Alectinib compared with chemotherapy in previously treated patients with *ALK*-positive NSCLC

This summary of the clinical trial called ALUR (MO29750) was prepared in November 2017 to provide patients who participated in the trial with information on why the trial was done, and the first results from the trial. Roche, the sponsor of this trial, would like to thank the participants for their contribution. If you have any queries about treatment options in your country, please speak with your healthcare professional.

What was this trial about?

Non-small-cell lung cancer (NSCLC) is a common form of lung cancer. There are different types of NSCLC, based on the type of cell the cancer starts in, and changes in different genes. Patients who took part in this clinical trial, ALUR (MO29750), had a change in the gene called *ALK* (anaplastic lymphoma kinase), and are described as having *ALK*-positive NSCLC. The number of cases of *ALK*-positive NSCLC is low, and these patients are more likely to be young and female, and they have a higher chance that the cancer will spread to the brain. The aim of this trial was to look at how well a new drug (called alectinib) worked in patients with *ALK*-positive NSCLC, compared with standard chemotherapy.

When this study took place, treatment options for patients with *ALK*-positive NSCLC included platinum-based chemotherapy, and the drug crizotinib. For patients whose cancer did not improve or got worse with crizotinib, treatment was stopped and patients went on to receive standard chemotherapy (pemetrexed or docetaxel). The new drug alectinib was investigated as an alternative to standard chemotherapy for patients already treated with platinum-based chemotherapy and crizotinib, whose cancer did not improve or got worse.

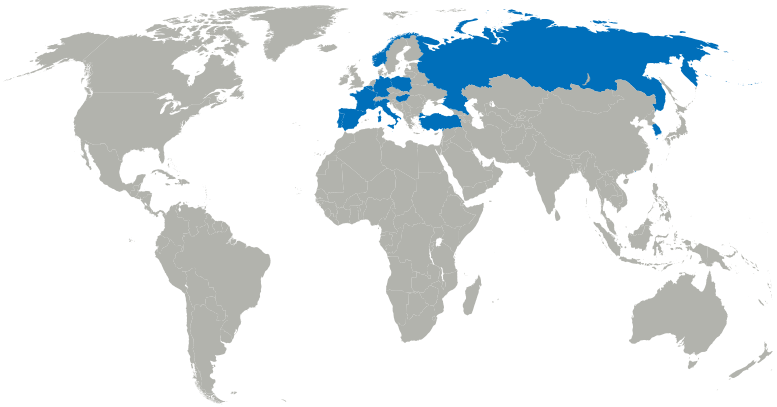
This phase III trial looked at whether alectinib can stop the cancer from getting worse and is a well-tolerated alternative compared with the standard chemotherapy available for patients whose cancer had previously worsened when they were treated with chemotherapy and crizotinib. The objective of the trial was to see if alectinib should be offered as treatment instead of chemotherapy after crizotinib.

Who took part?

The trial started in November 2015, and here we report results collected until January 2017. Patients from 40 different hospitals in 13 countries across Europe and Asia have taken part.

In total, 107 patients chose to take part and met all of the following requirements:

- Aged over 18 years old
- Diagnosed with lung cancer (NSCLC)
- *ALK*-positive NSCLC confirmed by a specific test
- Had a tumour that could be measured
- Had already received platinum-based chemotherapy and crizotinib for their NSCLC
- Expected to live for more than 12 weeks
- Were light or non-smokers



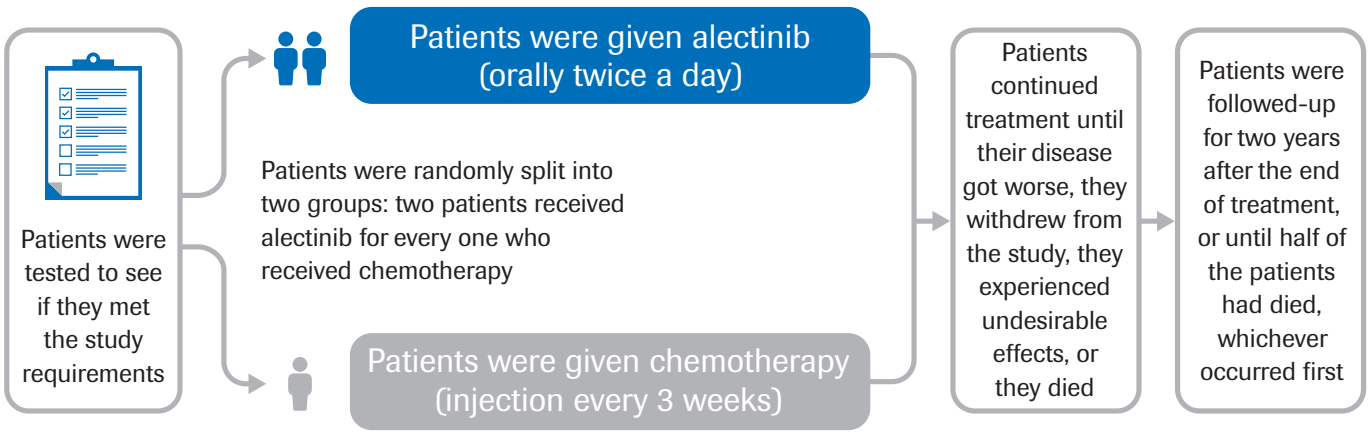
107 patients

40 centres

13 countries

Trial design

Patients were chosen at random to be treated with either alectinib or chemotherapy. For every two patients who received alectinib, one patient received chemotherapy. Patients 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. Patients who were being treated with chemotherapy were allowed to change from chemotherapy to alectinib if their cancer got worse.



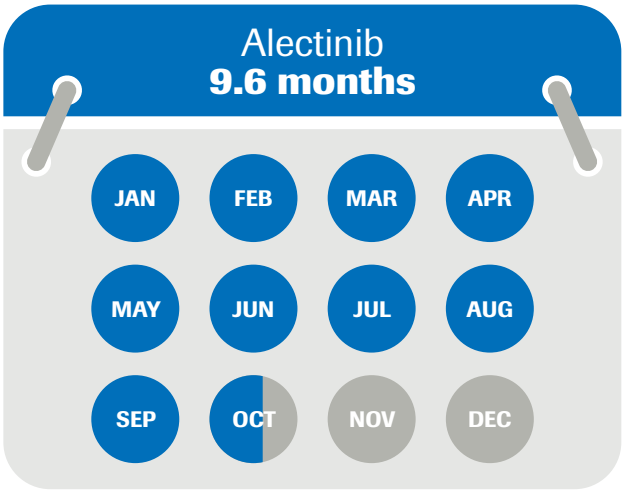
Results

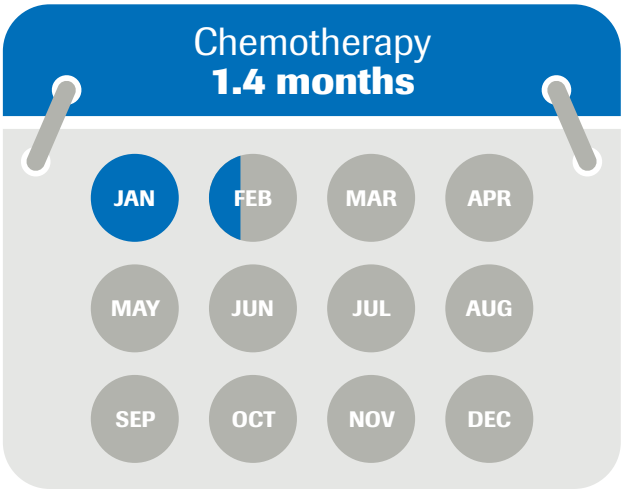
Here, we report the key results for the first 107 patients to be treated, of whom 72 received alectinib and 35 received chemotherapy. A total of 76 patients also had brain tumours at the start of the study. Of these, 50 patients received alectinib treatment, and 26 received chemotherapy.

How long did patients live without their cancer getting worse?

A key objective of this trial was to measure how long it took from the start of treatment with alectinib or chemotherapy until a patient's cancer got worse, the patient experienced undesirable effects from the treatment that caused them to withdraw from the study, or until the patient died. This is known as progression-free survival.

When chemotherapy was given after crizotinib, it took on average between 1 and 2 months for the cancer to get worse. For patients who received alectinib, it took on average between 9 and 10 months for their cancer to get worse. Statistical analysis showed that patients receiving alectinib were more likely to live for longer without their cancer getting worse than patients receiving chemotherapy.

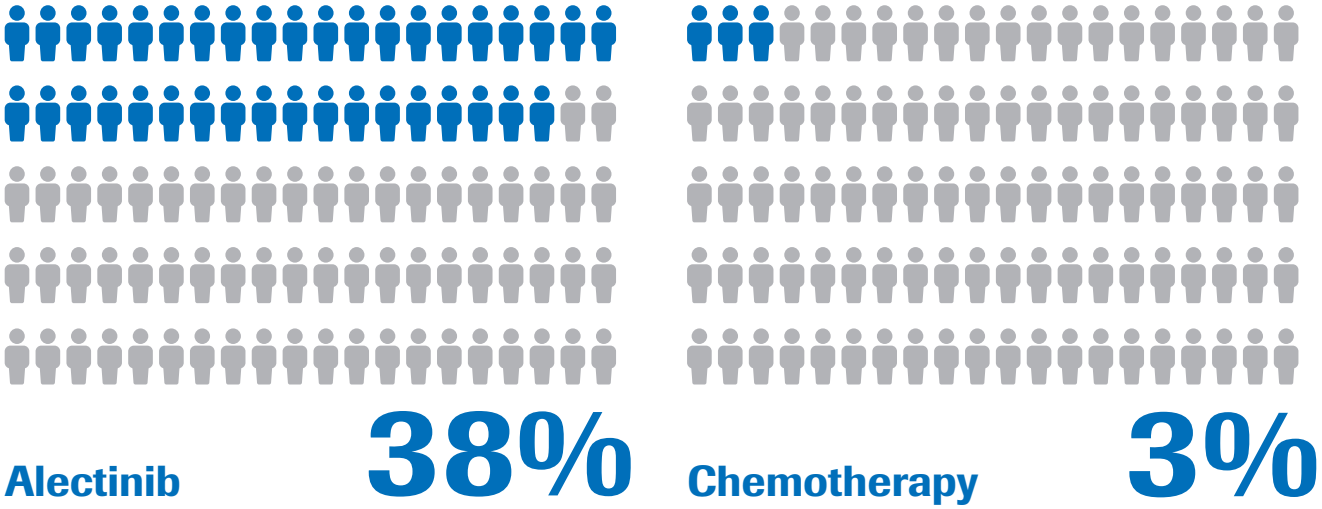




Reduction in the size of the tumour

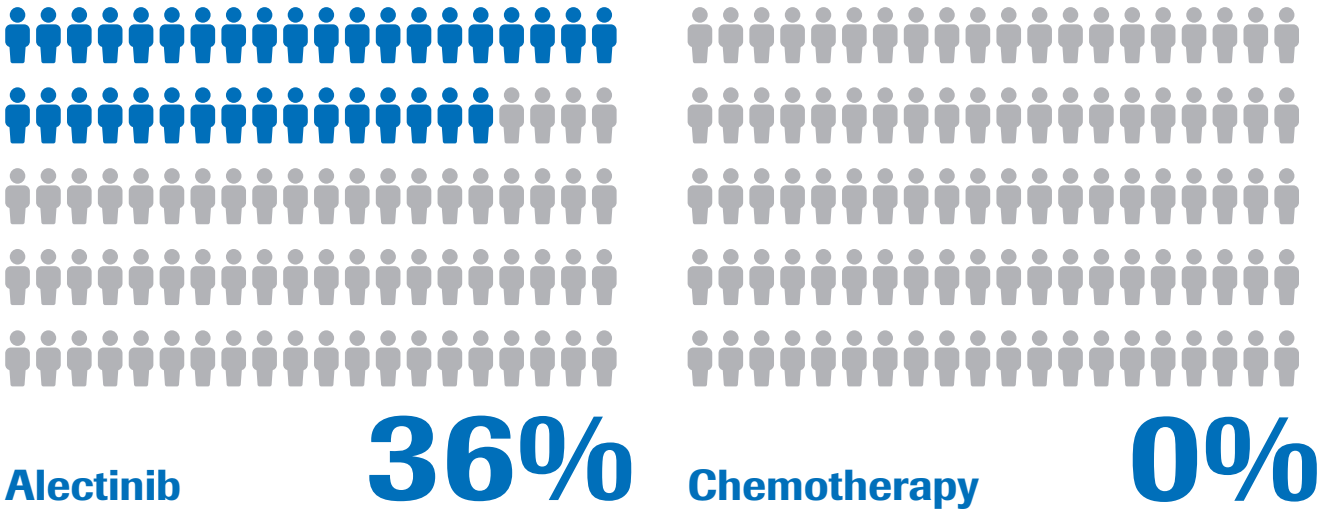
Another important measure of whether a treatment is working is whether the tumour is reduced in size. In this study, more patients treated with alectinib had a reduction in the size of their tumour compared with patients treated with chemotherapy.

In patients who received alectinib, almost four-in-ten (38%) had a reduction in their tumour size. In patients who received chemotherapy, 3% had a reduction in their tumour size.



Treatment of cancer that has spread to the brain

In 76 patients cancer had spread to their brain (metastatic disease) before the trial started. Of these, 50 patients received alectinib, and 26 received chemotherapy. The trial looked at whether alectinib or chemotherapy could treat this cancer that had spread to the brain. In those patients who received alectinib, just over one-in-three (36%) had a reduction in their metastatic disease. No patients who received chemotherapy had a reduction in their metastatic disease.



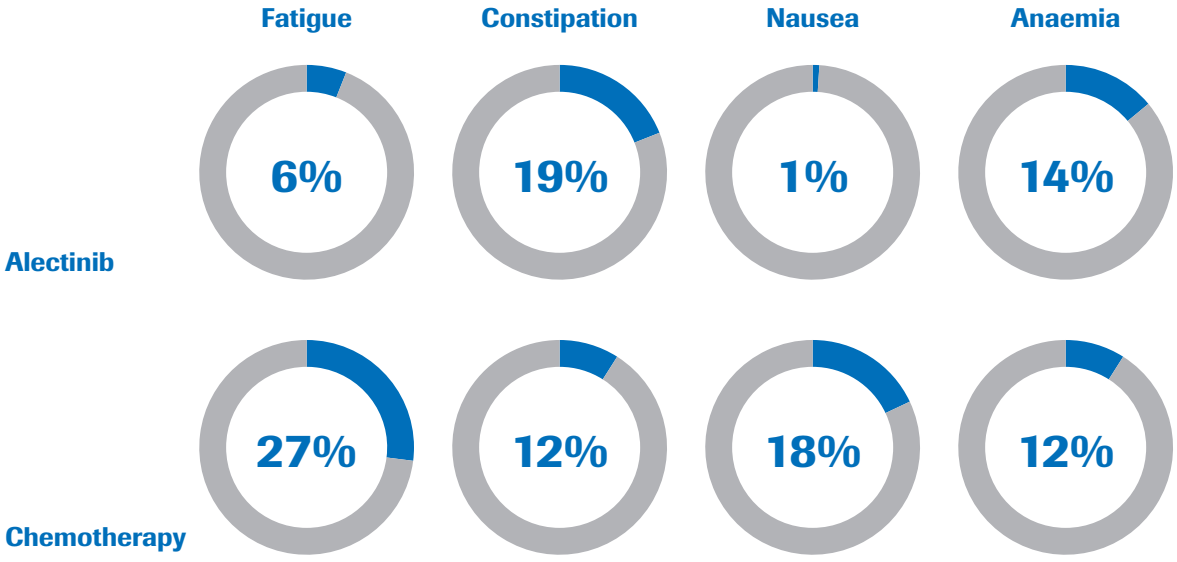
The trial also looked at the time it took from when these patients with *ALK*-positive NSCLC had a reduction in their metastatic disease in the brain until their cancer got worse. For patients who had a reduction in their metastatic disease, measurements were still ongoing in January 2017 when these results were collected. None of the patients who received chemotherapy had a reduction in their metastatic disease; for these patients this means that an average time from their tumour shrinking to their tumour growing again could not be calculated.

For patients who had metastatic disease in their brain before the trial started, those who received alectinib were less likely to have an increase in metastatic disease in their brain compared with patients who received chemotherapy. For patients who did not have metastatic disease in their brain at the beginning of the trial, patients who received alectinib took longer to develop tumours in the brain compared with patients who received chemotherapy.

Adverse events

An adverse event is an unfavourable medical occurrence associated with the use of a drug; it may or may not be thought to be related to the drug. Adverse events are different from side effects, which are known effects of a drug beyond the intended effect. Moderate adverse events are those that are not life-threatening, but result in a patient needing additional treatment. Severe adverse events are those that could result in death. It may be possible to reduce the number and severity of adverse events, for example, by lowering the dose of study drug received, or with supportive treatment.

The trial looked at whether alectinib is well-tolerated compared with chemotherapy, by measuring the number and type of adverse events in all patients. More patients who received chemotherapy had adverse events compared with patients who received alectinib. In patients who received alectinib, the most common adverse events were constipation (bowel movements occur less often) and anaemia (reduced number of red blood cells). In patients who received chemotherapy, nausea (feeling sick) and fatigue (overwhelming tiredness) were the most common adverse events.



Four-in-ten (41%) patients who received chemotherapy had a moderate or severe adverse event, compared with almost three-in-ten (27%) who received alectinib. The number of adverse events that caused patients to stop treatment was lower with alectinib (6%), than with chemotherapy (9%).

These safety results are similar to those seen in other alectinib trials.

What was the overall outcome?

Alectinib was shown to be a more effective treatment than standard chemotherapy in patients with *ALK*-positive NSCLC whose disease had got worse on crizotinib treatment. Patients who received alectinib lived for longer before their cancer got worse, and responded better to treatment. Patients with additional metastatic disease in the brain also lived for longer before their cancer got worse and responded better with alectinib than with chemotherapy.

Patients who received alectinib had fewer adverse events than patients who received chemotherapy.

The results of this trial suggest that alectinib can slow down the rate at which the cancer gets worse, is well-tolerated, and is a good alternative to standard chemotherapy in patients with *ALK*-positive NSCLC who have already received platinum-based chemotherapy and crizotinib.

Future studies

This trial was funded by F. Hoffmann-La Roche. There are other clinical trials that have been completed and that are ongoing using alectinib.

Any more questions?

Follow this link to ClinicalTrials.gov for more information on this trial. The trial number is NCT02604342. If you have any further questions, please contact a representative at your local Roche office.