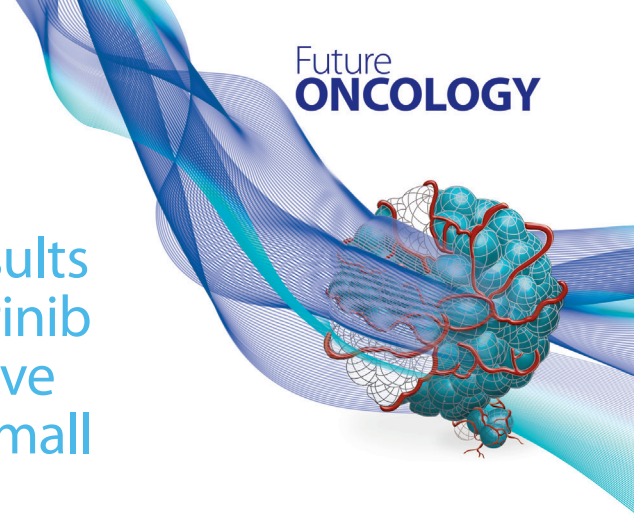
Future ONCOLOGY

Plain Language Summary of Publication

A plain language summary of results from the ADAURA study: osimertinib after surgery for patients who have early-stage EGFR-mutated non-small cell lung cancer



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Summary

Here, we summarize the initial results from the ADAURA clinical study looking at treatment with osimertinib in patients with a specific type of non-small cell lung cancer. Osimertinib (TAGRISSO®) is a medication used to treat a type of NSCLC with a change (mutation) in the EGFR gene, known as EGFR-mutated NSCLC. EGFR stands for 'epidermal growth factor receptor'. It is a protein present on the surface of both healthy and cancer cells that can regulate how cells grow and divide. Sometimes, certain mutations in EGFR can result in the EGFR protein malfunctioning, which can lead to the formation of cancer, like EGFR-mutated NSCLC. Based on previous clinical studies, osimertinib is already approved for use in patients with EGFR-mutated NSCLC that has spread beyond the lung (metastatic disease). This medication works to stop, prevent, or slow the growth of EGFR-mutated NSCLC tumors, by specifically blocking the activity of EGFR.

How to say (double click to play sound)...

- **Osimertinib:** oz-ee-mer-ti-nib

In the ADAURA clinical study, participants had resectable EGFR-mutated NSCLC, which means they had tumors that can be removed by surgery. Participants took either osimertinib or a placebo (a dummy drug with no active ingredient) after having their tumors removed by surgery. Post-surgery chemotherapy was allowed, but not compulsory (this was decided by the participant and their doctor). To date, the study has shown that osimertinib could be beneficial for patients with resectable EGFR-mutated NSCLC. Participants who took osimertinib have stayed cancer-free for longer than those who took the placebo, regardless of whether or not they received chemotherapy after surgery. Osimertinib treatment also reduced the risk of tumors spreading to the brain and spinal cord, otherwise known as the central nervous system (also called CNS). The side effects experienced by the participants taking osimertinib have been consistent with what we already know. Based on the results from ADAURA, osimertinib has been approved for the treatment of resectable EGFR-mutated NSCLC after tumor removal. The ADAURA study is still ongoing and more results are expected to be released in the future.

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Who should read this article?

This summary may be helpful for patients with EGFR-mutated NSCLC and their families, as well as patient advocates, caregivers and healthcare professionals, including those who are helping someone to find the best treatment for their diagnosis.

Who sponsored this clinical study?

The pharmaceutical company AstraZeneca (the manufacturers of osimertinib) funded and were responsible for conducting this clinical study.

What are the different stages of lung cancer?

Lung cancer occurs when there is an abnormal growth of cells (known as a tumor) in the lungs. Numbered stages are often used to categorize lung cancer. The ADAURA clinical study included patients with stage IB, IIA/B or IIIA NSCLC. The stage of disease was determined using the American Joint Committee on Cancer (7th edition) staging categories, which are summarized below. Stages I–IIIA are often referred to as 'early stage'.

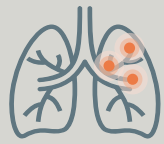
Stage IA	Stage IB	Stage IIA/B	Stage IIIA/B	Stage IV
When the cancer is less than 3 cm in size and has not spread anywhere else	When the cancer is less than 5 cm in size and has not spread anywhere else	When the cancer is larger than 5 cm in size or has spread to some surrounding areas (e.g., nearby lymph nodes)	When the cancer has grown and spread to surrounding areas (e.g., the lymph nodes), known as regional metastasis	When the cancer has spread to areas that are further away (e.g., another organ of the body), known as distant metastasis

What is EGFR-mutated NSCLC?

- Non-small-cell lung cancer (also known as NSCLC) is the most common type of lung cancer.
- Around one third (1/3) of patients with NSCLC have tumors that can be removed by surgery (also known as 'resectable' NSCLC).
- After surgery, chemotherapy is often recommended for patients with stage II–IIIA resected NSCLC and sometimes recommended for patients with stage IB.
- However, the cancer can unfortunately still come back in around half of patients with stage IB–IIIA NSCLC, even if post-surgery chemotherapy is received.
- The cancer may also spread to other parts of the body, such as the brain and spinal cord, otherwise known as the central nervous system (also called CNS). Almost half of patients with NSCLC develop brain metastases, which can have a big impact on patient quality of life.

What is EGFR-mutated NSCLC? (continued)

- New and improved therapies, such as personalized (targeted) treatment, are therefore needed for patients with resectable NSCLC.
- EGFR stands for 'epidermal growth factor receptor'. It is a protein present on the cell surface that can control how cells grow and divide.
- Some patients with NSCLC have a mutation in the gene for EGFR. This can cause lung cancer tumors to grow more quickly, due to a change in how the EGFR protein functions.



EGFR **10–20%**

- Almost half of all patients with NSCLC of Asian ethnicity and around 10–20% of patients in other parts of the world have tumors with a mutation in the EGFR gene, which is known as EGFR-mutated NSCLC. This type of lung cancer can be identified by testing for changes in genes or the activity of proteins, known as biomarkers (including EGFR mutation), by testing either blood or a sample of the tumor.
- Common types of EGFR mutation include exon 19 deletion and L858R substitution, which each account for around 45% of all EGFR mutations.

What is osimertinib?

The medication being studied in the ADAURA clinical study is osimertinib. It is taken by mouth (tablet) at a dose of 80 mg once per day, to treat resectable EGFR-mutated NSCLC.

Unlike chemotherapy, osimertinib is a personalized treatment option, targeted specifically for patients with EGFR mutations.

Osimertinib belongs to a group of EGFR-targeted medicines known as EGFR-tyrosine kinase inhibitors, or EGFR-TKIs.

Osimertinib is a next generation treatment that works by blocking the activity of EGFR. Over time, this can slow, prevent, or stop the growth of NSCLC tumors.

Osimertinib is currently recommended for the treatment of EGFR-mutated NSCLC that has spread to other parts of the body (metastatic disease).

In December 2020, osimertinib was approved for the treatment of resectable EGFR-mutated NSCLC after tumor removal (early-stage disease), based on results from the ADAURA clinical study.

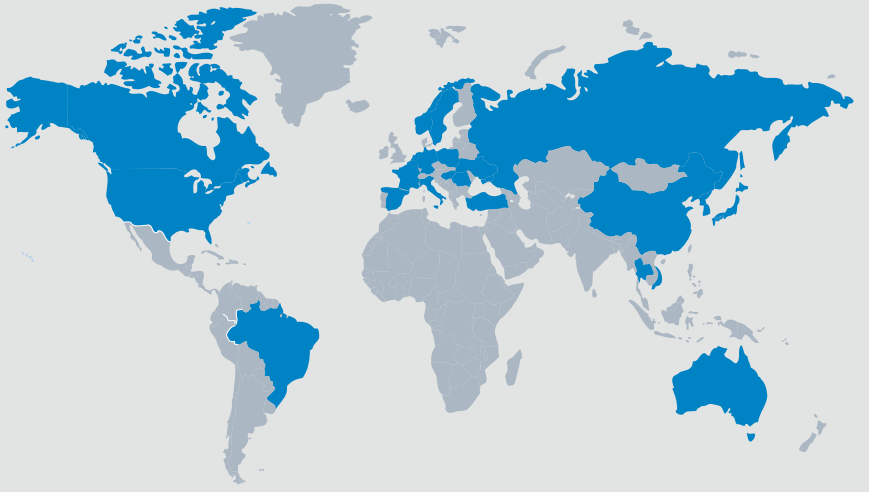
What was the ADAURA clinical study designed to look at?

- The aim of the ADAURA clinical study was to see how long participants in the study with resectable EGFR-mutated NSCLC would remain alive and cancer-free with osimertinib treatment (known as cancer-free survival), after having their tumors completely removed by surgery.
- Post-surgery chemotherapy was allowed, but not mandatory (this was decided by the participant and their doctor).
- The study compared results in participants who received osimertinib versus participants who took a placebo (a dummy drug with no active ingredient). Cancer-free survival was assessed in participants with resectable EGFR-mutated NSCLC (stage IB, II or IIIA). The safety of the treatment was also assessed.

- The ADAURA clinical study is still ongoing and more results are expected to be released in the future.
- Here, we summarize results from the study's primary data analysis.
- The primary analysis was completed earlier than planned due to results that were expected to change clinical practice. An Independent Data Monitoring Committee (known as IDMC) recommended that the results be made public.

The ADAURA clinical study included 682 participants. The study included participants from 231 hospitals and cancer centers across 26 different countries worldwide.

Participants were randomly assigned to take either osimertinib or a placebo. Neither the participant nor their doctor knew which treatment they were taking.

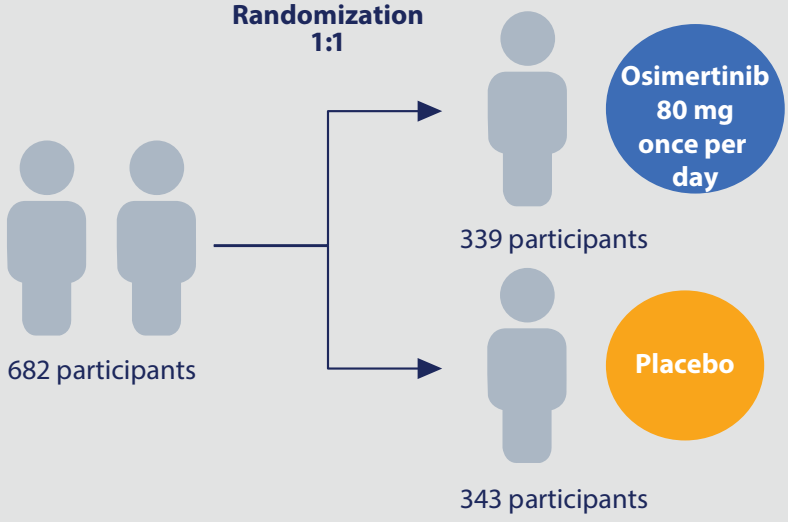


What was the ADAURA clinical study designed to look at? (continued)

The characteristics of participants included in each treatment group were similar:

	Osimertinib	Placebo	All patients	
Female (%)	68%	72%	70%	Approximately two thirds (2/3) of participants were female.
Average age (range)	63 (30–86)	62 (31–82)	62 (30–86)	The participants were aged 30–86 years. The average age was 62 years.
Smoking history				
Yes	32%	25%	29%	Approximately two thirds (2/3) of participants had no history of smoking.
No	68%	75%	72%	
Race				
Asian	36%	36%	36%	Approximately two thirds (2/3) of participants were Asian.
Non-Asian	64%	64%	64%	

Treatment was planned to continue for 3 years, unless the cancer came back, or the participant decided to stop treatment for other reasons



*In randomized clinical studies, unequal patient numbers can sometimes occur between treatment groups due to random variation during the allocation process.

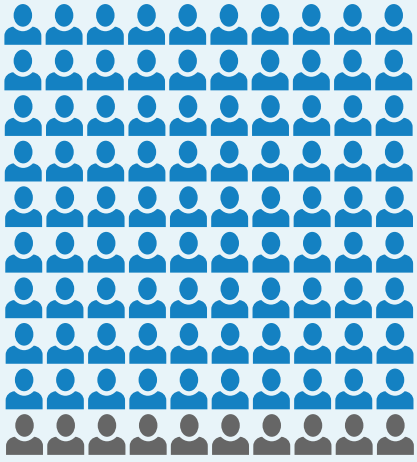
What were the overall results of the study?

To date, the participants who took osimertinib had longer cancer-free survival than those who took placebo.

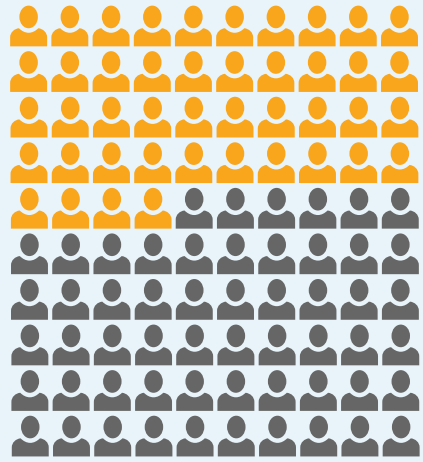
In participants with resectable stage II–IIIA NSCLC, there was an 83% reduction in the risk of the cancer returning or death in participants who took osimertinib compared to placebo.

In participants with resectable stage IB–IIIA NSCLC, 89% of those who took osimertinib were alive and cancer-free at 2 years, compared with 52% of participants who took placebo.

90% of participants who took osimertinib were alive and cancer-free at 2 years



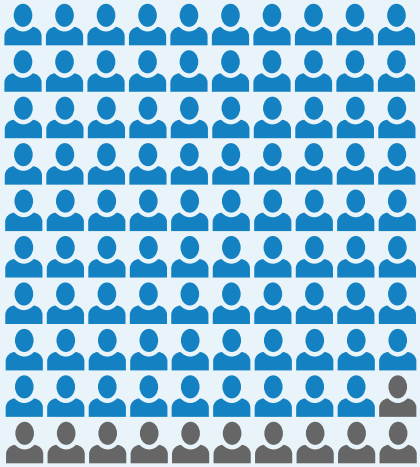
44% of participantswho took a placebo were alive and cancer-free at 2 years



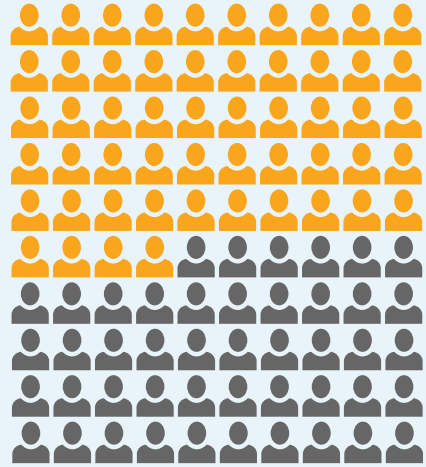
In participants with resectable stage II–IIIA NSCLC, 90% of those who took osimertinib were alive and cancer-free at 2 years, compared with 44% of participants who took placebo.

In participants with resectable stage IB–IIIA NSCLC, there was an 80% reduction in the risk of the cancer returning or death in participants who took osimertinib compared to placebo.

89% of participants who took osimertinib were alive and cancer-free at 2 years



52% of participants who took a placebo were alive and cancer-free at 2 years



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

60% of participants who took osimertinib, and 60% of those who took placebo, received chemotherapy before their treatment began

Among all participants who received chemotherapy, 89% of those who took osimertinib were alive and cancer-free at 2 years, compared with 49% of participants who took placebo.

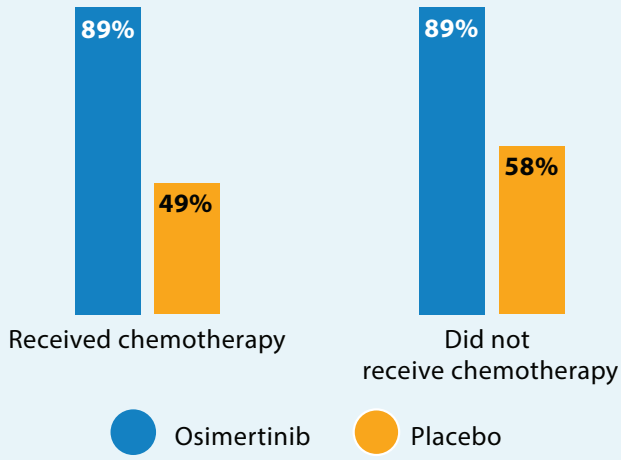
Among all participants who did not receive chemotherapy, 89% of those who took osimertinib were alive and cancer-free at 2 years, compared with 58% of participants who took placebo.

Osimertinib treatment also reduced the risk of tumors spreading to the CNS.

- Among all participants with resectable NSCLC, only 1% of those who took osimertinib had cancer that came back and spread to the CNS, compared with 10% of participants who took placebo.
- This meant there was an 82% reduction in the risk of CNS-related cancer or death in participants who took osimertinib.

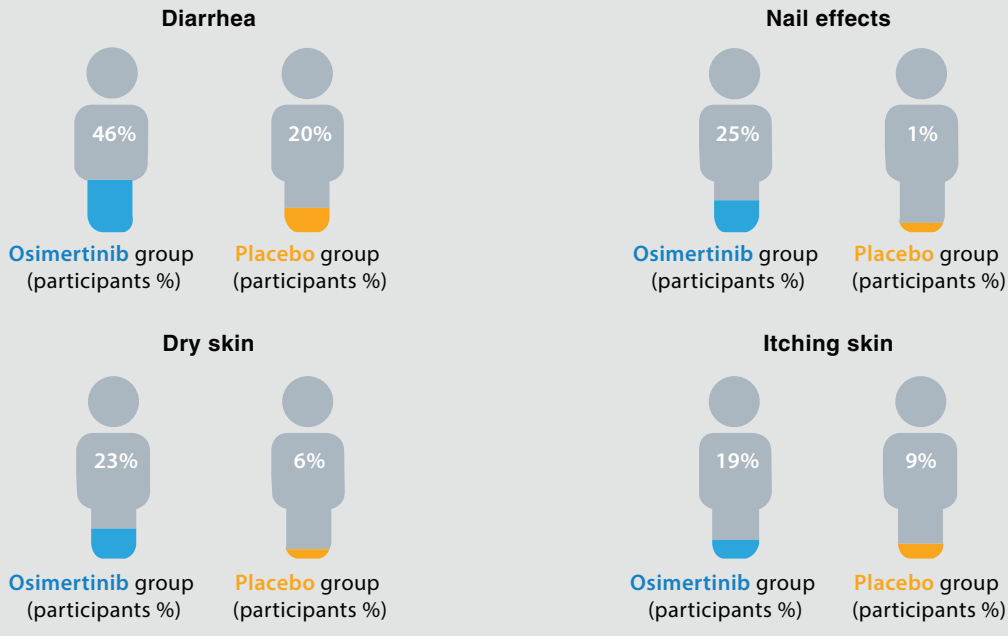
The chance of participants who took osimertinib remaining free of CNS-related cancer at 2 years was 98%. In participants who took placebo, the chance of remaining free of CNS-related cancer at 2 years was 85%.

89% of participants who took osimertinib were alive and cancer-free at 2 years, regardless of whether or not they received chemotherapy after surgery



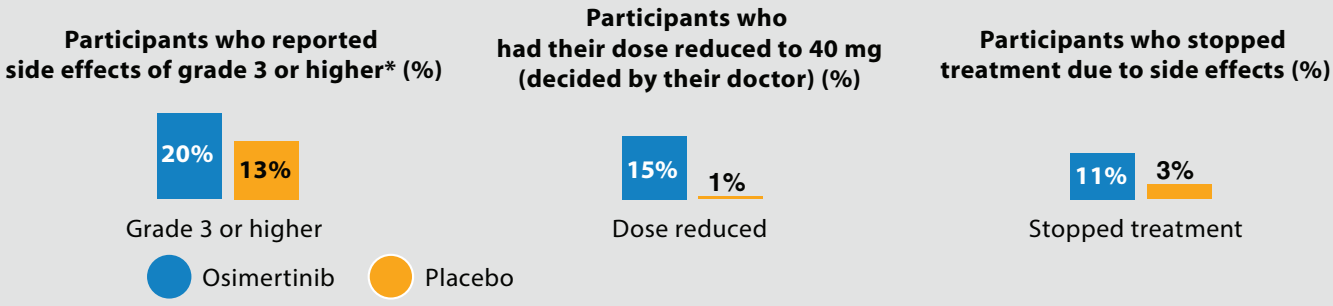
What were the most common side effects?

The most common side effects (of any severity) experienced by participants are shown in the figure.



What were the most common side effects? (continued)

- Side effects of grade 3 or higher (for example, those considered medically important, requiring hospitalization or significant treatment) were reported in 20% of participants who took osimertinib and 13% of participants who took placebo.
- 15% of participants who took osimertinib and 1% of participants who took placebo had their dose reduced to 40 mg (decided by their doctor).
- The number of participants who stopped treatment due to side effects was low (11% of participants who took osimertinib and 3% of participants who took placebo).
- The side effects observed were consistent with what we already know about osimertinib.



*For example, those considered medically important, requiring hospitalization or significant treatment

What do the results of this study mean?

- To date, this study has shown that participants who took osimertinib after having their tumors removed by surgery had longer cancer-free survival compared with participants who took placebo.
- The cancer-free benefit with osimertinib was seen regardless of whether participants received chemotherapy after their surgery or not.
- The number of participants who stopped treatment due to side effects was low. The side effects observed were consistent with what we already know about osimertinib.
- The ADAURA study is still ongoing and more results are expected to be released in the future.

Educational resources

Learn about the European Society for Medical Oncology (ESMO) clinical practice guidelines for the treatment of non-small cell lung cancer. These guidelines assist physicians in determining the best treatment for their patients. Read the guidelines for patients at: https://www.esmo.org/for-patients/patient-guides/non-small-cell-lung-cancer

Where can I find more information?

The full title of the original publication in the New England Journal of Medicine is: 'Osimertinib in Resected EGFR-Mutated Non-Small-Cell Lung Cancer'

You can read the original article at: www.nejm.org/doi/full/10.1056/NEJMoa2027071
You can read more about the ADAURA study on the following websites:

- Type the study number, NCT02511106, into the search bar of the ClinicalTrials.gov website at www.clinicaltrials.gov
- Type the EudraCT identifier 2015-000662-65 into the search field at www.clinicaltrialsregister.eu/ctr-search
- If you are or were a study participant and have questions about the results of this study, please speak with the doctor or staff at your study center.
- Patients should ask their healthcare providers for more information about the benefits and risks of any treatment.
- More information about clinical trials in general can be found at: https://www.clinicaltrials.gov/ct2/about-studies/learn

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