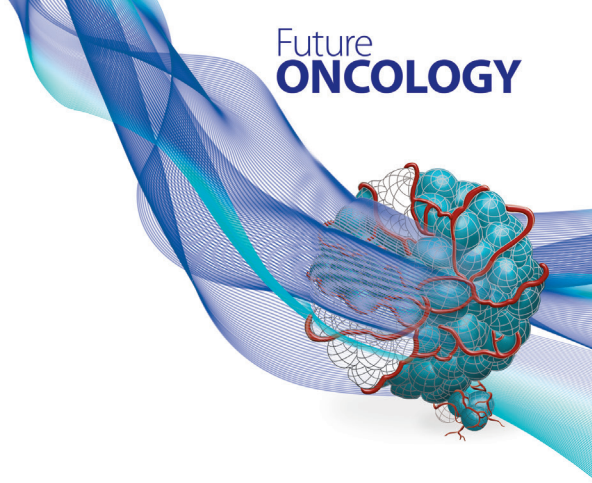
Plain Language Summary of Publication



Future ONCOLOGY

Plain language summary of MARIPOSA-2: amivantamab-chemotherapy either with or without lazertinib for treatment of non-small-cell lung cancer

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

The original article is titled 'Amivantamab plus chemotherapy with and without lazertinib in *EGFR*-mutated advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study.'

You can read the original article at: https://doi.org/10.1016/j.annonc.2023.10.117

Summary

What is this summary about?

This plain language summary describes the first results of the **phase 3 MARIPOSA-2 study** in patients with **locally advanced** or **metastatic** NSCLC with **common alterations** (**exon 19 deletion alteration [Ex19del]** or **exon 21 L858R substitution alteration [L858R]**) in the **epidermal growth factor receptor** (*EGFR*) **gene** whose **disease progressed** while on or after they received the osimertinib, a third generation **tyrosine kinase inhibitor (TKI)**. Osimertinib, a drug given for NSCLC that helps block the growth and multiplication of cancer cells, is currently a preferred option for patients who have not received prior treatment, as recommended by the National Comprehensive Cancer Network® (NCCN®).

Phase 3 study: Clinical research is performed in phases to ensure that there are multiple studies that confirm the study treatment is safe and effective prior to the treatment's approval. Phase 3 trials confirm the findings of phase 2 trials by comparing the effectiveness and safety of the study drug against the current standard-of-care treatment.

Locally advanced disease: When the cancer has spread to other parts of the organ where it first formed.

Metastatic disease/metastasis: When the cancer has spread from where it first formed (for example, lung cancer in the lung) to another area of the body (for example, lung cancer that spreads to the liver).

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

- **Amivantamab:** am-ee-VAN-tuh-mab
- **Anemia:** uh-nee-mee-uh
- **Bispecific antibody:** by-speh-SIH-fik AN-tee-BAH-dee
- **Carboplatin:** KAR-boh-pla-tin
- **Chemotherapy:** kee-moh-ther-uh-pee
- **CHRYSALIS:** kris-uh-lis
- **Epidermal:** ep-ee-DER-mal
- **Epithelial:** ep-ee-THEL-ee-ul
- **Exon:** ek-son
- **Intravenous:** in-truh-vee-nuhs
- **Lazertinib:** lay-ZER-tuh-nib
- **Mesenchymal:** meez-en-KY-mul
- **Metastases:** muh-ta-stuh-sees
- **MARIPOSA:** mare-EE-pose-ah
- **Neutropenia:** noo-truh-pee-nee-uh
- **Osimertinib:** OH-sih-MER-tih-nib
- **Pemetrexed:** peh-meh-TREX-ed
- **Tyrosine kinase:** tai-ruh-seen kai-nays

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Summary (cont.)

Amivantamab in combination with **chemotherapy** was approved by the **US Food and Drug Administration (FDA)** and the **European Medicines Agency (EMA)** for the treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* Ex19del or L858R whose disease had progressed on or after treatment with an EGFR TKI. The NCCN recommends amivantamab plus chemotherapy (carboplatin and pemetrexed) as a preferred treatment option for patients with *EGFR* Ex19del or L858R who have multiple tumors, or **lesions**, and experience disease progression after receiving **first-line** osimertinib.

What were the results?

657 patients were randomly assigned to treatment groups (patients received amivantamab plus chemotherapy, amivantamab plus lazertinib plus chemotherapy, or chemotherapy alone). Patients who received amivantamab plus chemotherapy and amivantamab plus lazertinib plus chemotherapy had their risk of their cancer getting worse or dying reduced by 52% and 56%, respectively, compared with patients who received chemotherapy alone. Similar benefits with amivantamab plus chemotherapy were seen for reducing the risk of cancer growing in the brain. Furthermore, more than 6 in 10 patients who received amivantamab plus chemotherapy or amivantamab plus lazertinib plus chemotherapy had tumors that shrank by at least 30% or were no longer detectable. This only happened in approximately 3 in 10 patients who received chemotherapy alone.

Side effects can be seen with all cancer treatments. Most side effects are known and manageable. The most common side effects in patients treated with amivantamab plus chemotherapy and amivantamab plus lazertinib plus chemotherapy were **hematologic**. Few patients who received amivantamab plus chemotherapy or amivantamab plus lazertinib plus chemotherapy stopped all treatments due to side effects.

What do the results mean?

In patients with NSCLC with *EGFR* Ex19del or L858R, amivantamab-containing combinations reduced the risk of a patient's cancer getting worse or dying. Therefore, they are effective treatment options for patients with NSCLC with *EGFR* Ex19del or L858R after disease progression on an EGFR TKI.

Genetic alteration: A change to the DNA sequence.

Exon 19 deletion alteration (Ex19del): 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.

Exon 21 L858R substitution alteration (L858R): A change to the DNA sequence of *EGFR* that changes the function of the EGFR protein. In the case of L858R, a small part of DNA is replaced with a different one within the *EGFR* gene.

Receptor: A protein used by cells to pass along chemical signals.

Epidermal growth factor receptor (EGFR): A protein that relays chemical signals that tell the cell to grow, divide, or survive. EGFR refers to a protein while *EGFR* refers to a gene.

Gene: Made up of sequences of deoxyribonucleic acid, or DNA, that contain the information needed for expression of physical characteristics or traits, or for a particular function in a cell.

Disease progression: The growth or spread of cancer.

Tyrosine kinase inhibitor: A type of medication that blocks certain proteins in the body (named tyrosine kinases) to help slow down or stop the growth of cancer cells.

Chemotherapy: A treatment that uses drugs to kill or slow down the growth of cancer cells in the body.

US Food and Drug Administration (FDA): An agency in the United States that is responsible for protecting the public health by making sure that drugs, medical devices, and equipment are safe and effective.

European Medicines Agency (EMA): An agency that protects and promotes human health by evaluating, supervising, and monitoring the safety of medicines within the European Union (EU).

Lesions: Any damage or unhealthy changes to an organ, such as the lungs during lung cancer.

First-line: The initial therapy a patient receives after they are diagnosed.

Side effect: An undesirable effect of a drug or treatment.

Hematologic: Relating to effects on various types of blood cells.

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What is the purpose of this plain language summary?

The purpose of this plain language summary is to help you understand the findings from recent research. Amivantamab plus chemotherapy 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 patients, their families, and health care teams involved with patients who have NSCLC with *EGFR* Ex19del or L858R after disease progression on an EGFR TKI.

Who sponsored this study?

Janssen Biotech, a pharmaceutical company of Johnson & Johnson and 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?

A patient's journey includes the sum of events that occur starting from the patient's diagnosis through the treatments they receive. To better understand the needs of patients and provide better care for them, it is important to understand the patient's journey. Patients who have lung cancer may differ in the causes or alterations that led to the development of their cancer and understanding these differences can help patients and health care providers to decide on treatment, which may have a large impact on how long a patient can live without their cancer getting worse. To identify these alterations, **genetic (biomarker) testing** is used when NSCLC is diagnosed to help medical professionals choose the most appropriate cancer treatment earlier, which may lead to better results.

Genetic (biomarker) testing: A test that examines genetic alterations (called biomarkers) in a patient's DNA that are known to cause lung cancer.

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

NSCLC accounts for 80% to 85% of lung cancer cases, making it the most common form of lung cancer. EGFR is a protein found on the surface of many cell types, including normal and cancer cells, and alterations in the *EGFR* gene can lead to NSCLC. *EGFR* Ex19del and L858R make up 85% to 90% of *EGFR* alterations and are called common *EGFR* alterations. These alterations can occur at any point in an individual's lifetime and can cause cells to grow abnormally. Furthermore, unlike many other lung cancers that are often linked to tobacco use, *EGFR* alterations can happen by chance and can occur regardless of tobacco use.

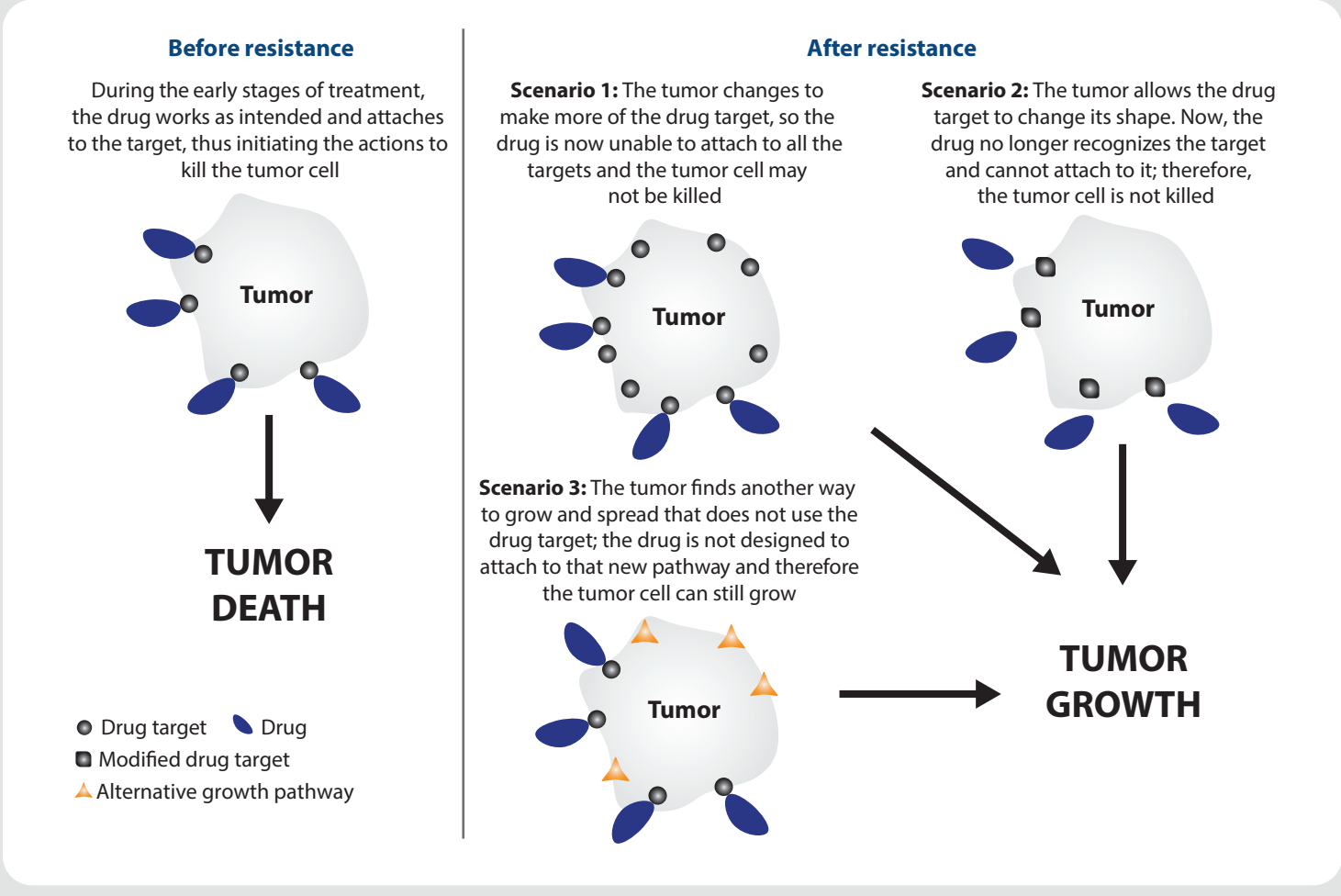
Identifying which genetic alteration is present in different cases of NSCLC is important for choosing the correct treatment and improving the chance of treatment success. **Targeted therapies** are developed to focus treatment toward an alteration that is thought to be the cause of a cancer. Genetic testing can identify *EGFR* Ex19del and L858R, which can guide medical teams to recommend targeted therapies for better treatment results.

Targeted therapy: A drug or other treatment that works on cells that have certain DNA alterations or proteins.

How are patients usually treated after disease progression on osimertinib?

Initial treatment for *EGFR*-mutated advanced NSCLC is typically a targeted therapy called osimertinib, which belongs to a family of medications called TKIs. Unfortunately, almost all patients will eventually develop **resistance mechanisms** to osimertinib, therefore requiring a different treatment for their cancer. Often, chemotherapy is given next, specifically a platinum-containing chemotherapy such as carboplatin-pemetrexed. However, the average patient on platinum-based chemotherapy has less than 6 months before their cancer grows or the patient dies. After treatment with osimertinib, patients lack treatment options that are better than chemotherapy. Until recently, there were no approved targeted therapies for these patients.

Resistance mechanism: The way through which cancer cells gain the ability to survive and grow despite being treated.



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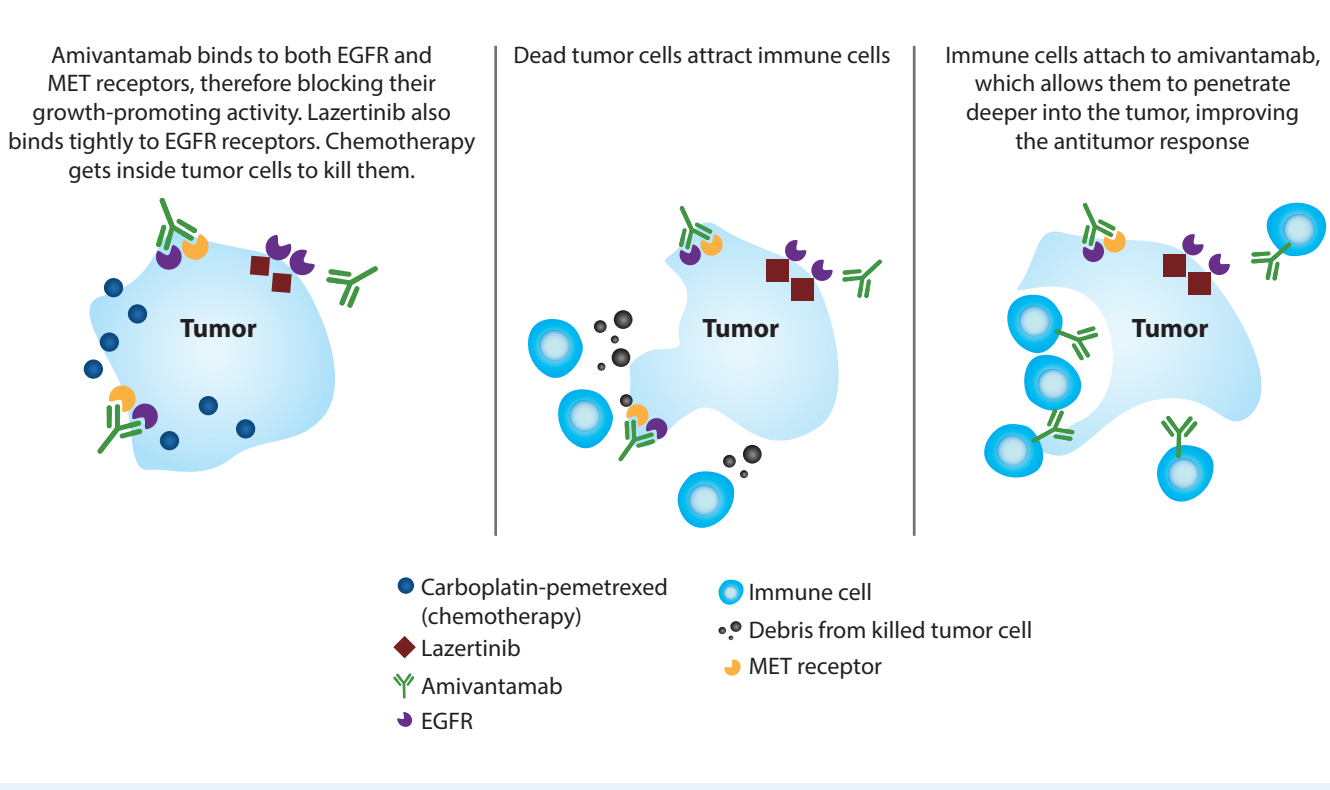
What is amivantamab and how does it work with chemotherapy and lazertinib?

Amivantamab is a bispecific antibody, meaning it can bind to 2 targets. Amivantamab is able to bind to EGFR and MET receptors, both of which are needed for cancer cells to grow and survive. By binding to these receptors, amivantamab blocks the binding of other proteins to these receptors and prevents the growth and spread of tumor cells. Amivantamab also has the ability to potentially boost the body's own natural defense system that helps protect against illness, known as the immune system, to help kill cancer cells.

On the other hand, lazertinib is a highly selective TKI that targets *EGFR* alterations. The addition of lazertinib is thought to be important since brain metastases are often observed in these patients and lazertinib is known to cross into the brain. Amivantamab plus lazertinib has previously shown positive results in patients with *EGFR*-mutated NSCLC after disease progression on osimertinib.

Carboplatin and pemetrexed are types of chemotherapy that are commonly used to treat NSCLC. Chemotherapy works by targeting all rapidly dividing cells and not just cells with specific alterations. Adding amivantamab or amivantamab plus lazertinib to chemotherapy could overcome some of the resistance that is seen in patients whose cancer has grown after treatment with osimertinib.



What was the MARIPOSA-2 study looking at?

MARIPOSA-2 is a phase 3 clinical study that evaluated the safety and effectiveness of amivantamab plus chemotherapy and amivantamab plus lazertinib plus chemotherapy compared with chemotherapy alone in patients with *EGFR*-mutated advanced NSCLC whose disease had progressed on or after receiving osimertinib. Patients chosen for this study were divided into groups at random to receive either amivantamab plus lazertinib plus chemotherapy, amivantamab plus chemotherapy, or chemotherapy alone.

Who were the patients?

Patients in the MARIPOSA-2 study had *EGFR*-mutated NSCLC that already had progressed while on or after receiving osimertinib. Researchers collected demographics (information about the characteristics of each patient, such as their age, sex, and race) at the beginning of the study.

Out of 970 patients who were interested in this study, a total of 657 patients from multiple countries took part in this study between December 2021 and April 2023. Before starting, patients were randomly put into treatment groups: 131 patients received amivantamab plus chemotherapy, 263 patients received amivantamab plus lazertinib plus chemotherapy, and 263 patients received chemotherapy alone.

Corticosteroids: Common medications that reduce swelling and inflammation in the body. They are often used for patients with brain metastases, as the spread of cancer to the brain can cause swelling and inflammation and lead to symptoms like headaches and trouble with coordination.

Corticosteroids are not used to treat cancer, but they can provide relief from symptoms and improve a patient's quality of life.

Radiation therapy: The use of high-energy radiation to kill cancer cells.

Eligible patients were 18 years of age or older and had *EGFR*-mutated NSCLC that had progressed on or after receiving osimertinib. Patients with brain metastases were able to participate if the tumor within the brain was clinically stable (not getting worse), the patients were showing no symptoms, and if requiring **corticosteroids**, they were on a fixed dose (same amount of drug at each dose) that had not changed recently. Prior treatment with **radiation therapy** or surgery was not mandatory for patients with brain metastases. Demographic and disease characteristics at the start of the study were similar between each treatment group.

Characteristics of patients in MARIPOSA-2

Amivantamab plus lazertinib plus chemotherapy (263 patients)
Amivantamab plus chemotherapy (131 patients)
Chemotherapy alone (263 patients)

Female

64%
62%
60%

Over half of the patients were female

Median age, years

61 (range, 23 to 83)
62 (range, 36 to 84)
62 (range, 31 to 85)

Ages of the patients ranged from 23 to 85 years

Smoking history

	No	Yes
	67%	33%
	69%	31%
	64%	36%

Over half of the patients had no history of smoking

Race

Asian	48%	48%	48%
White	49%	46%	47%
Other	3%	6%	5%

Almost half of the patients were Asian

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What was evaluated in the study?
The effectiveness and safety of the amivantamab plus chemotherapy and amivantamab plus lazertinib plus chemotherapy combinations were evaluated and compared with chemotherapy alone. The effectiveness of each treatment was assessed by its ability to:

- Stop tumor growth/spread (including in the brain) or delay death
- Shrink the tumor
- Prolong patient survival
- Provide a treatment benefit for an extended period of time

The safety of each treatment was assessed by the number, severity (seriousness), and type of side effects that all patients had, including those side effects that forced the patient to stop treatment or reduce the dose of treatment. The study started in December 2021 and the results for this study were collected by researchers until 10 July 2023.

How much of each treatment was given to patients?
Amivantamab was given intravenously by infusion (directly into a vein), weekly for the first 4 weeks, then every 3 weeks until the tumor grew or spread within the body. The first infusion was split over 2 days to reduce the risk of side effects known as **infusion-related reactions**.

Lazertinib was given orally (by mouth) as a pill daily.

Carboplatin was given for the first 4 cycles only (a treatment cycle was 21 days), and pemetrexed was given until the tumor grew or spread in the body.

Patients were aware of the treatment they received (**unblinded**) due to differences in how the medications are given (orally versus intravenously), the medications given prior to infusions, and the side effects of the medications.

At the beginning of the study, patients in the amivantamab plus lazertinib plus chemotherapy group received all 4 treatments at the same time; however, these patients had worse hematologic and **gastrointestinal** side effects. To help prevent these side effects, the treatment plan was changed so that lazertinib was only started once carboplatin had been completed. The results of this updated treatment plan will be reported at a later date.

Infusion-related reaction: Common side effects caused by infused medicines that are similar to an immune response (antibodies).

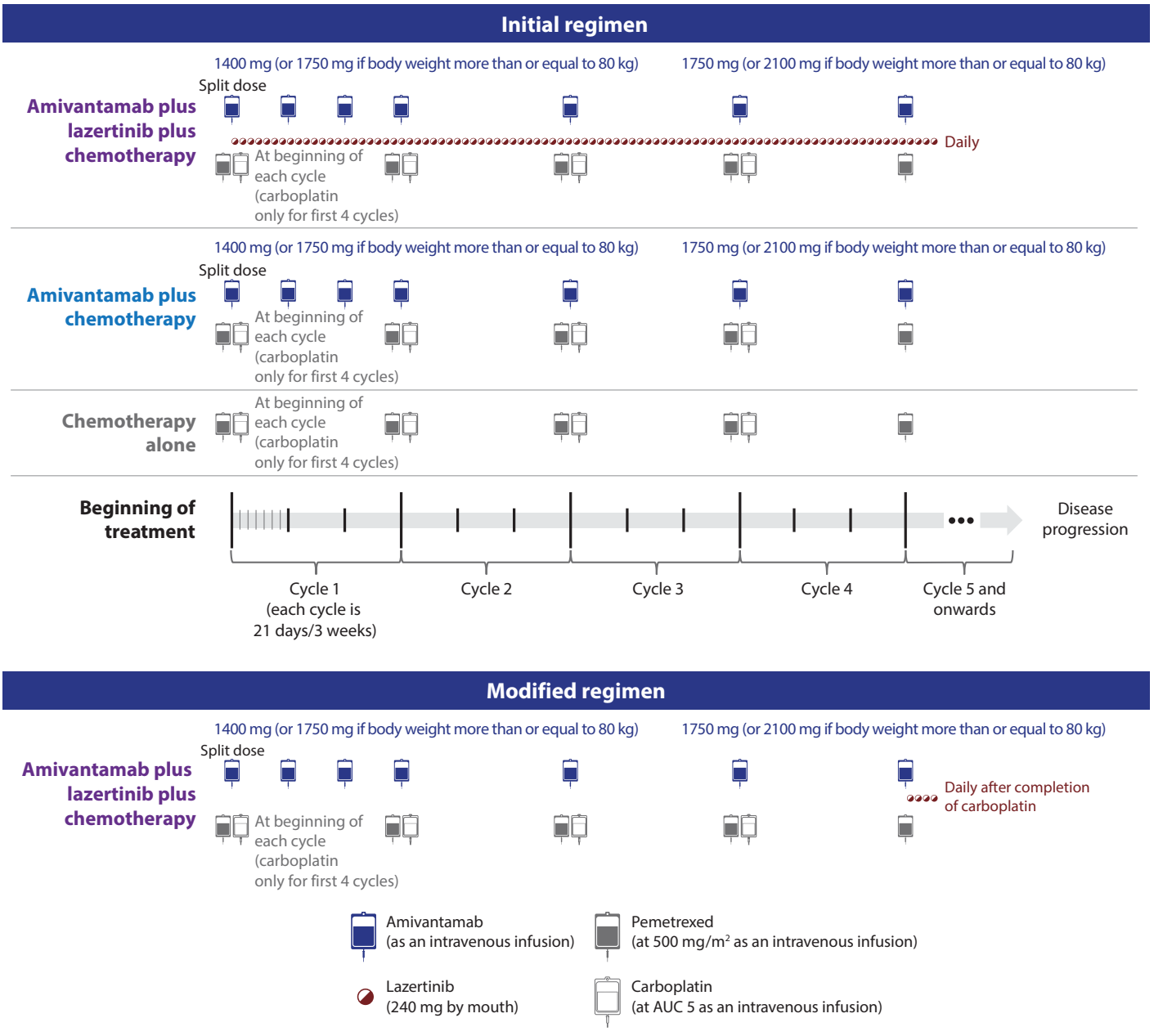
Unblinded treatment: A method used to assign study drugs in clinical studies where the patients are aware of whether they are receiving the tested drug or a placebo (an inactive substance).

Gastrointestinal: Relating to the stomach and the intestines.

Computed tomography (CT): A test that uses x-ray techniques to make detailed images of the body.

Magnetic resonance imaging (MRI): A way to make detailed images of parts of the body using magnets and radio waves.

How did researchers measure the effects of amivantamab plus lazertinib plus chemotherapy?
Patients were checked for changes to their treatment, side effects, and disease condition throughout the MARIPOSA-2 study. **Computed tomography (CT)** or **magnetic resonance imaging (MRI)** was used to monitor the status of the disease and see if cancer had spread to the brain in patients prior to and during the course of treatment.



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What were the overall results of the study?

Patients who received amivantamab plus chemotherapy had a 52% lower chance of their disease worsening or dying compared with chemotherapy alone. Similarly, patients who received amivantamab plus lazertinib plus chemotherapy had a 56% lower chance of progression or death compared with chemotherapy alone. This benefit was seen regardless of a patient's alteration type, history of brain metastases, or if osimertinib was given as a first or second therapy.

Patients who received amivantamab plus chemotherapy had a 45% lower chance of their cancer growing in the brain or dying compared with chemotherapy alone. Similarly, patients who received amivantamab plus lazertinib plus chemotherapy had a 42% lower chance of their cancer growing in the brain or dying compared with chemotherapy alone.

64% of patients who received amivantamab plus chemotherapy and 63% of patients who received amivantamab plus lazertinib plus chemotherapy had their tumors shrink or become no longer detectable compared with 36% of patients who received chemotherapy alone.

The amount of time from the start of treatment that half of all patients in the study lived without their tumor growing or spreading was 6.3 months with amivantamab plus chemotherapy, 8.3 months with amivantamab plus lazertinib plus chemotherapy, and 4.2 months with chemotherapy alone.

The **median** amount of time that patients' tumors shrank or were no longer detectable was 6.9 months with amivantamab plus chemotherapy, 9.4 months with amivantamab plus lazertinib plus chemotherapy, and 5.6 months with chemotherapy alone.

Median: The middle value of a set of numbers.

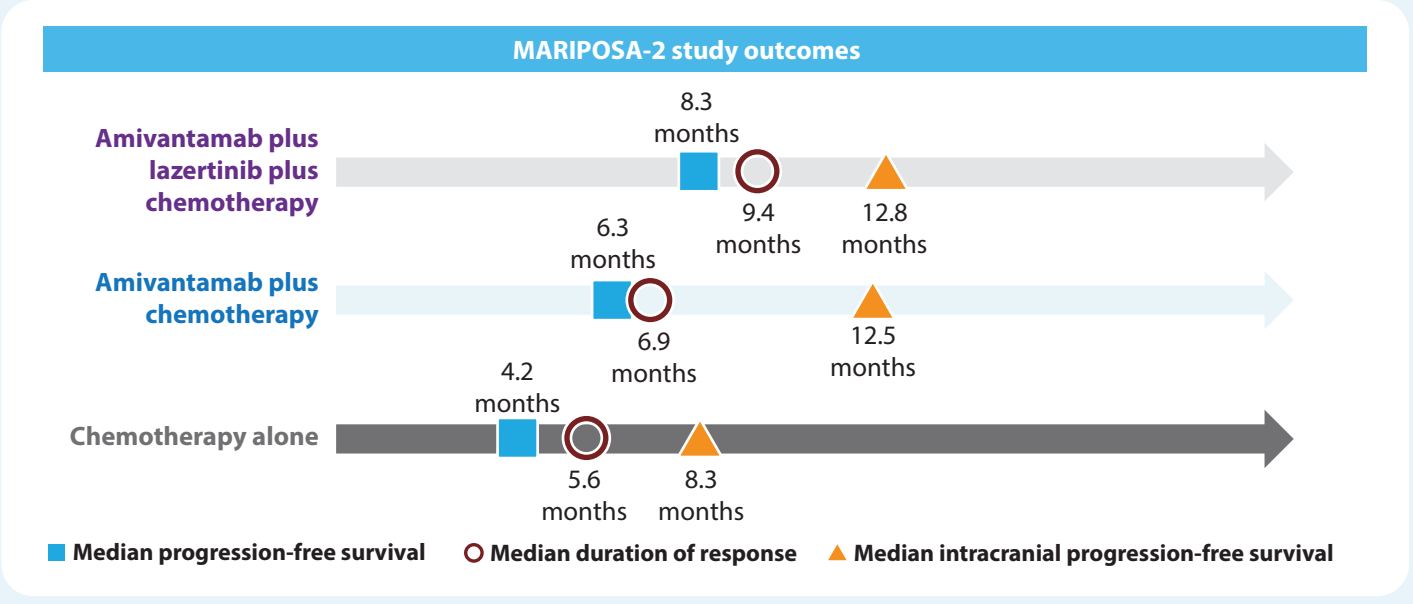
Objective response rate: The percentage of study patients whose tumor had measurable shrinkage or was no longer detectable after receiving a medication.

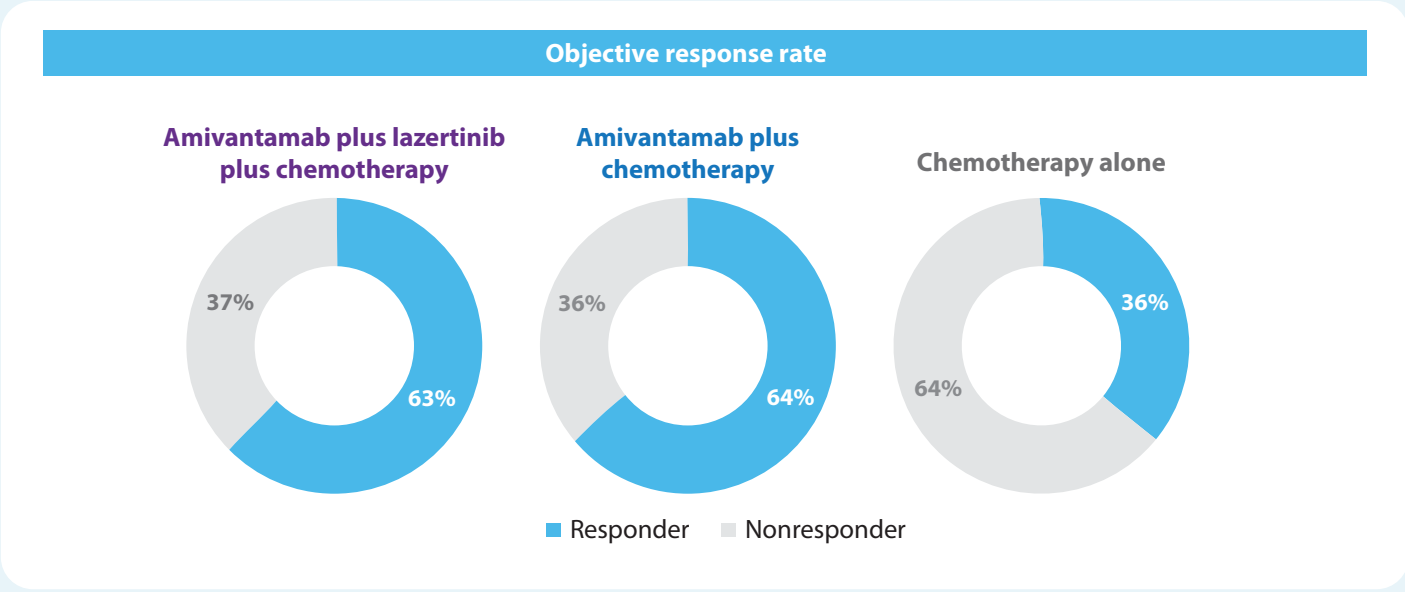
Median duration of response: The length of time from the start of treatment to when half of the patients had complete responses – defined as tumors that are no longer detectable over a specified time period – and partial responses – defined as measurable tumor shrinkage that is still detectable over a specified time period.

Median intracranial progression-free survival: The amount of time when half of the patient's cancer in the brain did not worsen (progressive disease).

Median progression-free survival: The amount of time when half of the patient's cancer did not worsen (progressive disease).

Based on initial data, there was a trend towards patients receiving amivantamab plus chemotherapy living longer overall than patients who received chemotherapy alone. No detrimental trend was observed for amivantamab plus chemotherapy plus lazertinib. However, this was an initial analysis of these data, and more data will be collected to assess whether amivantamab combination treatment improves the amount of overall time a patient is still alive.





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

A side effect is an unwanted or unintentional reaction that may or may not be related to the treatment. The 3 most common side effects, other than infusion-related reactions, for all groups included **neutropenia**, **thrombocytopenia**, and **anemia**. These hematologic side effects are common with the use of chemotherapy, and most patients were able to continue in the study without stopping treatment despite having side effects.

Neutropenia: A condition where a person has too few of one type of white blood cell called neutrophils.

Thrombocytopenia: A condition where a person has too few blood platelets, which can impair blood clotting.

Anemia: A condition where a person does not have enough healthy blood cells or has difficulty transporting oxygen in their blood.

Other than infusion-related reactions, the 3 most common side effects for amivantamab plus chemotherapy were neutropenia (observed in 57% of patients), nausea (feeling sick; 45%), and thrombocytopenia (44%). For amivantamab plus lazertinib plus chemotherapy, the 3 most common side effects were neutropenia (69%), thrombocytopenia (60%), and anemia (54%). For chemotherapy alone, the 3 most common side effects were neutropenia (42%), anemia (40%), and nausea (37%). Neutropenia and thrombocytopenia mostly occurred early, within the first 21 days of treatment (cycle 1). However, neutrophil (type of white blood cell that fights infection) and platelet (small blood particles that help stop bleeding) numbers increased and stabilized by cycle 2, which indicates that these side effects could be resolved. Febrile neutropenia, which is the presence of a fever with low counts of white blood cells, was seen in 2% of patients with amivantamab plus chemotherapy, 8% with amivantamab plus lazertinib plus chemotherapy, and 2% with chemotherapy alone, meaning that treatment largely did not negatively impact the body's ability to fight against infection for most patients.

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Another commonly experienced side effect of amivantamab was rash. Forty-three percent of patients who received amivantamab plus chemotherapy and 48% of patients who received amivantamab plus lazertinib plus chemotherapy experienced rash. Rash and other types of skin side effects are known with amivantamab and other EGFR inhibitors due to the way these drugs work.

Serious side effects, which are those that require significant medical care or hospitalization, occurred in 32% of patients who received amivantamab plus chemotherapy, 52% of patients who received amivantamab plus lazertinib plus chemotherapy, and 20% of patients who received chemotherapy alone.

84 patients (65%) in the amivantamab plus chemotherapy group, 202 patients (77%) in the amivantamab plus lazertinib plus chemotherapy group, and 81 patients (33%) in the chemotherapy alone group briefly interrupted (delayed or skipped) their treatment due to side effects. 53 patients (41%) in the amivantamab plus chemotherapy group, 171 patients (65%) in the amivantamab plus lazertinib plus chemotherapy group, and 37 patients (15%) in the chemotherapy alone group reduced the treatment dose due to side effects.

24 patients (18%) in the amivantamab plus chemotherapy group, 90 patients (34%) in the amivantamab plus lazertinib plus chemotherapy group, and 9 patients (4%) in the chemotherapy alone group had side effects that led to them completely stopping any of the study treatments.

The most common side effects that led to a patient stopping treatment in the amivantamab plus chemotherapy group were infusion-related reactions (5%) and thrombocytopenia (1%). For amivantamab plus lazertinib plus chemotherapy, the most common side effects that led to a patient stopping treatment were thrombocytopenia (5%), infusion-related reactions (3%), and **stomatitis** (3%). For chemotherapy alone, thrombocytopenia (1%) was the most common side effect that led to stopping treatment.

As of the date the data were analyzed, 27 patients (21%) in the amivantamab plus chemotherapy group and 69 patients (26%) in the amivantamab plus lazertinib plus chemotherapy group died during the study compared with 65 patients (27%) in the chemotherapy alone group. Most of these deaths (17 in the amivantamab plus chemotherapy group, 46 in the amivantamab plus lazertinib plus chemotherapy group, and 56 in the chemotherapy alone group) were due to worsening of the patient's lung cancer.

Stomatitis: Inflammation in the mouth, including blisters and ulcers.

Premedication: Medication that is given prior to another treatment to alleviate symptoms of the treatment.

Subcutaneous: Something that is applied under the skin; subcutaneous administration refers to drugs given with a needle that goes just under the skin.

What is an infusion-related reaction?

An infusion-related reaction is a side effect that may occur during or shortly after medication is given to a patient via intravenous infusion. Amivantamab is an antibody that is given through the vein as an infusion. Infusion-related reactions were common in the 2 groups that received amivantamab. 58% of patients who received amivantamab plus chemotherapy and 56% of patients who received amivantamab plus lazertinib plus chemotherapy had infusion-related reactions. Infusion-related reactions have been previously seen with amivantamab alone (67%). Patients were given **premedication** prior to infusion with amivantamab-containing combinations to reduce the chance of infusion-related reactions. Infusion-related reaction symptoms include, but are not limited to, nausea, reddening of the skin, shortness of breath, and chills.

A **subcutaneous** version of amivantamab is also being developed. Subcutaneous amivantamab was designed with the intention to reduce infusion-related reactions in patients receiving amivantamab while offering a more convenient option for patients.

Most common side effects in patients

Amivantamab plus lazertinib plus chemotherapy (263 patients)
Amivantamab plus chemotherapy (130 patients)
Chemotherapy alone (243 patients)

Low white blood cell count

69% of patients
57% of patients
42% of patients

Severe reactions:
55%, 45%, and 21%

Low platelet count

60% of patients
44% of patients
30% of patients

Severe reactions:
37%, 15%, and 9%

Infusion-related reaction

56% of patients
58% of patients
0.4% of patients

Severe reactions:
3%, 5%, and none

Anemia

54% of patients
39% of patients
40% of patients

Severe reactions:
18%, 12%, and 9%

Nail infections

51% of patients
37% of patients
0.4% of patients

Severe reactions:
4%, 2%, and none

Nausea (feeling sick)

50% of patients
45% of patients
37% of patients

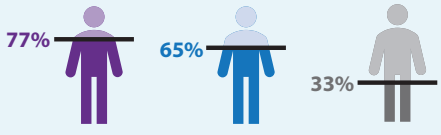
Severe reactions:
6%, 1%, and 1%

Rash

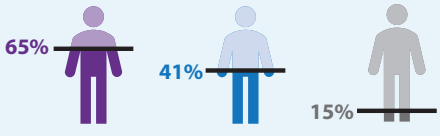
48% of patients
43% of patients
5% of patients

Severe reactions:
6%, 6%, and none

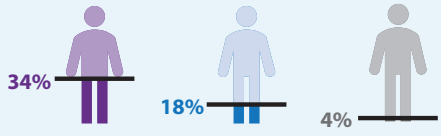
Treatment interrupted due to side effects



Treatment dose reduced



Treatment discontinued due to side effects



Severe reactions: Also known as 'Grade 3' side effects, include side effects that cause extreme distress and have a significant impact upon normal everyday activities, but are not immediately life-threatening.

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What is a venous thromboembolism?
Venous thromboembolism (VTE), another side effect of interest, is a condition that occurs when a blood clot forms in a vein and can commonly occur in patients with lung cancer. VTEs may be managed with anticoagulation therapy, also known as blood thinners, which prevents the blood from clotting.

Ten percent of patients who received amivantamab plus chemotherapy, 22% of patients who received amivantamab plus lazertinib plus chemotherapy, and 5% of patients who received chemotherapy alone experienced VTEs.

No patients died due to VTEs, most VTEs occurred early in treatment, and most VTEs were mild in severity. Stopping treatment due to VTEs was infrequent and similar across the treatment groups.

Since VTEs were more commonly seen in patients who received amivantamab plus lazertinib plus chemotherapy and more frequently occurred early on in treatment, patients are recommended to receive blood thinners during the first 4 months of treatment with amivantamab and lazertinib to prevent their occurrence.

The use of blood thinners can potentially increase a patient's risk of bleeding. One percent of patients who received amivantamab plus chemotherapy and 3% of patients who received amivantamab plus lazertinib plus chemotherapy experienced severe or life-threatening (grade 3 or 4) bleeding events. None of the patients who received chemotherapy alone had such events.

What do the results of this study mean?

The MARIPOSA-2 study found that amivantamab-containing treatments are the first to reduce the risk of the cancer growing or dying compared with chemotherapy alone in patients with *EGFR*-mutated advanced NSCLC who had their disease progress after receiving osimertinib. Amivantamab plus chemotherapy reduced the chance of a patient's tumor growing or a patient dying by 52% and amivantamab plus lazertinib plus chemotherapy reduced the chance by 56% compared with chemotherapy alone. This benefit was consistently seen regardless of the patient's *EGFR* alteration type, if osimertinib was received as the first or second therapy, and whether or not the patient had a history of brain metastases. In addition, patients who received amivantamab-containing treatments had improved disease responses that were longer-lasting and less likely to have their cancer spread to the brain compared with patients who received chemotherapy alone.

The side effects with amivantamab plus chemotherapy and amivantamab plus lazertinib plus chemotherapy were similar with what has been observed when those treatments are administered separately. The side effects were mostly hematologic and also related to amivantamab's ability to block EGFR or MET. Notably, patients who received amivantamab plus lazertinib plus chemotherapy did experience more frequent hematologic side effects than patients who received the other treatment plans. To potentially address this issue, changes were made so that lazertinib was only started after one of the chemotherapy drugs (carboplatin) had been completed. Results for this updated dosing schedule will be reported at a later date after patients are followed for a longer period of time.

The results of the MARIPOSA-2 study show that amivantamab plus chemotherapy is an option for patients with *EGFR*-mutated advanced NSCLC who had their tumor grow or spread after receiving osimertinib. Based on these findings, the combination of amivantamab plus chemotherapy has been approved by the FDA and EMA and is considered a new standard of care after osimertinib. In August 2024, the FDA also approved amivantamab plus lazertinib as a first-line treatment of *EGFR*-mutated NSCLC, with the European Commission approving this combination in January of 2025. Amivantamab plus lazertinib plus chemotherapy is still being investigated and to date has not been approved.

These results also highlight the importance of genetic testing for *EGFR* alterations to select the right treatment. Similar to that seen in patients with NSCLC and *EGFR* exon 20 insertion alterations who took part in the PAPILLON study (see 'Where can I find more information?'), patients with *EGFR* Ex19del or L858R respond better to amivantamab-containing treatments compared with chemotherapy alone. Overall, the MARIPOSA-2 study suggests that patients with *EGFR* Ex19del or L858R benefit from amivantamab plus chemotherapy after their lung cancer has worsened following standard therapy with an EGFR TKI. Based on the findings from MARIPOSA-2, the NCCN updated their guidelines to recommend amivantamab plus chemotherapy as a preferred treatment option for patients with *EGFR* Ex19del or L858R who have multiple lesions and disease progression after receiving first-line osimertinib.

Educational resources

Learn about the NCCN as well as the 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.esmo.org/for-patients/patient-guides/non-small-cell-lung-cancer (ESMO)
https://www.nccn.org/patients/guidelines/content/PDF/lung-metastatic-patient.pdf (NCCN – late-stage NSCLC)

Where can I find more information?

You can access and read the original article for free here:
Passaro A, Wang J, Wang Y, et al. Amivantamab plus chemotherapy with and without lazertinib in *EGFR*-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study. *Ann Oncol.* 2024;35(1):77-90. doi:10.1016/j.annonc.2023.10.117
https://www.annalsofoncology.org/article/S0923-7534(23)04281-3/fulltext

The MARIPOSA-2 study started on 17 November 2021 and is estimated to complete on 8 December 2025. You can read more about the MARIPOSA-2 study at the following website:
https://clinicaltrials.gov/study/NCT04988295

At ClinicalTrials.gov, type the following ClinicalTrials.gov Identifier into the 'Other Terms' section: NCT04988295

European Cancer Patient Coalition: https://ecpc.org/

More information on clinical studies of amivantamab can be found at:
https://clinicaltrials.gov/search?intr=amivantamab

More information about 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/
- Lung cancer: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00312-3/abstract
- Targeted therapies for lung cancer:
  https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/treatment/types-of-treatment/targeted-therapies
- Osimertinib or platinum-pemetrexed in *EGFR* T790M-positive lung cancer: https://pubmed.ncbi.nlm.nih.gov/27959700/
- Gefitinib plus chemotherapy versus placebo plus chemotherapy in *EGFR*-mutation-positive non-small-cell lung cancer after progression on first-line gefitinib (IMPRESS): a phase 3 randomised trial: https://pubmed.ncbi.nlm.nih.gov/26159065/
- Nivolumab (NIVO) + chemotherapy (chemo) vs chemo in patients (pts) with *EGFR*-mutated metastatic non-small cell lung cancer (mNSCLC) with disease progression after EGFR tyrosine kinase inhibitors (TKIs) in CheckMate 722:
  https://www.annalsofoncology.org/article/S0923-7534(22)04541-0/fulltext
- Pemetrexed and platinum with or without pembrolizumab for tyrosine kinase inhibitor (TKI)-resistant, EGFR-mutant, metastatic nonsquamous NSCLC: phase 3 KEYNOTE-789 study: https://meetings.asco.org/abstracts-presentations/218083
- 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.

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- NCCN Patient Guidelines: https://www.nccn.org/patientresources/patient-resources/guidelines-for-patients/guidelines-for-patients-details?patientGuidelineId=23

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/
- Predictive biomarkers for treatment with amivantamab plus lazertinib among *EGFR*-mutated NSCLC in the post-osimertinib setting: analysis of tissue IHC and ctDNA NGS: https://meetings.asco.org/abstracts-presentations/226378
- Lazertinib versus gefitinib as first-line treatment in patients with *EGFR*-mutated advanced non-small-cell lung cancer: results from LASER301: https://pubmed.ncbi.nlm.nih.gov/37379502/
- 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.tandfonline.com/doi/epdf/10.2217/fon-2023-0284
- A plain language summary of PAPILLON: amivantamab plus chemotherapy in untreated *EGFR*-mutated non-small-cell lung cancer: https://www.tandfonline.com/doi/epdf/10.1080/14796694.2024.2371698

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Generative AI (ChatGPT) was used to simplify technical language throughout.

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AP serves in a consulting or advisory role for AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo Europe, Johnson & Johnson Innovative Medicine, Merck Sharp & Dohme, Novartis, Pfizer, and Roche/Genentech; and participated in a speakers bureau for AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo Europe, Johnson & Johnson, and Merck Sharp & Dohme. ABC participated on a data safety monitoring board or advisory board for InhaTarget and Merck. RDG participated on a data safety monitoring board or advisory board for AstraZeneca, Blueprint Medicines, Daiichi Sankyo, Gilead, Jazz Pharmaceuticals, Johnson & Johnson, Mirati, Oncocyte, Sanofi, and Takeda; is a member of the ASCO Scientific Review Committee and the NCI Investigational Drug Steering Committee; is a co-chair for the Hoosier Cancer Research Network and the Thoracic Clinical Trial Working Group; and is an associate editor for ASCO meeting abstracts and the Journal of Clinical Oncology. WNWJr participated on a data safety monitoring board or advisory board for Io9; and holds an unpaid leadership or fiduciary role in Sociedade Brasileira de Oncologia Clinica and the Latin American Cooperative Oncology Group. BCC participated in an advisory board for BridgeBio Therapeutics, Cyrus Therapeutics, Guardant Health, KANAPH Therapeutics, and Oscotec.

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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 Yale Open Data Access (YODA) Project site at http://yoda.yale.edu.

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