Plain Language Summary of Publication

Plain language summary of first-line amivantamab-lazertinib in previously untreated high-risk *EGFR*-altered non-small-cell lung cancer in MARIPOSA

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Where can I find the original article on which this summary is based?

You can read the original article 'Amivantamab plus lazertinib versus osimertinib in first-line *EGFR*-mutant advanced non-small-cell lung cancer with biomarkers of high-risk disease: a secondary analysis from MARIPOSA' for free at: https://doi.org/10.1016/j.annonc.2024.05.541

Summary

What is this summary about?

This plain language summary describes the efficacy results from high-risk subgroups in the **phase 3** MARIPOSA study. The study evaluated the safety and **efficacy** of amivantamab plus lazertinib, a third-generation **tyrosine kinase inhibitor (TKI)**, compared with osimertinib, another third-generation TKI, or lazertinib in patients with **advanced** non-small-cell lung cancer (NSCLC) with **exon 19 deletions (Ex19del)** or **exon 21 L858R** substitution alterations in the **epidermal growth factor receptor (*EGFR*) gene** who had not received treatment before. Among all patients, at a **median follow-up** of 22 months, the median **progression-free survival (PFS)** for amivantamab plus lazertinib was 23.7 months compared with 16.6 months for osimertinib, with a 30% lower risk of their disease getting worse or dying. Median **duration of response** was 9 months longer with amivantamab plus lazertinib compared with osimertinib. Here, we report the results from a secondary analysis of the MARIPOSA study in patients with high-risk cancer characteristics associated with poor disease outcomes, such as *TP53* gene alterations, cancer DNA in the bloodstream, and liver or brain **metastases**. We will refer to patients with high-risk cancer traits as 'high-risk subgroups'.

What were the results?

1074 adults with locally advanced or metastatic *EGFR*-altered NSCLC were randomly divided into 3 treatment groups (patients who received amivantamab plus lazertinib, osimertinib alone, or lazertinib alone) in a 2:2:1 **ratio**. Here, we report the results for the amivantamab plus lazertinib and osimertinib **monotherapy** groups. Among high-risk subgroups, the median PFS was 20.3 months for amivantamab plus lazertinib compared with 15.0 months for osimertinib. PFS benefits were seen for those without *TP53* alterations, cancer DNA in the bloodstream, and liver or brain metastases.

As with treatments for NSCLC and other cancers, **side effects** occurred in most patients, many of which are commonly seen with amivantamab and other **EGFR-targeting therapies**. **Venous thromboembolic events (VTE)**, commonly associated with lung cancer, occurred more often in patients receiving amivantamab plus lazertinib compared with those receiving osimertinib.

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Severe VTEs were rare (less than 1%). However, few patients received **anticoagulants** to prevent VTEs (5%) or stopped taking amivantamab plus lazertinib due to these side effects (amivantamab plus lazertinib: 3%; osimertinib: less than 1%).

What do the results mean?
Most patients with advanced NSCLC have at least one high-risk feature. Among high-risk subgroups, amivantamab plus lazertinib compared with osimertinib extended the time that their cancer did not worsen. These results could be relevant to a wide range of patients with amivantamab plus lazertinib as a potential treatment option.

How to say (download PDF and double click sound icon to play sound)...

- **Amivantamab:** am-ee-VAN-tuh-mab
- **Anticoagulant:** an-tee-koh-AG-yuh-luhnt
- **Biomarker:** bai-ow-maar-kr
- **Bispecific antibody:** BY-speh-SIH-fik AN-tee-BAH-dee
- **Chemotherapy:** kee-moh-ther-uh-pee
- **CHRYSALIS:** kris-uh-lis
- **Epidermal:** ep-ee-DER-mal
- **Epithelial:** ep-ee-THEL-ee-ul
- **Exon:** ek-sn
- **Lazertinib:** lay-ZER-tin-nib
- **MARIPOSA:** mar-ee-POSE-ah
- **Mesenchymal:** meez-en-KY-mul
- **Metastases:** muh-ta-stuh-sees
- **Metastatic:** meh-tuh-sta-tuhk
- **Osimertinib:** oh-SEE-mer-tin-nib
- **Paronychia:** peh-ruh-ni-kee-uh
- **Tomography:** TOH-mog-ruh-FEE
- **Tyrosine kinase:** tai-ruh-seen kai-nays
- **Venous thromboembolic event:** VEE-nuhs throm-boh-EM-buh-lic E-vent

Clinical trial phase: Research is done in phases to make sure a study treatment is safe and then to confirm whether it works before it is approved. These study phases build on each other, and each phase has a separate goal. Phase 3 trials confirm findings of phase 2 trials and compare the study treatment to standard of care or placebo.
Efficacy: In a clinical trial, this is the ability of a medicine to produce its desired effect or how well it works.
Tyrosine kinase inhibitor (TKI): A type of medication that works by specifically blocking the EGFR protein to help slow down or stop the growth of cancer cells.
Advanced or metastatic disease: Also referred to as late-stage disease, where the cancer has spread from its original location in the body (for example, if lung cancer spreads beyond the lung).
Exon 19 deletion (Ex19del) alteration: A change to the DNA sequence of *EGFR* that changes the function of the EGFR protein. In the case of Ex19del, DNA was deleted in the part of the *EGFR* gene called exon 19.
Substitution alteration: When a DNA alteration causes an amino acid in a protein to be substituted for another. In this case, this results in changes in the structure of the EGFR protein, which may lead to lung cancer.
Exon 21 L858R alteration: A change to the DNA sequence of *EGFR* that changes the function of the EGFR protein. In the case of exon 21 L858R, a small part of DNA is replaced with a different one within the *EGFR* gene.
Epidermal growth factor receptor (EGFR): A protein that signals the cell to grow, divide, or survive. EGFR refers to a protein while *EGFR* refers to a gene.
Receptor: A protein used by cells to pass along chemical signals.
Gene: Sequences of DNA that determine your traits. Some genes are used as instructions to make molecules called proteins.
Median: The middle value of a set of numbers.
Follow-up: A follow-up visit is when a patient goes back to the doctor after receiving treatment to check on how the patient is feeling and how well the treatment is working.
Progression-free survival: The amount of time that patients lived without their cancer growing or spreading.
Duration of response: Length of time from the start of treatment to the time when half of the patients had complete responses (defined as tumors that are no longer detectable over a specified time period) and partial responses (defined as measurable tumor shrinkage that is still detectable over a specified time period).
***TP53* gene:** A gene that normally inhibits cancer development and growth. If alterations happen in this gene, it can lead to highrisk lung cancer.

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Metastases: When the cancer has spread from where it first formed to another part of the body (for example, if lung cancer spreads beyond the lung).
Ratio: In the context of clinical trials, a randomization ratio is the way we ensure fair assignment of people in different treatment groups to reduce bias. In the case of MARIPOSA, the most important comparison was between amivantamab plus lazertinib and osimertinib, so for every patient who was assigned to the lazertinib-only group, 2 patients were assigned to either amivantamab plus lazertinib or osimertinib to allow a better comparison between the important groups.
Monotherapy: The only medicine a patient is receiving.
Side effect: An undesired effect of a drug or other type of treatment.
EGFR-targeting therapies: Treatments designed to fight cancer by focusing on a specific protein called the epidermal growth factor receptor (EGFR). This protein is often found in high amounts on the surface of some cancer cells and helps them grow and divide. By targeting EGFR, these therapies aim to block its action, which can slow down or stop the growth of cancer cells.
Venous thromboembolic event (VTE): When a blood clot forms in a vein. VTEs are further characterized by where the clot occurs and includes pulmonary embolisms (lung clot) and deep vein thrombosis (clots in a deep tissue, usually the lower leg, thigh, or pelvis).
Anticoagulant: A type of medication that prevents clots from forming.

What is the purpose of this plain language summary?

The purpose of this plain language summary is to help you understand the findings from a recent clinical trial. Amivantamab plus lazertinib is used to treat the condition under study that is discussed in this summary. Approval varies by country; please check with your local provider for more details. The study described is ongoing; therefore, the final outcomes of this study may differ from the outcomes described in this summary.

Who should read this article?

This summary is designed to be helpful for people diagnosed with NSCLC, their families and caregivers, and health care teams involved with people diagnosed with NSCLC with *EGFR* Ex19del or exon 21 L858R alterations and certain cancer traits that put them at an increased risk for worse disease, such as alterations in the *TP53* gene, circulating cancer DNA in the bloodstream, and liver and brain metastases.

Who sponsored this study?

The pharmaceutical company Janssen Biotech, the manufacturer of amivantamab, **sponsored** and conducted this clinical study.

Sponsor: A company or organization that oversees and pays for a clinical research study. The sponsor also collects and analyzes the information from the study.

Why is it important to understand the journey of patients with lung cancer?

There are different types of lung cancer, with NSCLC being the most common. Patients diagnosed with lung cancer might have one of several genetic alterations contributing to their cancer. Through clinical trials and experience, medical experts have identified treatment combinations for cancers having specific alterations. Therefore, knowing what alterations contribute to a patient's lung cancer can help medical experts give better targeted care, which can have an impact on how long a patient may live without their

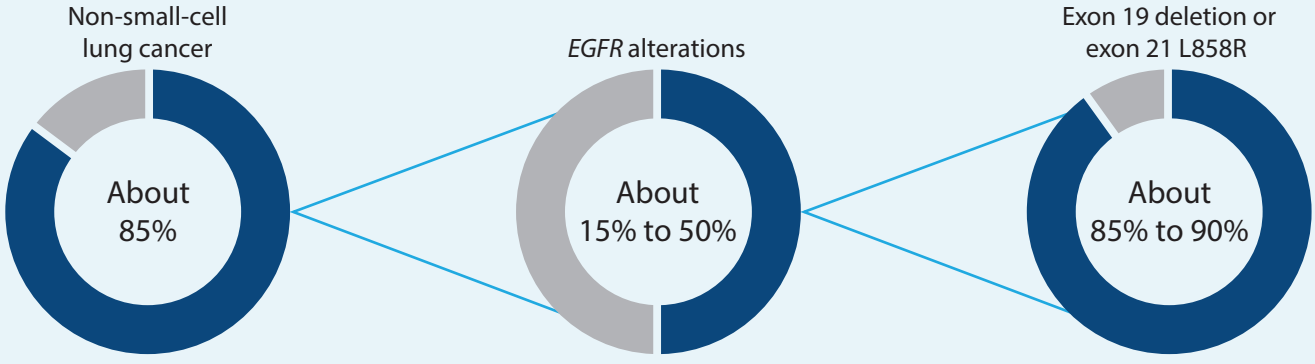
cancer getting worse. It is estimated that, following the most recent recommended treatment guidelines, 1 in 4 patients with NSCLC have rapid disease progression and do not live long enough to receive a second type of treatment. For this reason, **genetic (biomarker) testing** at the time of NSCLC diagnosis, which identifies alterations such as *EGFR* Ex19del and exon 21 L858R alterations, allows medical experts to choose a **targeted therapy** first, potentially leading to better results. For more information on the **patient journey** of those diagnosed with NSCLC, please read the plain language summary of the CHRYSALIS study in *Future Oncology*.

Genetic (biomarker) testing: A test where DNA is collected and examined for alterations (called biomarkers) that are known to cause lung cancer.
Targeted therapy: Treatments that will only work on cells that have certain characteristics, usually certain types of proteins.
Patient journey: The events experienced by a patient from the time they are diagnosed with a disease through the treatments they receive.

What is epidermal growth factor receptor (*EGFR*)–altered non-small-cell lung cancer?

NSCLC is the most common type of lung cancer. It can be attributed to alterations to the *EGFR* gene in specific cells, which means the DNA code is changed, leading these cells to multiply abnormally and thus become cancer cells. These types of changes can occur at any time in a person's lifetime and can happen in people with or without a history of tobacco use. The *EGFR* gene contains the blueprint to make the EGFR protein, which is found on both normal and cancer lung cells. The EGFR protein is also found on many normal cell types, including skin cells. The most common alterations to the *EGFR* gene that cause lung cancer are called Ex19del and exon 21 L858R. These alterations represent 85% to 90% of all alterations in *EGFR*-altered NSCLC.

Proportion of *EGFR* alterations in non-small-cell lung cancer



Non-small-cell lung cancer is the most common type of lung cancer, accounting for approximately 85% of all lung cancers

Globally, activating *EGFR* alterations are found in approximately 15% to 50% (depending on patient factors such as race) of advanced non-small-cell lung cancer cases

Exon 19 deletions and a substitution in exon 21 (L858R) are the most common activating *EGFR* alterations (approximately 85% to 90%)

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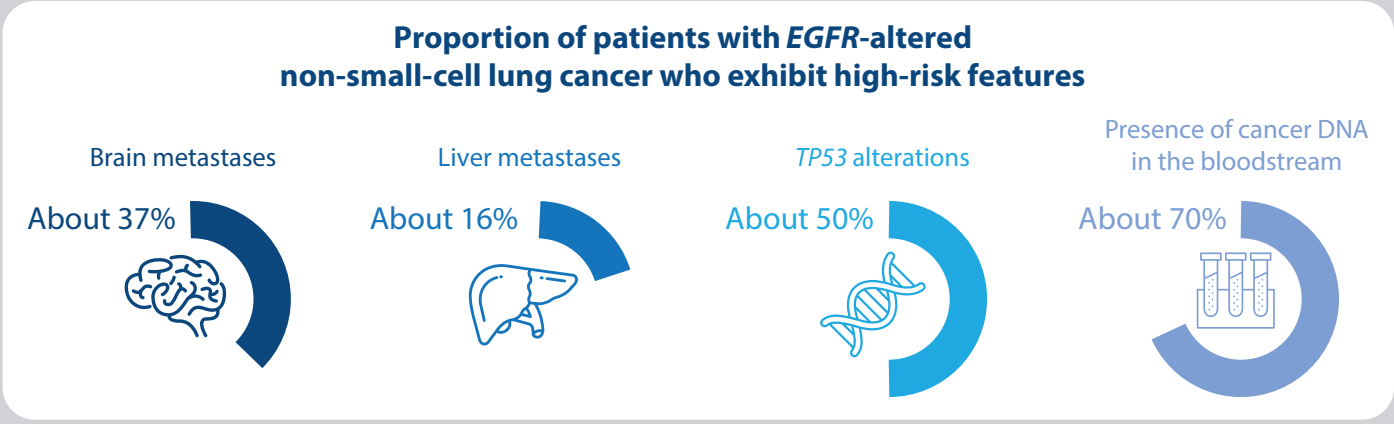
Which cancer characteristics increase a patient's risk of disease worsening?

Multiple cancer characteristics are associated with worse clinical outcomes in patients with *EGFR*-altered NSCLC. These features include brain or liver metastases, presence of alterations in the *TP53* gene, and circulating cancer DNA in the bloodstream. Most patients with advanced NSCLC have at least one of these high-risk characteristics.



After it is discovered, how is advanced *EGFR*-altered non-small-cell lung cancer currently treated?

Once an Ex19del or exon 21 L858R alteration is confirmed, many patients will initially receive osimertinib, an EGFR TKI, to treat their cancer. TKIs like osimertinib will eventually stop working against NSCLC when used alone due to the development of **resistance mechanisms**.

Amivantamab is approved by the US Food and Drug Administration (FDA) in combination with lazertinib as a **first-line** therapy for patients with *EGFR* Ex19del or exon 21 L858R-altered advanced NSCLC who have not received a prior therapy. Amivantamab is also approved in combination with **chemotherapy** for patients with *EGFR* Ex19del or exon 21 L858R alterations after their disease worsens with an EGFR TKI. These approvals were based on the results of the phase 3 MARIPOSA and MARIPOSA-2 studies. The **National Comprehensive Cancer Network® (NCCN®)** recommends these as first-line and **second-line** treatment options, respectively. Amivantamab is also approved as a monotherapy for patients with ***EGFR* exon 20 insertion (Ex20ins)–altered NSCLC** who previously received chemotherapy, or in combination with chemotherapy for the same patient population as a first-line treatment. These approvals were based

Resistance mechanisms: Genetic changes that help cancer cells survive against drugs or treatments.
First-line: Indicating that patients are untreated and this is the first therapy they are receiving.
Chemotherapy: Chemotherapy is a type of treatment that involves using powerful drugs to kill cancer cells or stop them from growing and spreading.
National Comprehensive Cancer Network (NCCN): A nonprofit alliance of cancer centers in the United States that develops guidelines for various types of cancer, which health care providers often use for reference when selecting treatments.
Second-line: Indicating that patients are receiving their second type of treatment after stopping their prior treatment due to disease worsening or side effects, among other reasons.
***EGFR* exon 20 insertion (Ex20ins)–altered NSCLC:** A type of lung cancer where cancer cells have a particular genetic alteration in a part of their DNA called exon 20. This mutation can make the cancer harder to treat with standard therapies.
Phase 1: Research is done in phases to make sure a study treatment is safe and then to confirm whether it works before it is approved. These study phases build on each other, and each phase has a separate goal. A phase 1 clinical trial is the first step in testing a new treatment, such as a drug, in humans. The main goals of this phase are to see if the treatment is safe and to determine the right dose of the drug.

on the results of the **phase 1** CHRYSALIS study and the phase 3 PAPILLON study. The NCCN also recommends amivantamab plus chemotherapy and amivantamab monotherapy as preferred first-line and second-line treatment options, respectively, for patients with *EGFR* Ex20ins-altered NSCLC. For more information on the results from the CHRYSALIS and PAPILLON studies, please read the plain language summary of each study in *Future Oncology*.

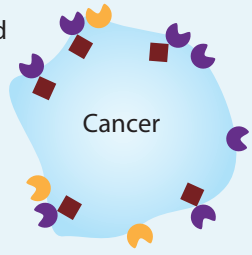
What are amivantamab and lazertinib? How do they work together?

Amivantamab is a bispecific antibody, which means that it can bind to 2 targets, EGFR and mesenchymal epithelial transition (**MET**) receptors. EGFR and MET receptors send signals to cells when signal-activating proteins bind to them, often leading to cell growth and division. By binding to these receptors first, amivantamab stops other proteins from binding to these receptors and prevents the cancer cells from growing and spreading.

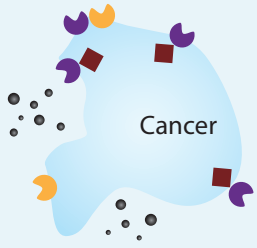
Mesenchymal epithelial transition (MET) receptor: A protein that signals to the cell to divide, spread, or survive. MET refers to a protein, while *MET* refers to a gene.

How does amivantamab work with lazertinib?

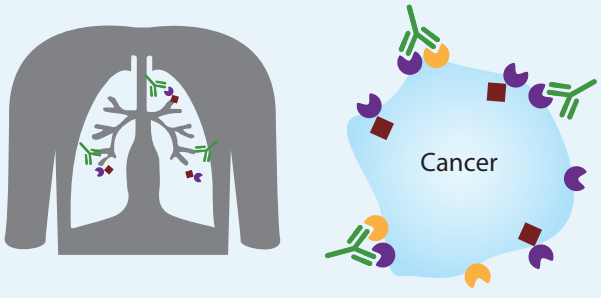
Lazertinib can access the brain and binds to the epidermal growth factor receptor (EGFR) of cancer cells that have spread to the brain, preventing them from surviving treatment and growing



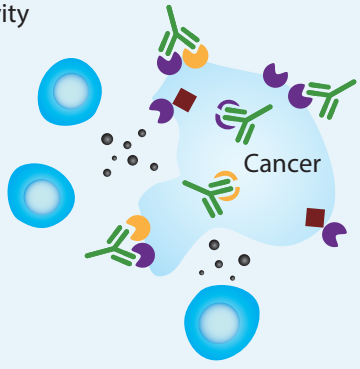
Cancer cells that rely on EGFR signaling to survive will die when lazertinib blocks their activity



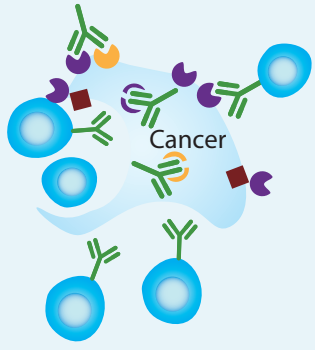
Amivantamab binds to both EGFR and mesenchymal epithelial transition (MET) receptors, therefore blocking their growth-promoting activity. Lazertinib selectively binds to EGFR, further blocking its activity



Dead cancer cells and the presence of amivantamab attract immune cells. EGFR and MET receptors are taken in by the cancer and destroyed, further preventing its growth-promoting activity



Immune cells bind to amivantamab, which allows them to go deeper inside the cancer, improving the drug's activity against the cancer



Lazertinib Immune cell EGFR Amivantamab Debris from killed cancer cell MET receptor

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Lazertinib is a third-generation EGFR TKI that works against several types of *EGFR* alterations and also can treat cancer that has spread to the brain. Together, amivantamab and lazertinib target NSCLC in multiple ways, including helping the body's **immune response** to kill cancer cells and direct cancer cell death, even if the cancer has metastasized to the brain. This is different from osimertinib, which targets and blocks signaling from the part of the EGFR protein within the cell. It should be noted that lazertinib is not considered an immunotherapy drug.

Immune response: An immune response is the body's defense mechanism against harmful agents, such as bacteria, viruses, and other foreign substances. When the immune system detects these invaders, it activates a series of actions to identify, attack, and eliminate them.

The primary reasons for combining amivantamab with lazertinib were to try to prevent resistance mechanisms that commonly occur with osimertinib. In 2 previous phase 1 trials, the combination of amivantamab plus lazertinib worked to treat *EGFR*-altered NSCLC. In a phase 1 study in patients whose disease worsened after treatment with osimertinib, amivantamab plus lazertinib worked across a wide range of resistance mechanisms.

What was the MARIPOSA high-risk analysis looking at?

MARIPOSA is a phase 3 clinical trial that looked at how safe and effective amivantamab plus lazertinib was compared with osimertinib monotherapy in patients with NSCLC with *EGFR* Ex19del or exon 21 L858R alterations. A secondary analysis was done to specifically look at patients who had cancer traits that put them at a high risk for worse outcomes and had not yet received treatment.

Who were the patients?

A total of 1074 patients took part in the study and were randomly placed into 1 of 3 groups in a ratio of approximately 2:2:1 – 429 patients into the amivantamab plus lazertinib group, 429 into the osimertinib monotherapy group, and 216 into the lazertinib monotherapy group. Lazertinib was evaluated as a monotherapy to determine how much of the effect seen with amivantamab plus lazertinib is due to lazertinib, but those results are not described here. The most important comparison was between amivantamab plus lazertinib and osimertinib; so for every patient who was assigned to the lazertinib monotherapy group, 2 patients were assigned to either amivantamab plus lazertinib or osimertinib monotherapy to allow a better comparison between the important groups.
As of the cutoff date for this analysis, 320 patients in the amivantamab plus lazertinib group and 316 in the osimertinib group had blood samples for this analysis.

For all patients, the prespecified treatment evaluations were measured until the cutoff date for this analysis. Eligible patients were 18 years of age or older and had not yet had treatment for locally advanced or metastatic NSCLC with *EGFR* Ex19del or exon 21 L858R alterations. Over half of the patients had no history of tobacco use. Patients with brain metastases that did not cause symptoms were able to enroll in the trial. Patient characteristics were similar between each treatment group

Characteristics of patients with high-risk features in the MARIPOSA study

Amivantamab plus lazertinib (320 patients)
Osimertinib (316 patients)

Female

65%
59%

Over half of the patients were female

Median age, years

64 (range, 25 to 88)
63 (range, 31 to 88)

The age of the patients ranged from 25 to 88 years

History of tobacco use

No	Yes
67%	33%
68%	32%

One-third of the patients had a history of tobacco use

Race

Asian	51%	51%
White	45%	45%
Other	4%	4%

More than half of the patients were Asian

History of brain metastases

No	Yes
59%	41%
59%	41%

Almost half of the patients had a history of brain metastases

History of liver metastases

No	Yes
86%	14%
85%	15%

Most patients did not have liver metastases

Presence of alterations in the *TP53* gene

No	Yes
53%	47%
54%	46%

Almost half of the patients had *TP53* alterations

Presence of cancer DNA in the bloodstream at the beginning of the study

No	Yes
17%	83%
13%	87%

Most patients had cancer DNA in the bloodstream at the beginning of the study

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What was evaluated in the study?

The effectiveness and safety of amivantamab plus lazertinib was evaluated and compared with osimertinib. The effectiveness of each treatment was measured by its ability to prevent cancer growth or spread.
The safety of each treatment was assessed by the number, severity, and type of side effects, including those that caused the patient to stop treatment or lower the treatment dose.
Patients' blood samples were evaluated for the presence of alterations in their cancers. Researchers were able to evaluate how cancer alterations changed throughout the study or if any new alterations were observed that might impact the effectiveness of amivantamab plus lazertinib.

How much of each treatment was given to patients?

Amivantamab was given through a vein (intravenously) by infusion at a dose of 1050 mg (1400 mg for a body weight of 80 kg [approximately 176 lbs] or greater) weekly for the first 4 weeks. The first infusion was split over 2 days, with 350 mg given on cycle 1 day 1 and the remainder given when the patient came back on cycle 1 day 2, to reduce the risk of a side effect known as an **infusion-related reaction**. Starting at week 5 of treatment, amivantamab was given at the same dose every 2 weeks until the cancer grew or spread. Lazertinib was given daily at a dose of 240 mg to patients and taken by mouth as a pill. Osimertinib was given once daily at a dose of 80 mg as a pill.

Infusion-related reaction: A side effect that may occur after receiving medicine through a vein, which commonly includes turning one's face red and/or hot, chills, difficulty breathing, nausea, chest discomfort, and vomiting.

How did researchers measure the effectiveness of amivantamab plus lazertinib?

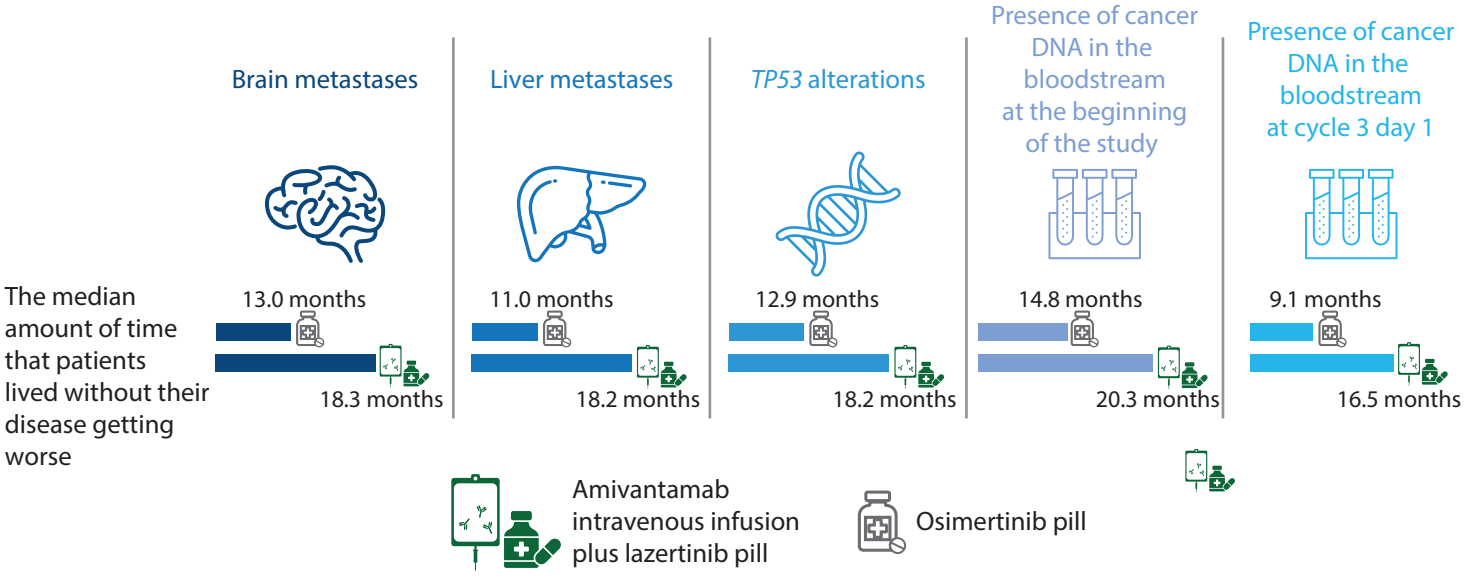
Patients were monitored for changes to their treatment and disease status throughout the MARIPOSA study. Patients were evaluated for the presence of alterations in blood DNA samples at the beginning of the study and within 30 days of their disease worsening and starting a new therapy. Two different methods of analysis were used.

	Patient monitoring schedule	
	Disease assessments (CT scan or MRI)	Genetic biomarker testing
Before receiving treatment	28 days	28 days
Receiving treatment, no worsening of disease	7 to 9 weeks after starting treatment for the first 30 months Every 11 to 13 weeks thereafter	Cycle 3 day 1
Worsening of disease	Stop after worsening of disease	Within 30 days of worsening of disease before next anticancer therapy

What were the overall results of the study?

When the data were analyzed, 320 patients in the amivantamab plus lazertinib group and 316 in the osimertinib group had blood DNA samples available. The effectiveness of amivantamab plus lazertinib was evaluated across several high-risk categories, including patients with brain or liver metastases, *TP53* alterations, and the presence of circulating cancer DNA in the bloodstream at the beginning of the study and at cycle 3 day 1. When the information from the amivantamab plus lazertinib group was compared with the information from the osimertinib group at the time of data analysis, the following was observed:

Results in patients with high-risk features for *EGFR*-altered non-small-cell lung cancer



Brain metastases:

- At the beginning of the MARIPOSA study, 41% of patients had a history of cancer that had spread to the brain
- Among these patients, the median amount of time that patients lived without their cancer growing or spreading, also known as PFS, was 18.3 months in the amivantamab plus lazertinib group compared with 13.0 months in the osimertinib group
- Similarly, this prolonged effect was also observed among patients with cancer that had not spread to the brain, with a median PFS of 27.5 months with amivantamab plus lazertinib compared with 19.9 months with osimertinib

Liver metastases:

- Overall, 136 patients (16%) had cancer that had spread to the liver at the beginning of the study (64 in the amivantamab plus lazertinib group and 72 in the osimertinib group)
- Among these patients, the median PFS was 18.2 months in the amivantamab plus lazertinib group compared with 11.0 months in the osimertinib group
- Similarly, this prolonged effect was also observed among patients with cancer that had not spread to the liver, with a median PFS of 24.0 months with amivantamab plus lazertinib compared with 18.3 months with osimertinib

***TP53* alterations:**

- 54% of patients had *TP53* alterations detected at the beginning of the study (149 patients in the amivantamab plus lazertinib group and 144 in the osimertinib group)

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- Among these patients, the median PFS was 18.2 months in the amivantamab plus lazertinib group compared with 12.9 months in the osimertinib group
- Similarly, this prolonged effect was also observed among the patients without *TP53* alterations, with a median PFS of 22.1 months with amivantamab plus lazertinib compared with 19.9 months with osimertinib

Cancer DNA in the bloodstream at the beginning of the study:

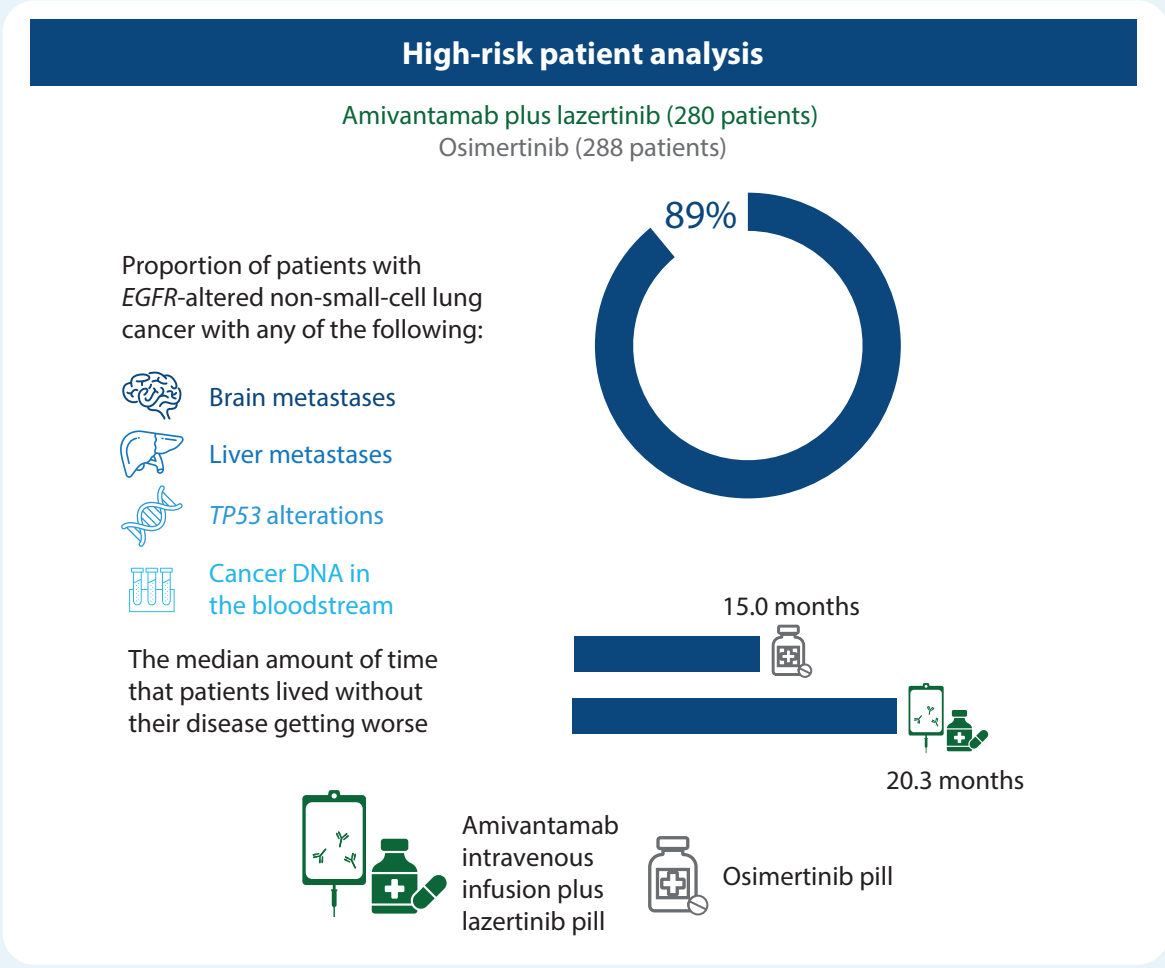
- At the beginning of the study, 70% of patients had cancer DNA in the bloodstream, which is also known as circulating tumor DNA, or ctDNA (231 in the amivantamab plus lazertinib group and 240 in the osimertinib group)
- Among these patients, the median PFS was 20.3 months in the amivantamab plus lazertinib group compared with 14.8 months in the osimertinib group
- Similarly, this treatment benefit was also seen for patients without cancer DNA in their bloodstream at the beginning of the study, with a median PFS of 27.7 months in the amivantamab plus lazertinib group compared with 21.9 months in the osimertinib group

Cancer DNA in the bloodstream at cycle 3 day 1 (29 days into treatment):

- In both treatment groups, 85% of patients no longer had cancer DNA in their bloodstream on cycle 3 day 1 of treatment
- In those patients who still had cancer DNA in their bloodstream on cycle 3 day 1, the median PFS was 16.5 months in the amivantamab plus lazertinib group compared with 9.1 months in the osimertinib group
- Improved outcomes were also seen for patients who no longer had cancer DNA in their bloodstream on cycle 3 day 1 of treatment, with a median of 24.0 months in the amivantamab plus lazertinib group compared with 16.5 months in the osimertinib group

High-risk patient analysis:

- At the beginning of the study, high-risk cancer traits, such as cancer DNA in the bloodstream, *TP53* alterations, and brain or liver metastases, were present in 89% of patients with blood samples available for analysis (280 in the amivantamab plus lazertinib group and 288 in the osimertinib group)
- Among these patients, the median PFS was 20.3 months in the amivantamab plus lazertinib group compared with 15.0 months in the osimertinib group



What were the most common side effects, and how did they compare between treatment groups?

Among all patients, the most common types of side effects in the MARIPOSA study were skin and nail related. Amivantamab, lazertinib, and osimertinib all block the EGFR protein, which is found on skin and nail cells; this means that these therapies may impact those types of cells, leading to side effects. Skin and scalp rashes may require the assistance of dermatology professionals. Additional studies, such as COCOON, are evaluating ways to prevent or to better manage skin-related side effects.

A VTE is when a blood clot forms in a vein, which is a serious side effect that can be life threatening in some cases. Taking anticoagulants can help prevent VTEs from happening; patients with cancer are often advised to take preventative anticoagulants along with other treatments if their health care providers are concerned about the possibility of VTEs. VTEs occurred more often in patients receiving amivantamab plus lazertinib compared with those receiving osimertinib. Severe VTEs were rare. However, few patients received anticoagulants to prevent VTEs (5% of all patients) or stopped taking amivantamab plus lazertinib due to VTEs (3% for amivantamab plus lazertinib; less than 1% for osimertinib).

Overall, the side effects observed were similar to those previously seen in other studies evaluating amivantamab, lazertinib, and osimertinib. For more information on the safety of amivantamab plus lazertinib and osimertinib in the MARIPOSA study, please read the article published in *The New England Journal of Medicine*.

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What do the results of this high-risk analysis mean?

This high-risk subgroup analysis of the MARIPOSA study found that the combination of amivantamab plus lazertinib extended PFS compared with osimertinib in patients with NSCLC with *EGFR* Ex19del or exon 21 L858R alterations and high-risk features, such as *TP53* alterations, cancer that had spread to the brain or liver, or cancer DNA in the bloodstream. Since most patients with advanced NSCLC have at least one of these high-risk characteristics that increase their risk for worse disease, these results are relevant to a wide group of patients.

The findings of the MARIPOSA study support the scientific reasoning for combining amivantamab and lazertinib as first-line therapy for certain patients with NSCLC with *EGFR* Ex19del or exon 21 L858R alterations with or without high-risk features.

Educational resources

Learn about the NCCN and the European Society for Medical Oncology (ESMO) guidelines for treating NSCLC. These guidelines help doctors to best care for their patients and help patients make informed decisions regarding their care. NCCN and ESMO guidelines for patients can be found at:
https://www.nccn.org/patients/guidelines/content/PDF/lung-metastatic-patient.pdf (NCCN; late-stage NSCLC)
https://www.esmo.org/for-patients/patient-guides/non-small-cell-lung-cancer (ESMO)

Where can I find more information?

The original article citation is: Felip E, Cho BC, Gutiérrez V, *et al.* Amivantamab plus lazertinib versus osimertinib in first-line *EGFR*-mutant advanced non-small-cell lung cancer with biomarkers of high-risk disease: a secondary analysis from MARIPOSA. *Ann Oncol.* 2024;35(9):805-816; it is free to access at: https://www.annalsofoncology.org/article/S0923-7534(24)00702-6/fulltext

You can read more about the MARIPOSA study, which took place November 2020 through May 2022, here and at the following websites:
Cho BC, Lu S, Felip E, *et al.* Amivantamab plus lazertinib in previously untreated *EGFR*-mutated advanced NSCLC. *N Engl J Med.* 2024;391(16):1486-1498. https://www.nejm.org/doi/full/10.1056/NEJMoa2403614 and https://clinicaltrials.gov/study/NCT04487080

- Type the ClinicalTrials.gov Identifier "NCT04487080" into the "Other Terms" section at: https://clinicaltrials.gov
- US Food and Drug Administration: https://www.fda.gov
- European Cancer Patient Coalition: https://ecpc.org

More information on clinical studies in general can be found at: https://www.clinicaltrials.gov/ct2/about-studies/learn

More information on NSCLC can be found at the following sources that were used to develop this plain language summary:

- Non–small cell lung cancer: epidemiology, screening, diagnosis, and treatment: https://pubmed.ncbi.nlm.nih.gov/31378236
- Comparative clinical outcomes for patients with advanced NSCLC harboring *EGFR* exon 20 insertion mutations and common *EGFR* mutations: https://pubmed.ncbi.nlm.nih.gov/34818606
- Lung cancer: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00312-3/fulltext
- Targeted therapies for lung cancer: https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/treatment/types-of-treatment/targeted-therapies
- What is lung cancer?: https://www.cancer.org/cancer/types/lung-cancer/about/what-is.html

- New driver mutations in non-small-cell lung cancer: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(10)70087-5/abstract
- Effect of epidermal growth factor receptor tyrosine kinase domain mutations on the outcome of patients with non-small cell lung cancer treated with epidermal growth factor receptor tyrosine kinase inhibitors: https://aacrjournals.org/clincancerres/article/12/14/4416s/284848/Effect-of-Epidermal-Growth-Factor-Receptor
- Activating and resistance mutations of *EGFR* in non-small-cell lung cancer: role in clinical response to EGFR tyrosine kinase inhibitors: https://pmc.ncbi.nlm.nih.gov/articles/PMC2849651/
- Targeting *EGFR* exon 20 insertion mutations in non-small cell lung cancer: https://www.nature.com/articles/s41392-019-0038-9
- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.3.2025. © National Comprehensive Cancer Network, Inc. All rights reserved. Accessed March 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
- NCCN Patient Guidelines: https://www.nccn.org/patientresources/patient-resources/guidelines-for-patients/guidelines-for-patients-details?patientGuidelineId=23

More information about the effects of the first therapy given to patients with Ex19del or exon 21 L858R mutations can be found at:

- Mortality among *EGFR*-mutated advanced NSCLC patients after frontline osimertinib treatment: a real-world, US attrition analysis: https://www.jto.org/article/S1556-0864(23)00273-3/fulltext
- Retrospective analysis of real-world management of *EGFR*-mutated advanced NSCLC, after first-line EGFR-TKI treatment: US treatment patterns, attrition, and survival data: https://pubmed.ncbi.nlm.nih.gov/35661118

More information on amivantamab and lazertinib can be found at the following sources:

- Amivantamab prescribing information: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/RYBREVANT-pi.pdf
- A novel bispecific antibody targeting EGFR and cMet is effective against EGFR inhibitor-resistant lung tumors: https://pubmed.ncbi.nlm.nih.gov/27216193
- Lazertinib approval review: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8217052/pdf/40265_2021_Article_1533.pdf

More information about how safe and effective amivantamab was in clinical trials can be found at the following sources:

- A plain language summary of the results from the group of patients in the CHRYSALIS study with *EGFR* exon 20 insertion-mutated non-small-cell lung cancer who received amivantamab: https://www.futuremedicine.com/doi/epdf/10.2217/fon-2023-0284
- Plain language summary of PAPILLON: amivantamab plus chemotherapy in untreated *EGFR*-mutated non-small-cell lung cancer: https://www.tandfonline.com/doi/full/10.1080/14796694.2024.2371698
- Enhanced dermatological care to reduce rash and paronychia in epidermal growth factor receptor (*EGFR*)-mutated non-small cell lung cancer (NSCLC) treated first-line with amivantamab plus lazertinib (COCOON): https://clinicaltrials.gov/study/NCT06120140

More information on the side effects related to EGFR inhibitors can be found at the following sources that were used to develop this plain language summary:

- Prevention and management of acneiform rash associated with EGFR inhibitor therapy: a systematic review and meta-analysis: https://onlinelibrary.wiley.com/doi/10.1111/ajco.13740
- Current recommendations and novel strategies for the management of skin toxicities related to anti-EGFR therapies in patients with metastatic colorectal cancer: https://pubmed.ncbi.nlm.nih.gov/31264159
- A national survey of medical oncologist's opinions and perceptions for managing rash among mCRC patients treated with panitumumab: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6522609/

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• Dougherty L, Lewis WE, O' Neill M, *et al.* Infusion-related reaction management with amivantamab for *EGFR* exon 20 insertion mutation NSCLC: a practical guide for advanced practitioners. *J Adv Pract Oncol.* 2024;15(4):245-252. https://www.jadpro.com/issues/volume-15-number-4-mayjun-2024/infusion-related-reaction-management-with-amivantamab-for-egfr-exon-20-insertion-mutation-nsclc-a-practical-guide-for-advanced-practitioners

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Ethical declaration

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Data availability statement

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access (YODA) Project site at http://yoda.yale.edu.