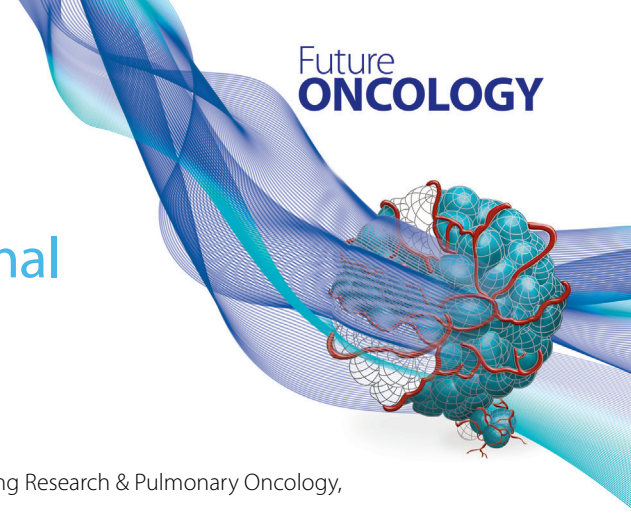
Future ONCOLOGY

Plain Language Summary of Publication

# Plain language summary of the final results from the GioTag study



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## Summary

The GioTag study assessed how drugs called afatinib and osimertinib affected people with non-small cell lung cancer (NSCLC) who had mutations in the epidermal growth factor receptor (*EGFR*) gene. Resistance mutations in our genes can lead to resistance to specific treatments, meaning that drugs no longer work. Patients in the current study all initially received afatinib treatment before they developed a certain resistance mutation in the *EGFR* gene, called T790M. Patients then started osimertinib treatment. The study aimed to identify for how long patients received treatment and for how long patients survived after their first dose of afatinib. Overall, 204 patients were included. Median overall time on treatment (afatinib and osimertinib) was 27.7 months. Median overall survival was 37.6 months. This study showed that afatinib followed by osimertinib treatment was effective in patients with NSCLC with *EGFR* mutations developing T790M resistance mutations on initial afatinib treatment.

### How to say.....

- **Afatinib:** a-fa-ti-nib
- **Dacomitinib:** da-co-mi-ti-nib
- **Erlotinib:** er-lo-ti-nib
- **Gefitinib:** je-fi-ti-nib
- **Osimertinib:** o-si-mur-ti-nib

## Who should read this article?

Patients and their caregivers, patient advocates and healthcare professionals, including those who are helping people learn about scientific discoveries and potential new therapeutic strategies.

## Who sponsored this review?

Boehringer Ingelheim.

## What was the focus of the study?

Patients with non-small cell lung cancer (NSCLC for short) have few treatment options. Some patients with NSCLC have a mutation in a gene called the epidermal growth factor receptor (*EGFR* for short). The most common *EGFR* mutations are called Del19 and L858R. Many patients with *EGFR* mutations receive drugs called EGFR tyrosine kinase inhibitors (TKIs for short). There are several different types of EGFR TKIs available, which fall into three different categories: first-generation, second-generation and third-generation.

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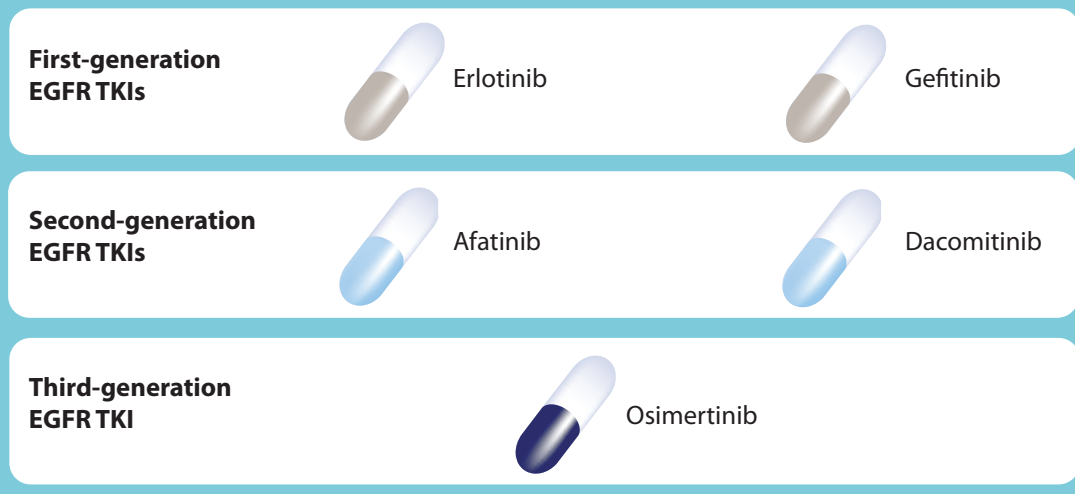
## What was the focus of the study? (continued)

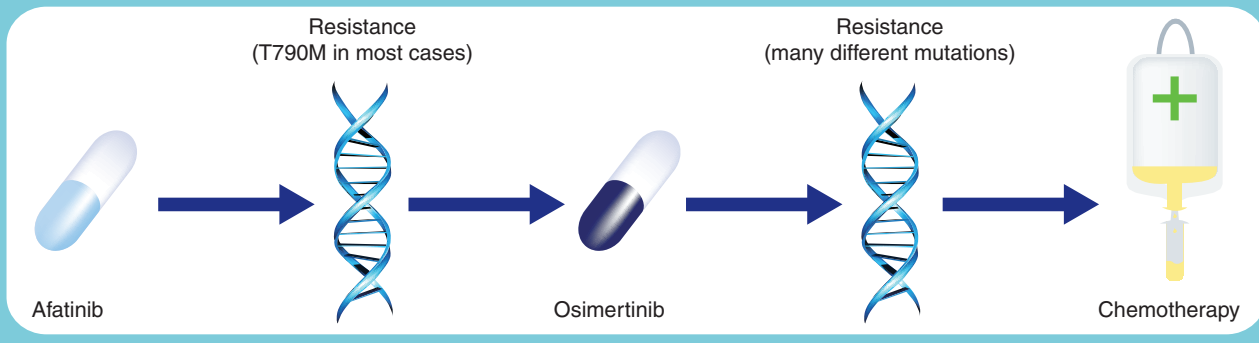
These categories include:




In previous clinical trials, all of these treatments were generally well tolerated; however, patients survived for longer when treated with second- and third-generation EGFR TKIs compared with first-generation EGFR TKIs. Numerically, patient survival was longest with osimertinib. However, the effects on patient survival from treatment with second-generation afatinib or dacomitinib have not been directly compared with third-generation osimertinib in a clinical study.

Different mutations in people's genes, which happen by chance, can lead to resistance, meaning that drugs no longer work. One of the most common mutations in NSCLC that leads to resistance is called the T790M mutation. This mutation occurs in up to 7 out of 10 patients who receive afatinib, erlotinib or gefitinib treatment. It is most common in patients who also have the Del19 *EGFR* mutation, which is also found in around 7 out of 10 patients. In previous trials, osimertinib treatment was effective in patients who had developed the T790M mutation, so it is a good option for further treatment in patients with NSCLC who have developed resistance to afatinib, erlotinib or gefitinib.

Patients who receive osimertinib can develop lots of different types of resistance mutations over time. This makes it very hard to know which treatment to use when a patient has developed resistance to osimertinib treatment. Therefore, patients who become resistant to osimertinib typically go on to receive chemotherapy, which can have unpleasant side effects. It has, therefore, been suggested that osimertinib could be used as a second-line treatment option after afatinib to increase the time patients can be chemotherapy-free.



## What did the GioTag study look at?

The GioTag study aimed to assess the outcomes of patients with NSCLC with *EGFR* mutations who received afatinib, developed the T790M resistance mutation, and then received osimertinib treatment.

Randomized clinical trials (RCTs for short) usually have strict entry criteria that do not allow patients with other clinical conditions like brain metastases or poor overall health to be included. Elderly patients are also often under-represented. Patient overall health is often categorized using criteria called Eastern Cooperative Oncology Group Performance Status (ECOG PS for short). Patients are rated from 0 (fully active and able to carry out all self-care tasks) to 4 (completely disabled and unable to carry out any self-care tasks) and, typically, those with ECOG PS of 2 and over are not included in RCTs.

However, the GioTag study included a much broader group of patients, including the elderly, those with other clinical conditions and those with an ECOG PS of 2 and over, making the results relevant to many patients with EGFR-mutated NSCLC.

Initial and updated data from the GioTag study have been reported previously, showing promising results. Here, we present the final results.

## How was the study carried out?

GioTag was a retrospective, observational study.

– Retrospective means that the study took place in the past, between December 2017 and December 2019.

– Observational means that the data were collected from patients who had previously been treated in the 'real-world' (that is, not in a clinical trial) and the study did not affect which treatments they received.

Patients were included if they met all of these criteria:

- Had *EGFR*-mutated NSCLC with a Del19 or L858R mutation
- Had received afatinib treatment and developed T790M resistance
- Had started osimertinib treatment at least 10 months before being enrolled

**204 patients** from 10 countries were included:

| | | |
|---|---|---|
| Austria | Italy | Slovenia |
| Canada | Japan | Spain |
| Israel | Singapore | Taiwan |
| | | USA |

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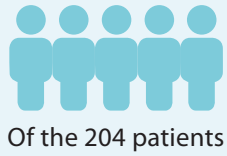
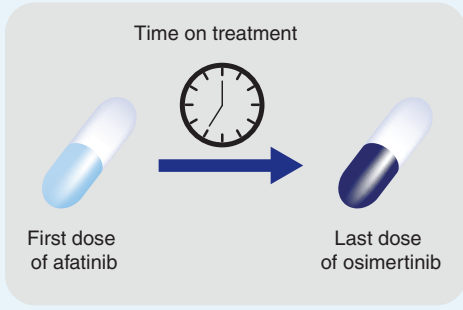
## How was the study carried out? (continued)

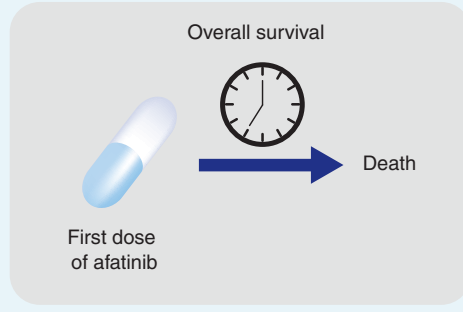



Most patients received the approved starting doses of afatinib (40 mg) and osimertinib (80 mg). These drugs are oral tablets which are taken daily.

The main aim of the study was to find out how long patients received EGFR TKI (afatinib and osimertinib) treatment. This was measured as the median time between the first dose of afatinib to the last dose of osimertinib. The median value is the middle value in a range of values.

Another goal was to find out how long patients receiving the treatment survived. This was measured as the median time from the first dose of afatinib until the patients died.

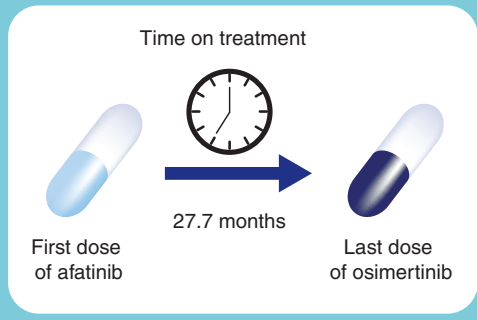


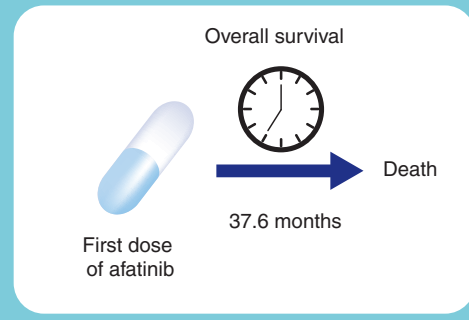




As this study collected data from previous medical record, and there is no way of knowing if all of the side effects were reported consistently, safety data was not analysed.

## What were the overall study results?

All patients:

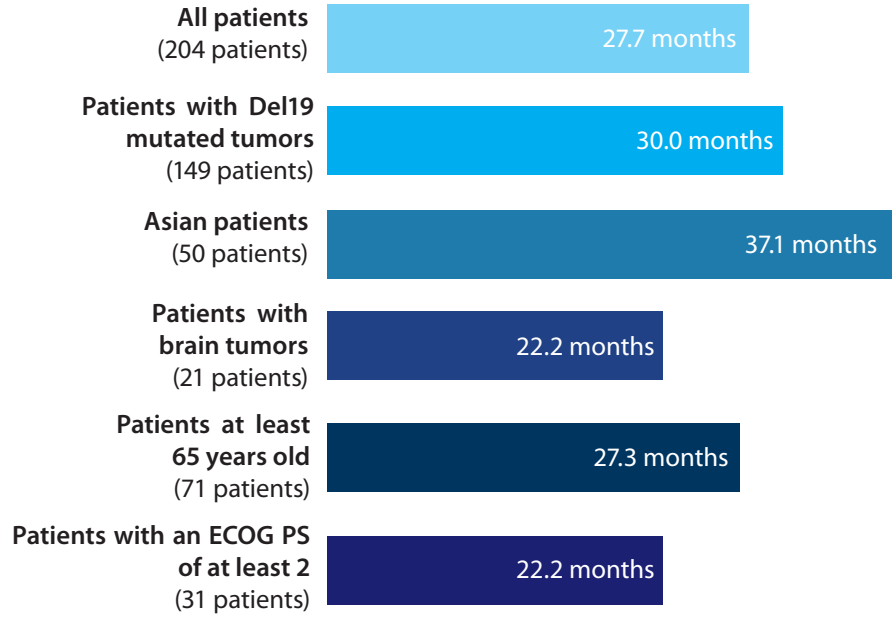


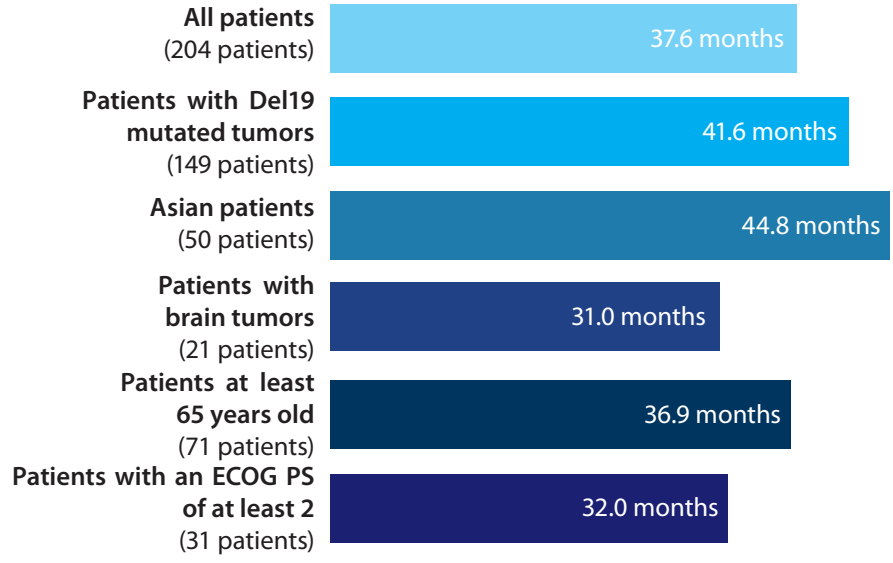
## What were the overall study results? (continued)

These study results were also analysed in subgroups. Results from patients with Del19 mutated tumors were analysed because this is the most common type of mutation in patients with NSCLC and *EGFR* mutations. Results from Asian patients were analysed as some EGFR TKIs appear to have different effects in different ethnic groups. Results from patients with brain tumors, patients at least 65 years old and those with ECOG PS of at least 2 were analysed as they are frequently under-represented in clinical trials and these patients often have poor outcomes.

Median time on treatment in each subgroup was:




Median overall survival in each subgroup was:



## What do these results mean?

As patients survived for a median of just over 3 years, afatinib treatment followed by osimertinib treatment appears to be an effective treatment option for patients with *EFGR* mutated NSCLC who develop T790M mutations.

The results were especially good in patients with Del19 mutations and in Asian patients. This suggests that afatinib followed by osimertinib treatment could allow these patients to remain chemotherapy-free for a long period of time.

Benefits were also seen in patients with brain metastases, patients at least 65 years old and in patients with an ECOG PS of at least 2. This was important as these patients usually have poor outcomes and are generally under-represented in clinical trials.

It is important to consider the results in context with the study limitations. These include the fact that the GioTag study analysed data that was collected in the past and it did not include a 'control' group of patients who received placebo rather than the active treatments. However, despite these limitations, the results suggest that afatinib treatment followed by osimertinib treatment is an effective treatment option for patients with *EFGR* mutated NSCLC who develop T790M mutations.

Further studies investigating afatinib followed by osimertinib treatment are ongoing.

## Where can readers find more information on this study?

The original article discussed in this summary entitled 'Sequential afatinib and osimertinib in patients with *EGFR* mutation-positive non-small-cell lung cancer: final analysis of the GioTag study' was published in *Future Oncology* in August 2020. You can read the original article at: https://www.futuremedicine.com/doi/10.2217/fon-2020-0740

## Acknowledgements

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### Financial & competing interests disclosure

MJ Hochmair reports personal fees from Speakers honorarium Boehringer Ingelheim, AstraZeneca and Roche. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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