who took part in the study were between 25 and 82 years of age. 35 of the 87 people (40%) were male and 52 of the 87 people (60%) were female.

Before receiving alectinib, 35 out of 87 people (40%) 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).
- Not received any other medicines for their *ALK*-positive lung cancer.

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

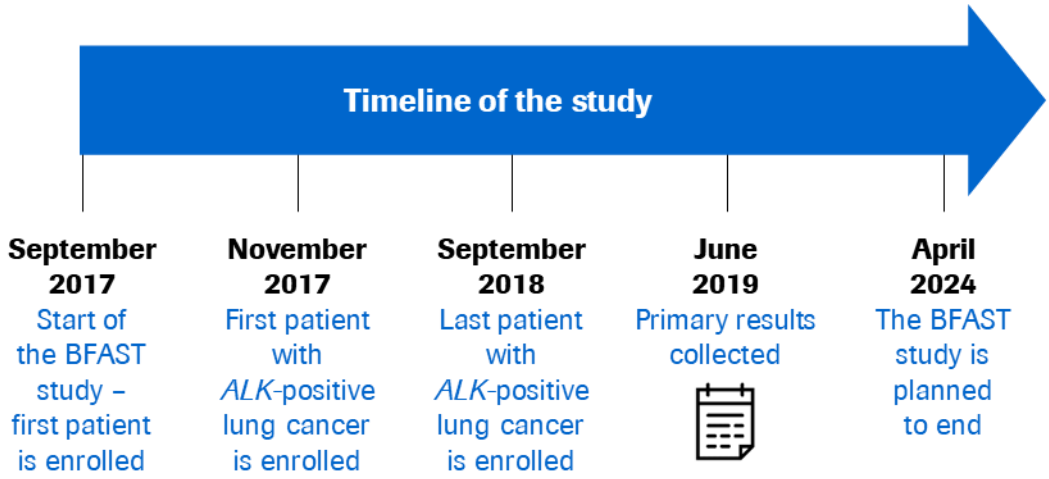
- Any other cancers in the last 5 years.
- Any stomach, gut or liver problems that could affect how well the body takes up (or 'absorbs') medicines.
- A slow heart rate, also known as 'symptomatic bradycardia'.

3. What happened during the study?

During the study, a blood sample was taken and tests were performed to identify people with an alteration in the *ALK* gene.

The study medicine was alectinib – given in capsule form (600mg dose) and taken by mouth twice daily.

This study is still happening so some people are still being treated with the study medicine. When the study finishes, the people who took part will be asked to go back to their study centre for more visits, to check their overall health. Look below to see more information about what has happened in the study so far – and what the next steps are.



This study is still happening so the symbol on the timeline (📋) shows when the information shown in this summary was collected – June 2019.

4. What were the results of the study?

Question 1: What proportion of people had tumours that got smaller or shrank completely, after receiving alectinib?

Researchers looked at how many people responded to the study medicine, alectinib; in other words, whether their *ALK*-positive lung cancer got smaller or shrank completely.

A total of 76 out of 87 people (**87%**) responded to treatment with alectinib as determined by the doctors who were treating the people:

- No one who was receiving alectinib had their *ALK*-positive lung cancer shrink completely (called a 'complete response').
- All of the people who responded to treatment with alectinib had their *ALK*-positive lung cancer shrink partly (called a 'partial response').

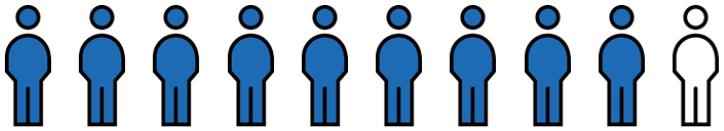
A total of 80 out of 87 people (**92%**) responded to treatment with alectinib as determined by an independent group of doctors not involved in treating people in this study:

- 11 out of 87 people (13%) had their *ALK*-positive lung cancer shrink completely (called a 'complete response').
- 69 out of 87 people (79%) had their *ALK*-positive lung cancer shrink partly (called a 'partial response').

Question 2: How long did people live with their *ALK*-positive lung cancer after receiving alectinib, without it getting worse?

Another piece of information that researchers wanted to collect was how long people lived with their *ALK*-positive lung cancer after receiving alectinib, without it getting worse.

This information was estimated by looking at a graph showing how many people had experienced their *ALK*-positive lung cancer getting worse over time, after receiving alectinib:



Around 9 in every 10 people (91%)
did not experience their *ALK*-positive lung cancer getting worse within **6 months** of starting alectinib treatment

Almost 8 in every 10 people (78%)
did not experience their *ALK*-positive lung cancer getting worse within **12 months** of starting alectinib treatment

Question 3: How long did people live overall with their *ALK*-positive lung cancer after receiving alectinib?

Another piece of information that researchers wanted to collect was how long people lived with their *ALK*-positive lung cancer after receiving alectinib.

This information was estimated by looking at a graph showing when people died after receiving alectinib:

Almost everyone (98%)
survived for at least **6 months** after starting alectinib treatment

Almost 9 in every 10 people (87%)
survived for at least **12 months** after starting alectinib treatment

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during 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 leaflet.
- 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, or causes lasting problems or death.

People took alectinib for a period of 11.1 months on average and 21 out of 87 people (24%) had at least one serious side effect in this time.

The most common serious side effects are shown in the following table – these are the six most common serious side effects that occurred in people taking alectinib in this study.

Serious side effects reported in this study	**People taking alectinib**
Being short of breath (dyspnoea)	7% (6 out of 87)
Liver damage – shown by higher levels of an enzyme called 'ALT' in the blood	2% (2 out of 87)
Liver, heart or kidney damage – shown by higher levels of an enzyme called 'AST' in the blood	2% (2 out of 87)
Constipation	2% (2 out of 87)
A type of infection which affects the lungs, called 'pneumonia'	2% (2 out of 87)
An infection that affects the parts of the body involved in breathing (respiratory tract infection)	2% (2 out of 87)

One person died due to a side effect that was considered unrelated to alectinib by the study doctor.

A small number of people experienced side effects that indicated that they may need to stop taking the study medicine. A total of 6 people (7%) stopped taking alectinib 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 five most common side effects that occurred in people taking alectinib in this study.

Most common side effects reported in this study	People taking alectinib
Constipation	38% (33 out of 87)
Swelling of the lower legs or hands (peripheral oedema)	37% (32 out of 87)
Feeling tired (fatigue)	25% (22 out of 87)
Liver, heart or kidney damage – shown by higher levels of an enzyme called 'AST' in the blood	24% (21 out of 87)
Liver damage – shown by higher levels of a substance called 'bilirubin' in the blood	24% (21 out of 87)

Other side effects

There were a small number of serious side effects that the study doctor believes were related to the treatment. During the study, 5 out of 87 people (6%) treated with alectinib had at least one serious side effect related to alectinib.

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 87 people with *ALK*-positive lung cancer. These results helped researchers learn more about *ALK*-positive lung cancer and alectinib.

The BFAST study is one of the first studies to see if you could use only a blood test to identify genetic alterations in the blood of people with a specific type of lung cancer and then see how well specific medicines for these types of lung cancer work.

The purpose of this part of the BFAST study was to see how well alectinib works when it is used to treat people who have had their *ALK*-positive lung cancer diagnosed using a blood test. Because 76 out of 87 (87%) people with *ALK*-positive lung cancer responded to treatment with alectinib, this study shows that a blood test can be an effective way of identifying people who may respond well to alectinib.

As it can be hard to remove samples of tissue for a biopsy in some people with lung cancer, this can sometimes lead to a delay in selecting a targeted treatment or the person only being given a standard form of chemotherapy (which may be less effective). This study shows that a blood sample (which is easier to get than a tissue sample) can be used to diagnose *ALK*-positive lung cancer, so that targeted treatment with alectinib can be selected. This may improve access to targeted treatment for more people with *ALK*-positive lung cancer.

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 parts of the BFAST study are still happening, in people whose blood test identified different genetic alterations:

- ***ALK* group** – this group is full.
- ***RET* group** – alectinib was tested in people with *RET*-positive lung cancer but this part of the study was closed sooner than planned, as the early results did not show a clear benefit. The data was presented by N. Peled at the World Lung Cancer Congress in 2020.
- **bTMB group** – this group is now full. An initial analysis (presented at the European Society of Medical Oncology in 2021 by R. Dziadziuszko) did not show any difference in benefit in patients with bTMB-positive lung cancer treated with atezolizumab or chemotherapy.
- ***ROS1* group** – this group is now full.
- ***BRAF* group** – this group is now full; analysis is about to start.
- ***EGFR* exon 20 group** – this group is looking for people with *EGFR* exon 20-positive lung cancer to join.

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/NCT03178552
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-000076-2/results
- https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-study-to-evaluate-efficacy-and-safety-of-multiple-targeted-the.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Blood First Assay Screening Trial (BFAST) in treatment-naïve advanced or metastatic NSCLC: initial results of the phase 2 *ALK*-positive cohort”. The authors of the scientific paper are: R. Dziadziuszko, T. Mok, S. Peters, J.-Y. Han, J. Alatorre-Alexander and others. The paper is published online in the journal ‘Journal of Thoracic Oncology’, 2021;Jul 24:S1556-0864(21)02321-2.

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

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-study-to-evaluate-efficacy-and-safety-of-multiple-targeted-the.html
- Contact a representative at your local Roche office.

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: “A Phase II/III Multicenter Study Evaluating the Efficacy and Safety of Multiple Targeted Therapies as Treatments for Patients With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) Harboring Actionable Somatic Mutations Detected in Blood (BFAST: Blood First Assay Screening Trial)”.

The study is known as ‘BFAST’.

- The ClinicalTrials.gov identifier for this study is: NCT03178552.
- The EudraCT number for this study is: 2017-000076-28.
- The protocol number for this study is: B029554.