elcc European Lung Cancer Congress 2025

Amivantamab Plus Lazertinib vs Osimertinib in First-line *EGFR*-mutant Advanced NSCLC

Final Overall Survival from the Phase 3 MARIPOSA Study

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Organisers ESMO IASLC International Association for the Study of Lung Cancer
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DECLARATION OF INTERESTS

James Chih-Hsin Yang

Consulting or Advisory Role: Boehringer Ingelheim, Novartis, AstraZeneca, Clovis Oncology, MSD Oncology, Celgene, Bayer, Pfizer, Ono Pharmaceutical, Bristol Myers Squibb, Yuhan, Hansoh, Blueprint Medicines, Daiichi Sankyo, G1 Therapeutics, AbbVie, Takeda, Amgen, Incyte, Eli Lilly, GSK, Merck KGaA, Daiichi Sankyo/AstraZeneca, Puma Biotechnology, Gilead Sciences, Taiho Pharmaceutical, Bayer, Roche/Genentech, Sanofi, ArriVent Biopharma

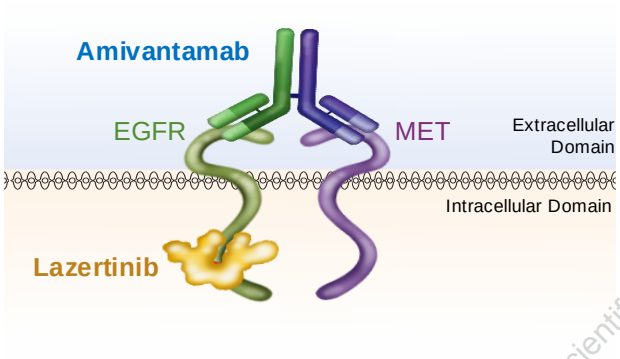
Honoraria: Boehringer Ingelheim, Roche, Merck Sharp & Dohme, AstraZeneca, Novartis, Bristol Myers Squibb, Ono Pharmaceutical, Takeda, Eli Lilly, Pfizer, Amgen, AstraZeneca/MedImmune, Dizal Pharma, Taiho Pharmaceutical, Roche/Genentech, Daiichi Sankyo/AstraZeneca, MSD Oncology, BeiGene, Gilead Sciences, Sanofi/Regeneron

Travel, accommodations, expenses: Pfizer, AstraZeneca, Dizal Pharma

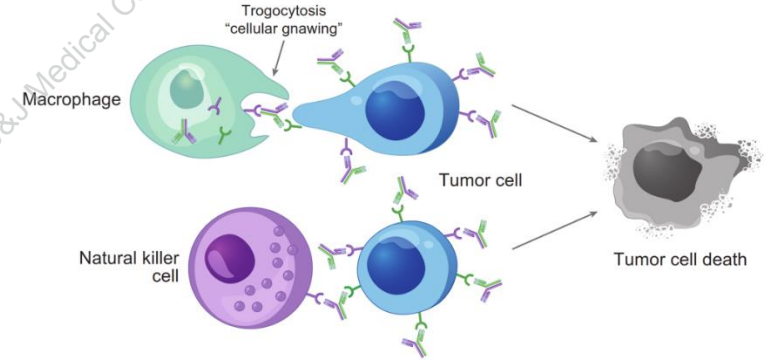
Research funding: AstraZeneca

Background

- In MARIPOSA, 1L amivantamab + lazertinib significantly improved PFS vs osimertinib (**HR, 0.70**; *P*<0.001)[1,2]
- Amivantamab + lazertinib is approved for patients with 1L *EGFR*-mutant advanced NSCLC[3,4]
- 1L amivantamab + lazertinib exhibits a triple mechanism of action with a reduction in the spectrum and complexity of acquired resistance[5]



Immune Cell–directing Activity of Amivantamab



Here, we report the protocol-specified final overall survival results of 1L amivantamab + lazertinib vs osimertinib from MARIPOSA

1. Cho BC, et al. *N Engl J Med*. 2024;24;391(16):1486-1498. 2. Cho BC, et al. Presented at the European Society for Medical Oncology (ESMO) Congress; October 20-24, 2023; Madrid, Spain. 3. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2025. 4. Johnson & Johnson. European Commission approves LAZCLUZE® (lazertinib) in combination with RYBREVANT® (amivantamab) for the first-line treatment of patients with EGFR-mutated advanced non-small cell lung cancer. January 21, 2025. Accessed January 27, 2025.5. Besse B, et al. Presented at the European Society for Medical Oncology (ESMO) Congress; September 13-17, 2024; Barcelona, Spain.

Phase 3 MARIPOSA Study Design

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS 0 or 1

Stratification Factors

- *EGFR* mutation type (Ex19del or L858R)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=1074)

Focus of this presentation

Amivantamab + lazertinib
(n=429; open-label)

Osimertinib
(n=429; blinded)

Lazertinib
(n=216; blinded)

Lazertinib monotherapy arm was included to assess the contribution of components

Serial brain MRIs were required for all participants
MARIPOSA did not allow treatment crossover[a]

Primary endpoint:

- PFS by BICR per RECIST v1.1

Key secondary endpoint:

- Protocol-specified final overall survival[b]

Other endpoints reported in this presentation:

- Intracranial PFS (icPFS)
- Intracranial ORR (icORR)
- Intracranial DoR (icDoR)
- Time to symptomatic progression (TTSP)
- Safety

OS was a key secondary endpoint with prespecified alpha to assess significance

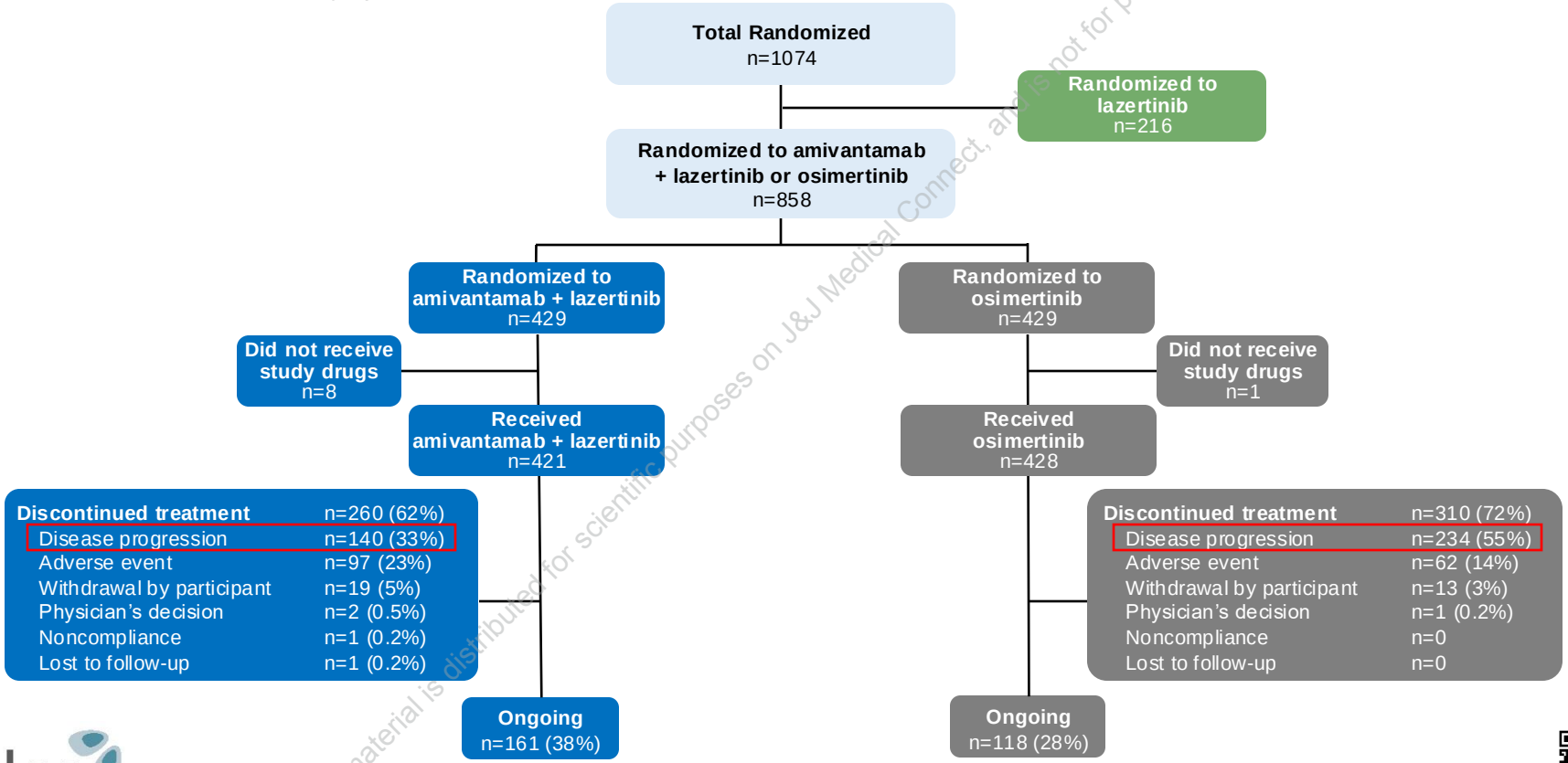
- Protocol-specified final OS analysis was planned for when ~390 deaths had occurred in the amivantamab + lazertinib and osimertinib arms
- OS was tested with a 2-sided alpha of 0.05, determined by O'Brien-Fleming alpha spending approach as implemented by the Lan-DeMets method
  - In the prespecified interim analysis, a 2-sided alpha of 0.005 was allocated for OS
  - The protocol-specified final analysis of overall survival was subsequently evaluated at a 2-sided significance level of 0.0484

MARIPOSA (ClinicalTrials.gov Identifier: NCT04487080) enrollment period: November 2020 to May 2022; clinical cut-off: 04 December 2024. OS analysis was evaluated by means of the *P*-value generated from the stratified log-rank test, with *EGFR* mutation type, Asian race, and history of brain metastases as stratification factors. HRs and 95% CIs were calculated using the stratified Cox regression model with treatment as the sole explanatory variable. Dosing (in 28day cycles): amivantamab: 1050 mg (1400 mg if ≥80 kg) weekly for the first 4 weeks, then every 2 weeks; lazertinib: 240 mg daily; osimertinib: 80 mg daily.

[a]MARIPOSA did not allow crossover as amivantamab-based regimens were not approved in the 2L setting during MARIPOSA enrollment. [b]Continued follow-up is planned to evaluate long-term overall survival.

Participant Disposition

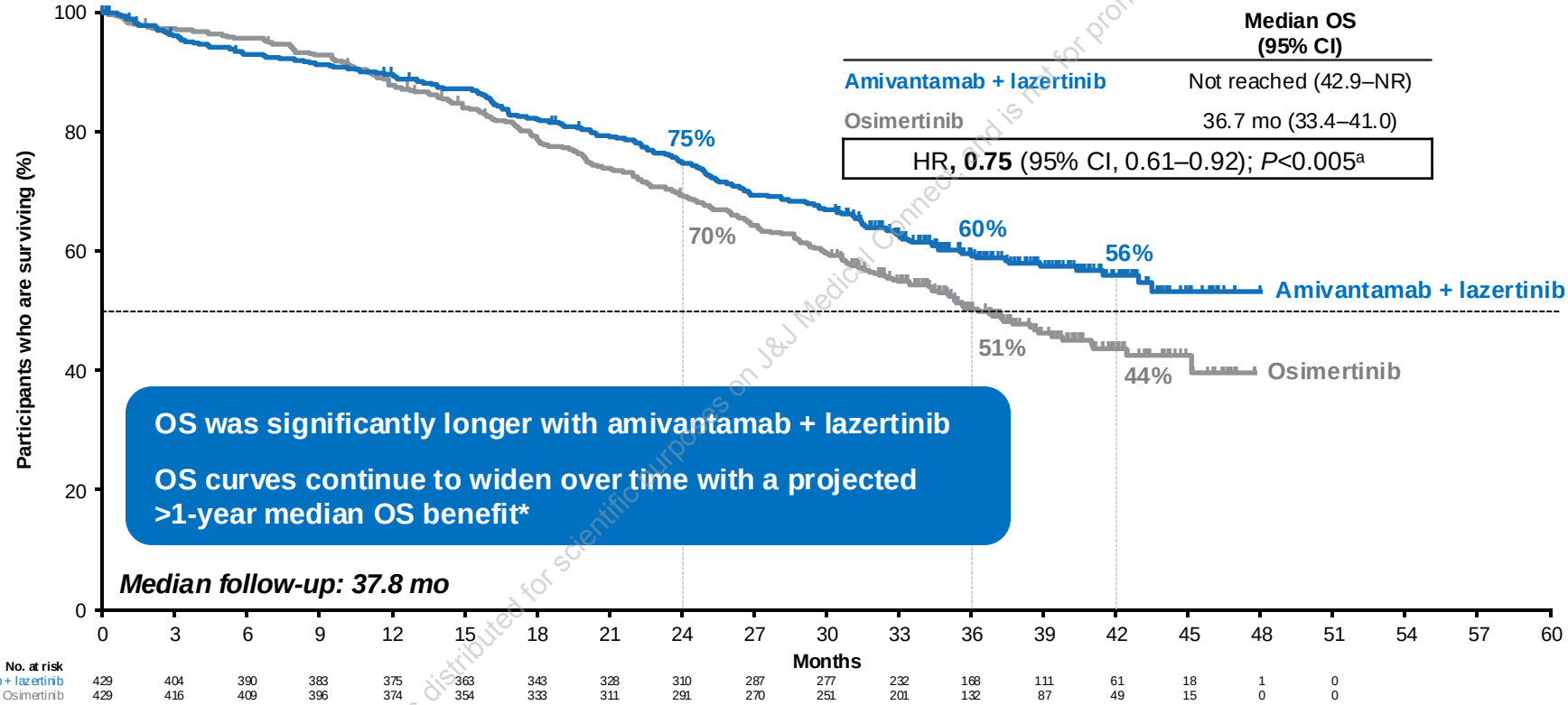
Demographics and baseline disease characteristics were well balanced between arms[1]



1. Cho BC, et al. *N Engl J Med*. 2024;24;391(16):1486-1498.

MARIPOSA: Overall Survival

MARIPOSA
Ami + Laz in 1L
EGFR+ NSCLC



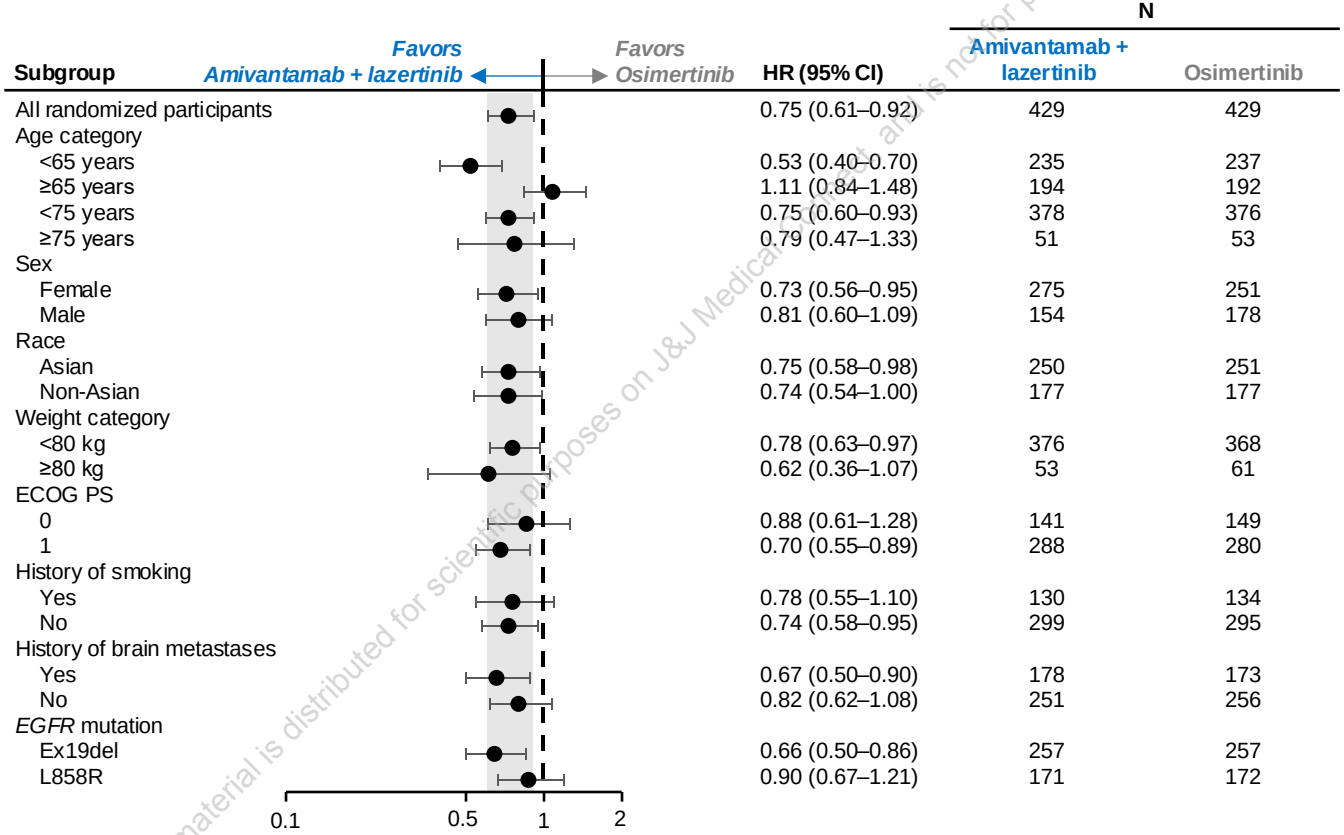
Based on an exponential distribution assumption of OS in both arms, the improvement in median OS is projected to exceed 1 year.

Note: Last participant was enrolled in May 2022. Clinical cutoff date was December 4, 2024. In total, 390 deaths had occurred in the amivantamab + lazertinib (173 deaths) and osimertinib (217 deaths) arms.

[a]*P*-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified Cox regression model.

Overall Survival in Predefined Subgroups[a]

A generally consistent OS benefit for amivantamab + lazertinib over osimertinib was observed across predefined subgroups

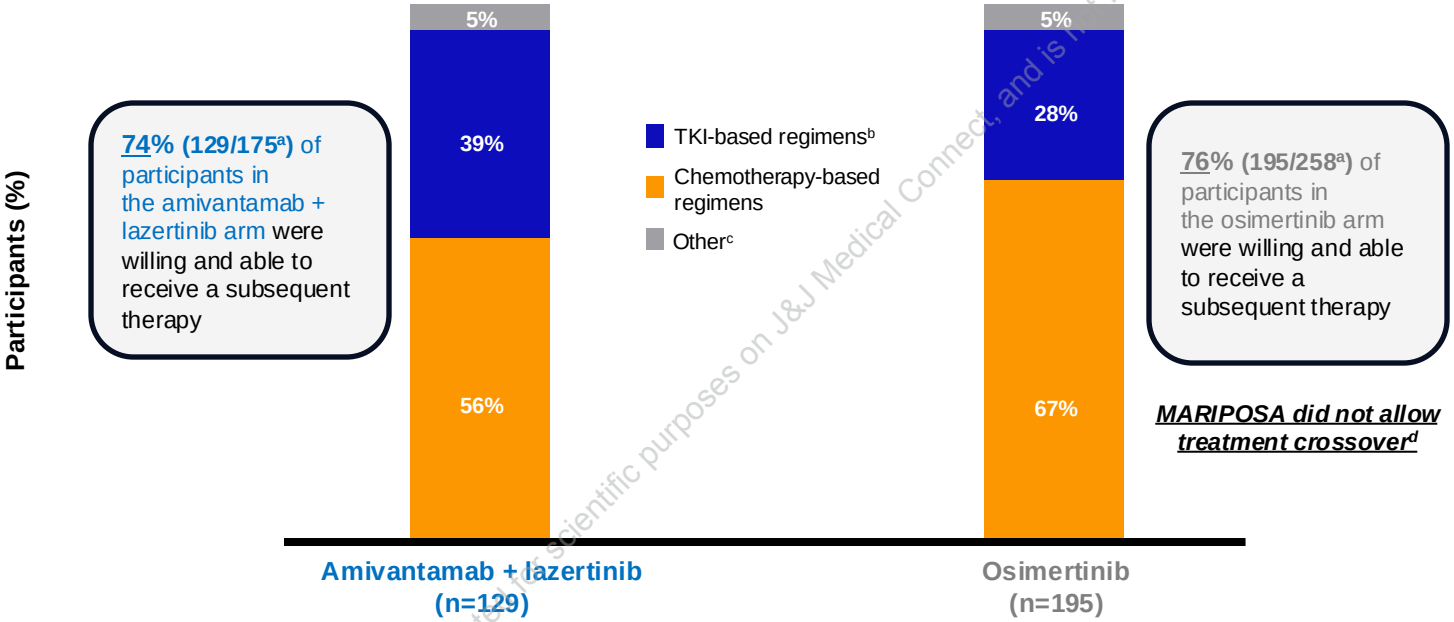


Subgroup	HR (95% CI)	N: Amivantamab + lazertinib	N: Osimertinib
All randomized participants	0.75 (0.61–0.92)	429	429
Age category			
<65 years	0.53 (0.40–0.70)	235	237
≥65 years	1.11 (0.84–1.48)	194	192
<75 years	0.75 (0.60–0.93)	378	376
≥75 years	0.79 (0.47–1.33)	51	53
Sex			
Female	0.73 (0.56–0.95)	275	251
Male	0.81 (0.60–1.09)	154	178
Race			
Asian	0.75 (0.58–0.98)	250	251
Non-Asian	0.74 (0.54–1.00)	177	177
Weight category			
<80 kg	0.78 (0.63–0.97)	376	368
≥80 kg	0.62 (0.36–1.07)	53	61
ECOG PS			
0	0.88 (0.61–1.28)	141	149
1	0.70 (0.55–0.89)	288	280
History of smoking			
Yes	0.78 (0.55–1.10)	130	134
No	0.74 (0.58–0.95)	299	295
History of brain metastases			
Yes	0.67 (0.50–0.90)	178	173
No	0.82 (0.62–1.08)	251	256
EGFR mutation			
Ex19del	0.66 (0.50–0.86)	257	257
L858R	0.90 (0.67–1.21)	171	172

Note: Gray box indicates 95% CI of HR for all randomized participants. [a]Subgroup analyses were not part of the hypothesis testing of the trial and should not be used to infer definitive treatment effects.

First Subsequent Therapy

Most common subsequent therapy class was chemotherapy-based regimens in both arms



74% received 2L therapy, suggesting a long-term treatment plan after 1L amivantamab + lazertinib is feasible

Note: Percentages may not sum to 100 due to rounding.

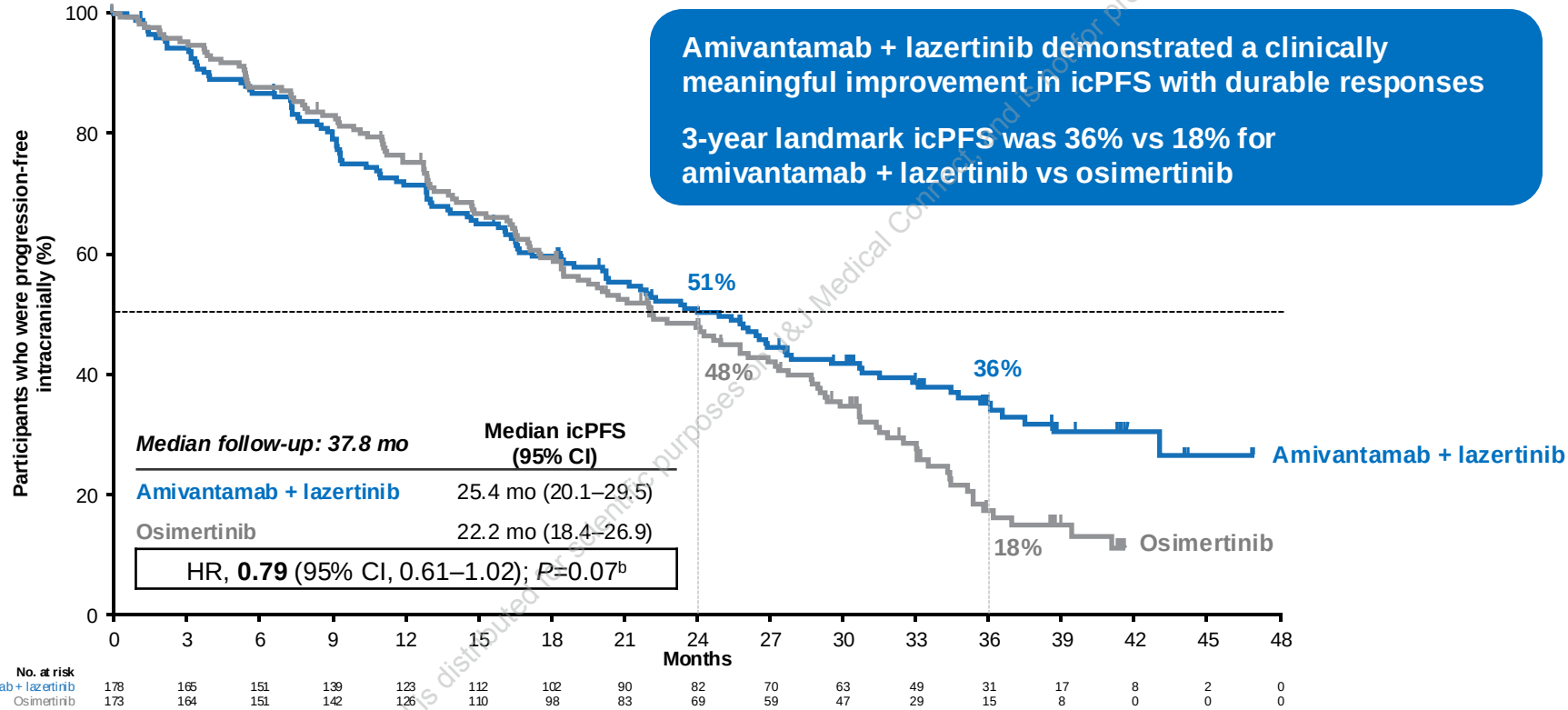
[a]Denominator is the number of participants who had disease progression and discontinued randomized treatment. [b]TKI-based regimens include TKI + chemotherapy (5% in both arms). [c]Other therapy included VEGFi alone, IO alone, herbals, antibody-drug conjugates, ALK tyrosine kinase inhibitors, c-MET tyrosine kinase inhibitors, amivantamab (1 participant received amivantamab-chemotherapy after amivantamab-lazertinib; after osimertinib, 1 participant received amivantamab-chemotherapy, 1 participant received amivantamab-lazertinib, and 1 participant received amivantamab monotherapy), and investigational agents. [d]MARIPOSA did not allow crossover as amivantamab-based regimens were not approved in the 2L setting during MARIPOSA enrollment.

Intracranial PFS[a]

MARIPOSA
Ami + Laz in 1L
EGFR+ NSCLC

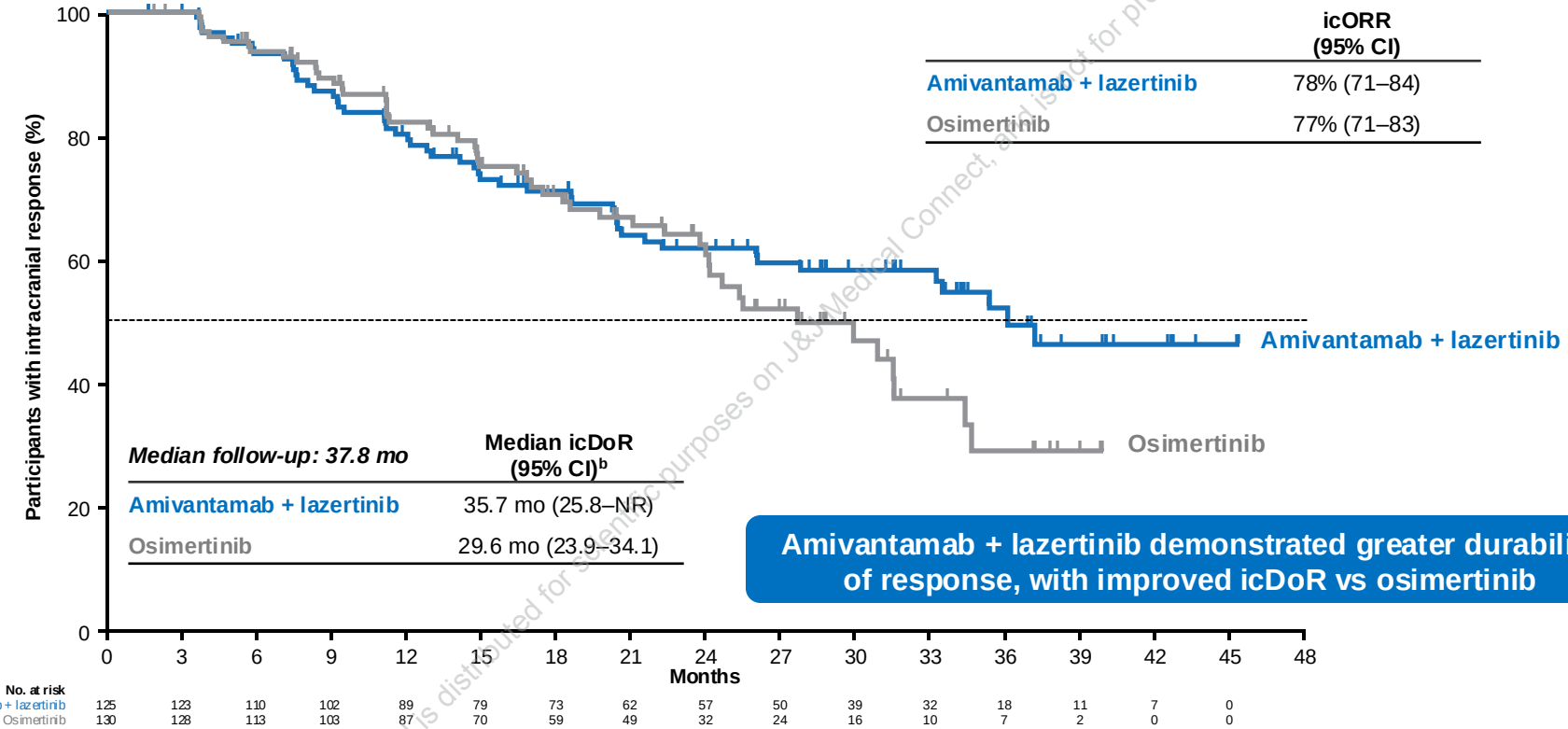
Amivantamab + lazertinib demonstrated a clinically meaningful improvement in icPFS with durable responses

3-year landmark icPFS was 36% vs 18% for amivantamab + lazertinib vs osimertinib



[a]Intracranial PFS was defined as time from randomization until the date of intracranial disease progression (progression of brain metastasis or occurrence of new brain lesions) or death, based on BICR using RECIST v1.1 among participants with a history of brain metastases. [b]*P*-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R) and race (Asian or Non-Asian). Hazard ratio was calculated from a stratified Cox regression model.

Intracranial DoR[a]



	icORR (95% CI)
Amivantamab + lazertinib	78% (71–84)
Osimertinib	77% (71–83)

Median follow-up: 37.8 mo	Median icDoR (95% CI)[b]
Amivantamab + lazertinib	35.7 mo (25.8–NR)
Osimertinib	29.6 mo (23.9–34.1)

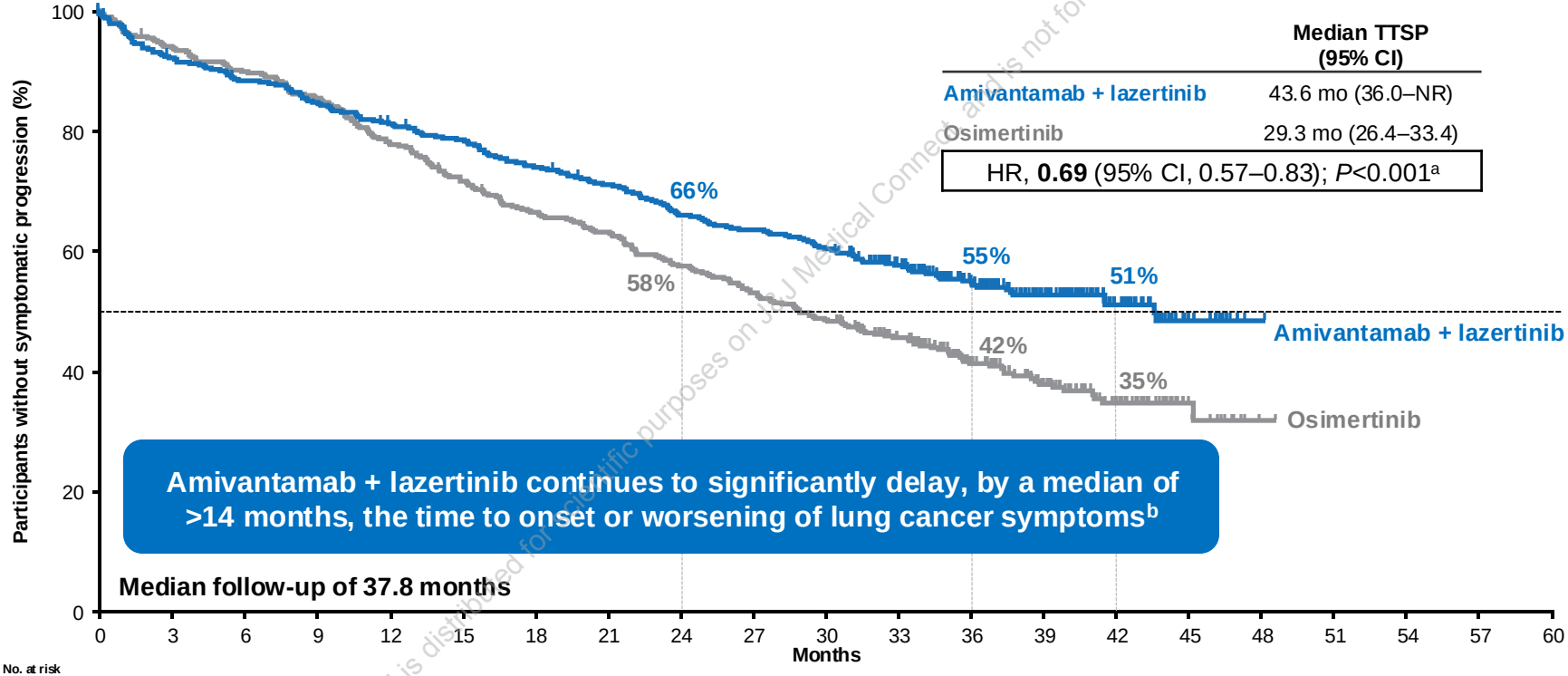
Amivantamab + lazertinib demonstrated greater durability of response, with improved icDoR vs osimertinib

[a]Intracranial DoR was analyzed as the time from the date of first documented intracranial response (CR or PR) until the date of documented intracranial progression or death, whichever occurred first, among participants with a brain lesion at screening who have intracranial CR or PR based on BICR using RECIST v1.1. [b]95% CIs were estimated with the Kaplan-Meier method.

Time to Symptomatic Progression (TTSP)

MARIPOSA
Ami + Laz in 1L
EGFR+ NSCLC

Symptomatic progression is a patient-relevant endpoint that measures time from randomization to the onset of new/worsening lung cancer symptoms requiring a change in therapy, clinical intervention, or death, based on investigator discretion



No. at risk

Amivantamab + lazertinib	429	390	373	358	342	329	310	296	275	265	252	215	159	106	57	17	1	0
Osimertinib	429	404	386	367	335	306	283	269	245	226	207	168	111	77	42	12	1	0

[a]*P*-value is calculated by log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified Cox regression model. [b]Data with median follow-up of 22.0 months were previously presented: Nguyen D, et al. Presented at the World Conference on Lung Cancer (WCLC); September 7-10, 2024; San Diego, CA, USA.

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Safety

- Median duration of treatment was **27.0 mo** for amivantamab + lazertinib and **22.4 mo** for osimertinib
- Safety profile was consistent with the primary analysis[1]
  - AEs were mostly EGFR- and MET-related and grades 1–2[1,2]
- A minority of participants were prescribed antibiotics for rash (21%) at study initiation[2]
- Few were on anticoagulation (**5%**) at baseline[2], with VTE[a] occurring in **40%** in the amivantamab + lazertinib arm and **11%** in the osimertinib arm

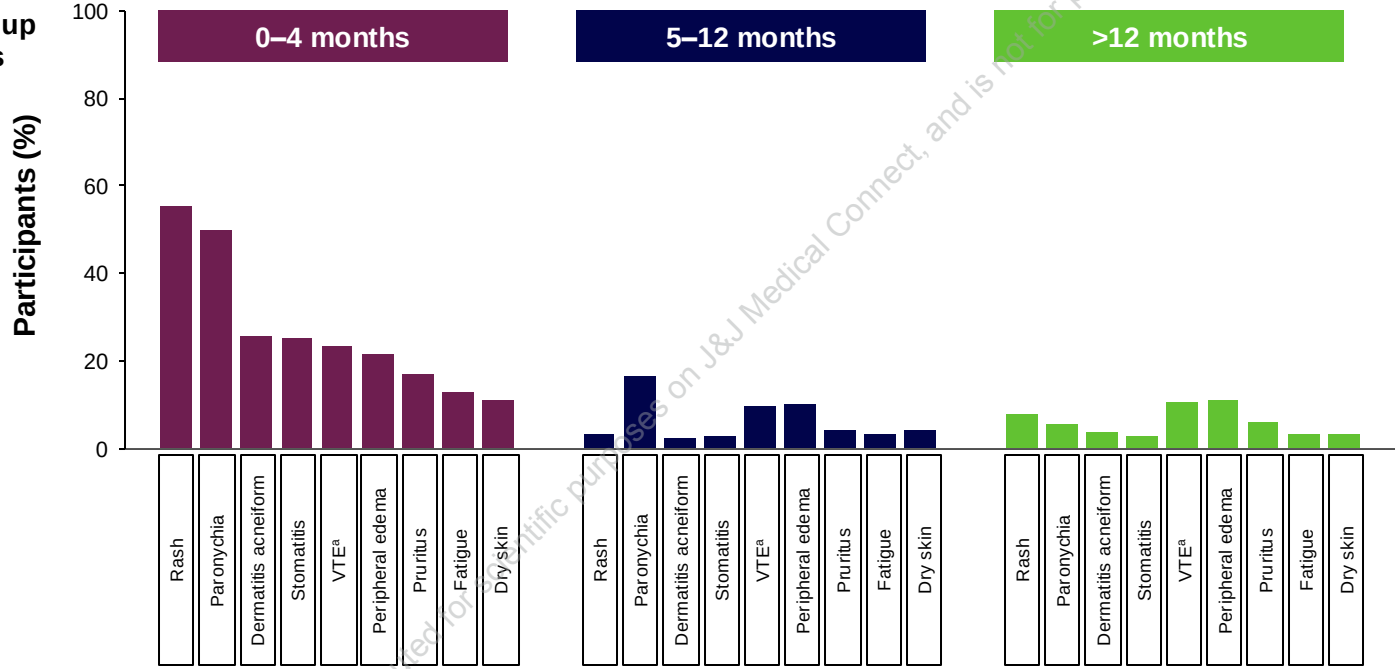
AEs by preferred term (≥20% of participants in either group)	Amivantamab + lazertinib (n=421)		Osimertinib (n=428)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Related to EGFR inhibition				
Paronychia	291 (69)	49 (12)	127 (30)	2 (<1)
Rash	271 (64)	73 (17)	136 (32)	3 (<1)
Diarrhea	133 (32)	9 (2)	200 (47)	4 (<1)
Dermatitis acneiform	127 (30)	37 (9)	55 (13)	0
Stomatitis	126 (30)	5 (1)	92 (21)	1 (<1)
Pruritus	107 (25)	2 (<1)	75 (18)	1 (<1)
Related to MET inhibition				
Hypoalbuminemia	216 (51)	26 (6)	29 (7)	0
Peripheral edema	162 (38)	8 (2)	29 (7)	1 (<1)
Other				
Infusion-related reaction	275 (65)	27 (6)	0	0
ALT increased	170 (40)	28 (7)	66 (15)	8 (2)
AST increased	139 (33)	15 (4)	68 (16)	6 (1)
Constipation	130 (31)	0	70 (16)	0
COVID-19	125 (30)	8 (2)	112 (26)	9 (2)
Anemia	114 (27)	20 (5)	112 (26)	10 (2)
Decreased appetite	114 (27)	4 (1)	84 (20)	7 (2)
Nausea	99 (24)	5 (1)	65 (15)	1 (<1)
Hypocalcemia	96 (23)	11 (3)	37 (9)	0
Asthenia	84 (20)	13 (3)	54 (13)	7 (2)
Muscle spasms	84 (20)	3 (<1)	36 (8)	0
Thrombocytopenia	74 (18)	4 (1)	92 (21)	6 (1)

[a]VTE is a grouped term, which included pulmonary embolism, deep vein thrombosis, limb venous thrombosis, venous thrombosis, thrombosis, superficial vein thrombosis, thrombophlebitis, embolism, venous embolism, jugular vein thrombosis, sigmoid sinus thrombosis, axillary vein thrombosis, pulmonary infarction, vena cava thrombosis, central venous catheterization, portal vein thrombosis, post thrombotic syndrome, pulmonary thrombosis, superior sagittal sinus thrombosis, transverse sinus thrombosis, pelvic venous thrombosis, and superior vena cava syndrome. 1. Cho BC, et al. *N Engl J Med*. 2024;391(16):1489-1498. 2. Spira AI, et al. Presented at: 2023 North America Conference on Lung Cancer (NACLC); December 1–3, 2023; Chicago, IL, USA.

First Onset of Key AEs for 1L Amivantamab + Lazertinib

MARIPOSA
Ami + Laz in 1L
EGFR+ NSCLC

Median follow-up of 37.8 months



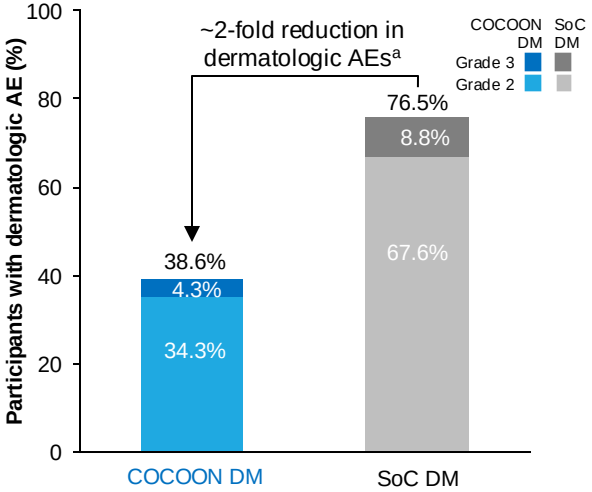
Most first onset AEs occur early (0–4 months), with longer-term follow-up showing no new safety signals and indicating that long-term treatment is feasible

[a]VTE is a grouped term, which included pulmonary embolism, deep vein thrombosis, limb venous thrombosis, venous thrombosis, thrombosis, superficial vein thrombosis, thrombophlebitis, embolism, venous embolism, jugular vein thrombosis, sigmoid sinus thrombosis, axillary vein thrombosis, pulmonary infarction, vena cava thrombosis, central venous catheterization, portal vein thrombosis, post thrombotic syndrome, pulmonary thrombosis, superior sagittal sinus thrombosis, transverse sinus thrombosis, pelvic venous thrombosis, and superior vena cava syndrome.

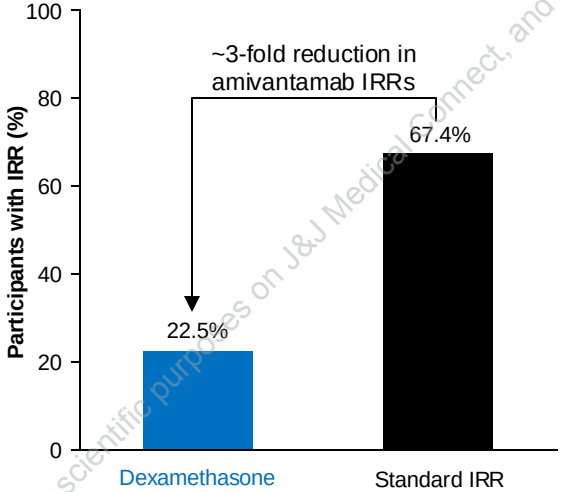
Early Onset AEs can be Significantly Reduced with Prophylactic Approaches

MARIPOSA
Ami + Laz in 1L
EGFR+ NSCLC

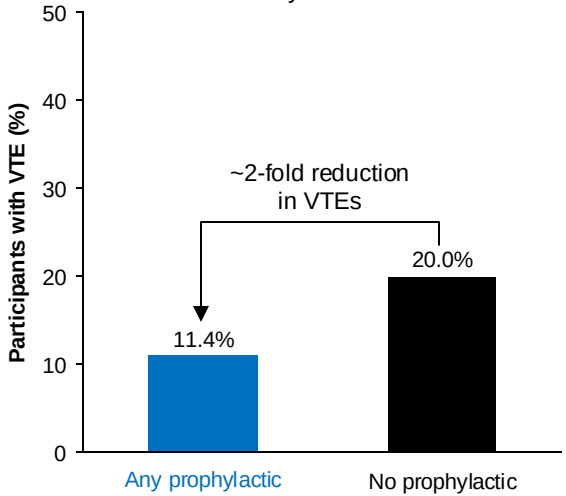
COCOON DM regimen substantially reduced grade ≥2 dermatologic AEs[1]



SKIPPirr regimen substantially reduced IRRs[2]



Prophylactic anticoagulation substantially reduced VTEs[3]



COCOON

Data from COCOON will be presented on Thursday, 27 March 2025 at 16:50–16:55 CET

Early onset AEs can be reduced using simple and accessible preventative approaches

[a]OR: 0.19 (95% CI, 0.09–0.40); *P*<0.0001.

1. Girard N, et al. To be presented at: The European Lung Cancer Congress (ELCC), March 26–29, 2025, Paris, France. 2. Spira AI, et al. *J Thorac Oncol*. 2025:S1556-0864(25)00051-6. 3. Scott SC, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA.

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Conclusions

- 1L amivantamab + lazertinib led to a statistically significant and clinically meaningful reduction in mortality vs osimertinib (HR, **0.75**; *P*<0.005) in participants with previously untreated *EGFR*-mutant advanced NSCLC
  - A **>12-month median OS benefit** is projected for amivantamab + lazertinib versus osimertinib[a]
  - **60% of participants were alive at 3 years in the amivantamab + lazertinib arm** vs 51% for osimertinib; benefit continued at 42-months with survival rates of 56% and 44%, respectively
- **Twice as many** participants receiving amivantamab + lazertinib were **intracranially progression-free** at 3 years (36% vs 18%) with a **longer intracranial DoR** vs osimertinib (35.7 vs 29.6 months)[b]
- Amivantamab + lazertinib delayed the time to a participant experiencing symptoms from their lung cancer by a median of >14 months (TTSP; *P*<0.001)
- AEs with 1L amivantamab + lazertinib occurred early; prophylactic interventions have now been shown to substantially **reduce the incidence of these key AEs** (dermatologic AEs, IRRs, and VTE)

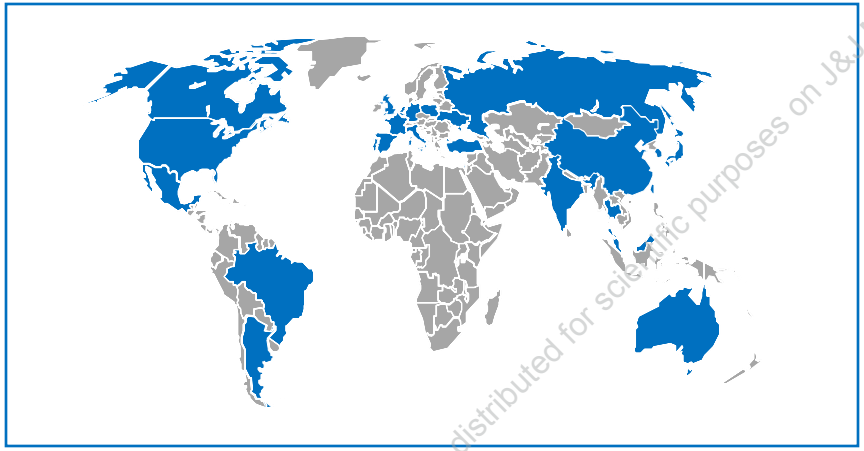
Patients live longer with 1L amivantamab + lazertinib, with MARIPOSA demonstrating practice-changing superior OS versus osimertinib and potentially extending median survival beyond 4 years

[a]Based on an exponential distribution assumption of OS in both arms, the improvement in median OS is projected to exceed 1 year. [b]Among participants with a history of brain metastases.

Acknowledgments

- Participants who were enrolled in the study and their families and caregivers
- Physicians and nurses who cared for participants and staff members who supported this clinical trial
- Staff members at the study sites and involved in data collection/analyses
- Medical writing assistance was provided by Lumanity Communications Inc. and funded by Johnson & Johnson

A total of 1074 participants from 28 countries randomized in the MARIPOSA study



Preventing AEs with Amivantamab + Lazertinib

Begin Amivantamab + Lazertinib

IRR Prophylactic Regimen (SKIPPirr)[1]	VTE Prophylactic Regimen (PALOMA-2, PALOMA-3)[2,3]
2 Days to 1 hour before start Oral 8-mg dexamethasone BID 2 days and 1 day prior and 8-mg 1 hour before first infusion[a]	**First 4 months** Oral anticoagulants as per NCCN or local guidelines

Dermatologic Prophylactic Regimen (COCOON)[b]

Antibiotic prophylaxis	**Weeks 1–12** 100-mg BID doxycycline or minocycline	**Weeks 13+** 1% Topical clindamycin lotion on the scalp daily
Nail cleaning agent	**Weeks 1+** 4% Chlorhexidine on the fingernails and toenails daily for 12 months	
Long-acting skin hydration	**Weeks 1+** Ceramide-based moisturizer at least daily for 12 months[c]	

[a]Includes standard premedication (antihistamines, antipyretics, and glucocorticoids). [b]Prophylactic antibiotics: oral doxycycline or minocycline 100 mg BID; topical clindamycin lotion 1% on scalp daily before bedtime. Paronychia prophylaxis: chlorhexidine 4% on the fingernails and toenails daily. Skin moisturization: La Roche Posay Lipikar AP+M moisturizer on the body and face at least daily. [c]La Roche Posay Lipikar AP+M moisturizer was used in COCOON.

BID, twice daily; IRR, infusion-related reaction; VTE, venous thromboembolism.

1. Spira AI, et al. *J Thorac Oncol*. 2025:S1556-0864(25)00051-6. 2. Scott SC, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA.
3. Leighl NB, et al. *J Clin Oncol*. 2024 Oct 20;42(30):3593-3605.