BARCELONA 2024 ESMO congress

MARIPOSA-2
Ami-chemo in 2L+ *EGFR*+ NSCLC

Amivantamab Plus Chemotherapy vs Chemotherapy in *EGFR*-mutated, Advanced Non-small Cell Lung Cancer After Disease Progression on Osimertinib

2nd Interim Overall Survival From MARIPOSA-2

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DECLARATION OF INTERESTS

Sanjay Popat

Participation in advisory boards: Boehringer Ingelheim, Novartis, Amgen, Janssen, Daiichi Sankyo, AstraZeneca, Bayer, Bristol Myers Squibb, Blueprint Medicines, Merck Serono, Guardant Health, BeiGene, Takeda, Lilly, Roche, Turning Point Therapeutics, GSK, Merck Sharp & Dohme, Pfizer, Sanofi, and EQRx

Invited speaker for: Medscape and VJOncology

Other relationships with: Elsevier, Amgen, Merck Sharpe & Dohme, and Blueprint Medicines

Coordinating/local PI for: ARIAD Pharmaceuticals, Boehringer Ingelheim, Celgene, Takeda, Turning Point Therapeutics, Roche, Janssen, Bristol Myers Squibb, Lilly, AstraZeneca, Roche, GSK, and Trizell

Research grants from Guardant Health

Leadership role for: British Thoracic Oncology Group and European Thoracic Oncology Platform

Advisory role for: ALK Positive UK, International Association for the Study of Lung Cancer, Lung Cancer Europe, and Ruth Strauss Foundation

Officer for the European Society of Medical Oncology

Member of the Board of Directors for the Mesothelioma Applied Research Foundation

Background

- Progression on or after TKI monotherapy is nearly inevitable, with resistance mechanisms that can be diverse and polyclonal[1–3]
- At a median follow-up of 8.7 months, MARIPOSA-2 met its primary endpoint, where **amivantamab-chemotherapy** significantly improved PFS vs chemotherapy in *EGFR*-mutant advanced NSCLC after disease progression on osimertinib (HR, 0.48; 95% CI, 0.36–0.64; *P*<0.001), as presented at ESMO 2023[4]
    - Additionally, amivantamab-chemotherapy vs chemotherapy demonstrated a favorable trend for OS (HR, 0.77; 95% CI, 0.49–1.21) at the first interim OS analysis[4]
- Amivantamab-chemotherapy is currently EMA approved and pending FDA approval for the treatment of patients with *EGFR*-mutant advanced NSCLC after disease progression on an EGFR TKI[5,6]

Here we report the prespecified second interim OS analysis at a median follow-up of 18.1 months for patients receiving amivantamab-chemotherapy vs chemotherapy in MARIPOSA-2

CI, confidence interval; EGFR, epidermal growth factor receptor; ESMO, European Society for Medical Oncology; HR, hazard ratio; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

1. Leonetti A, et al. *Br J Cancer* 2019;121:725-37. 2. Yu HA, et al. *J Clin Oncol* 2023;41:Suppl:9074. 3. Ramalingam SS, et al. *Ann Oncol* 2018;Suppl 8:VIII740-VIII740. 4. Passaro A, et al. *Ann Oncol*. 2024;35(1):77-90. 5. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024. 6. Johnson & Johnson Press Release. https://www.jnj.com/media-center/press-releases/european-commission-approves-rybrevant-amivantamab-in-combination-with-chemotherapy-for-the-treatment-of-adult-patients-with-advanced-egfr-mutated-non-small-cell-lung-cancer-after-failure-of-prior-therapy. Accessed: August 2024.

MARIPOSA-2 Study Design

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R
- *Progressed on or after osimertinib monotherapy (as most recent line)*
- ECOG PS 0 or 1

2:2:1 Randomization[a] (N=657)

- Amivantamab-Lazertinib-Chemotherapy[b] (n=263)
- Chemotherapy (n=263)
- Amivantamab-Chemotherapy (n=131)

Focus of this presentation

Secondary/Exploratory Efficacy Endpoints Reported:

- Overall survival (OS)
- Time to symptomatic progression (TTSP)
- Time to treatment discontinuation (TTD)
- Time to subsequent therapy (TTST)
- PFS after first subsequent therapy (PFS2)

- The second interim analysis of OS was prespecified for when ~75% of the planned OS events were observed
- The significance level at the second interim analysis for OS was determined based on the O'Brien-Fleming alpha spending approach (2-sided alpha: 0.0142) as implemented by the Lan-DeMets method

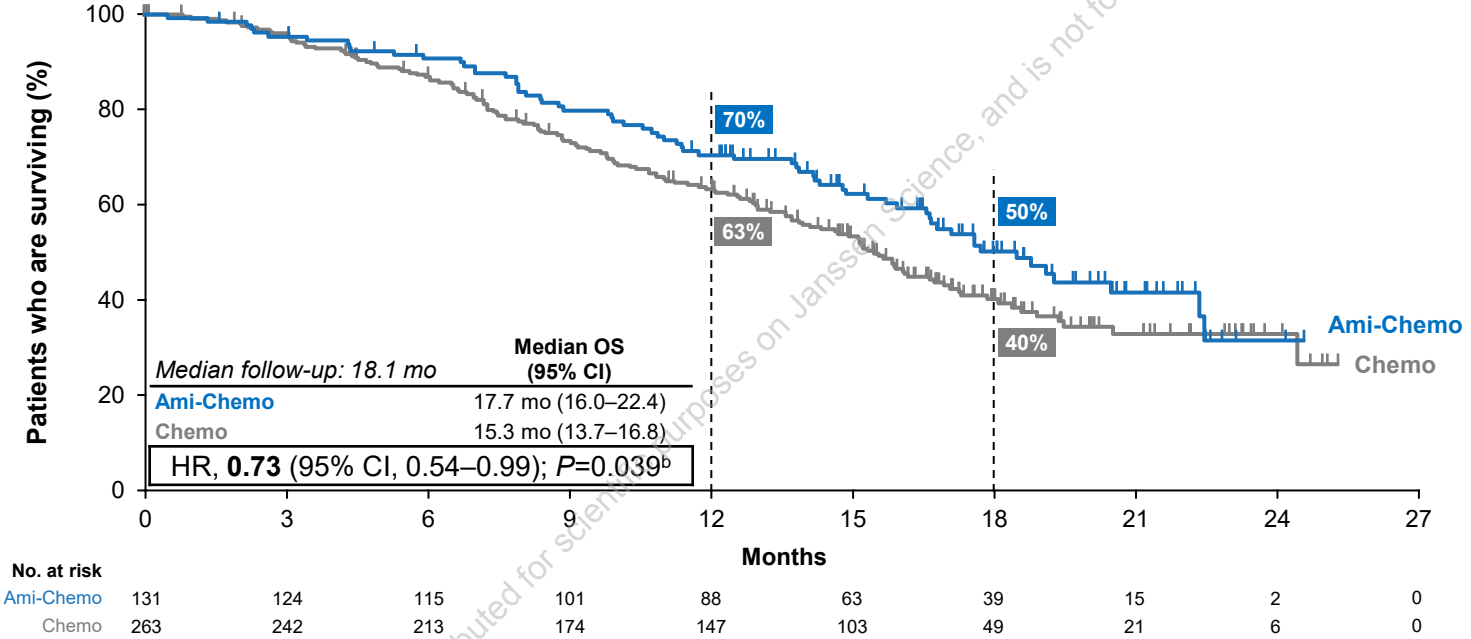
MARIPOSA-2 (ClinicalTrials.gov Identifier: NCT04988295); clinical cut-off: 26-Apr-2024.

[a]Analyses were further stratified based on osimertinib line of therapy (first-line vs second-line), history of brain metastases, and race (Asian vs non-Asian). [b]Dosing schedule of the amivantamab-lazertinib-chemotherapy arm was modified during the study. Results will be reported after additional follow-up.

ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; NSCLC, non-small cell lung cancer; OS, overall survival.

Overall Survival

Amivantamab-chemotherapy continues to demonstrate a clear and improving OS trend vs chemotherapy[a]



18-month landmark for OS was 50% for amivantamab-chemotherapy vs 40% for chemotherapy

[a]OS benefit of amivantamab-chemotherapy vs chemotherapy was generally consistent among pre-defined subgroups. [b]*P*-value is from a log-rank test stratified by osimertinib line of therapy (first-line vs second-line), history of brain metastases (yes or no), and Asian race (yes vs no). OS was evaluated at a 2-sided alpha of 0.0142.

Ami, amivantamab; chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; OS, overall survival.

Overall Survival

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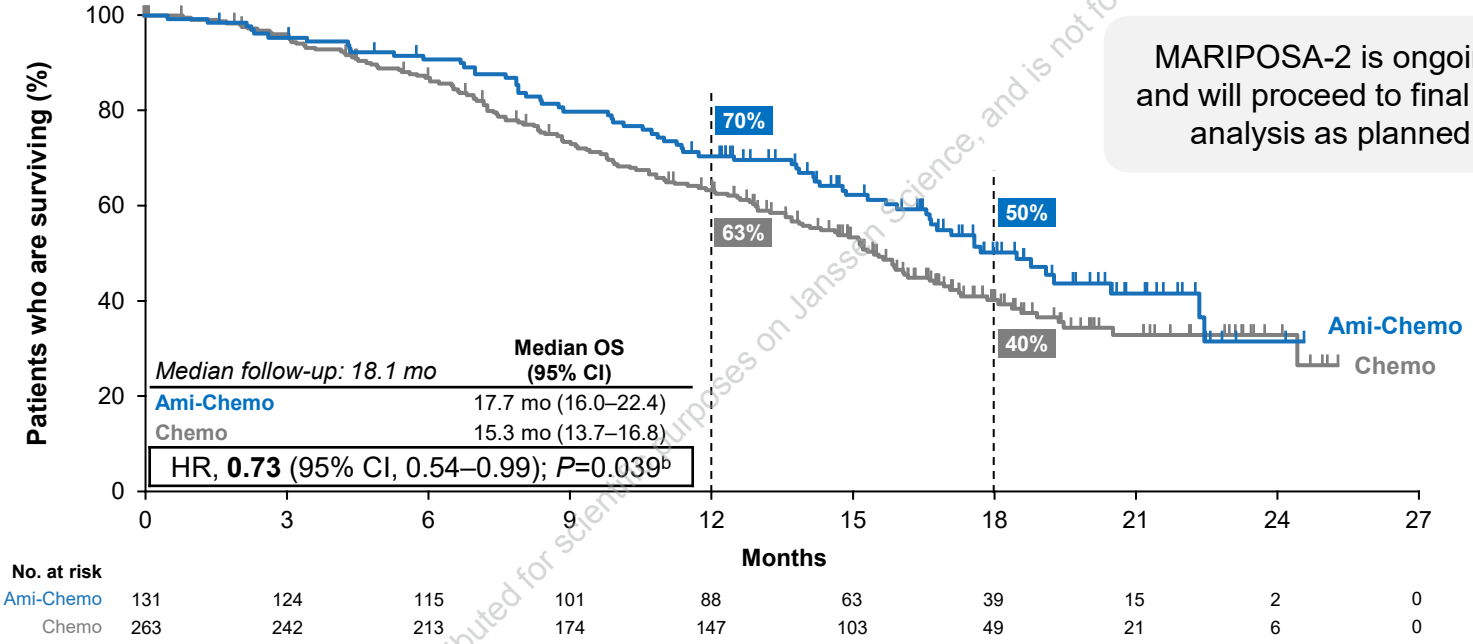

MARIPOSA-2 is ongoing and will proceed to final OS analysis as planned

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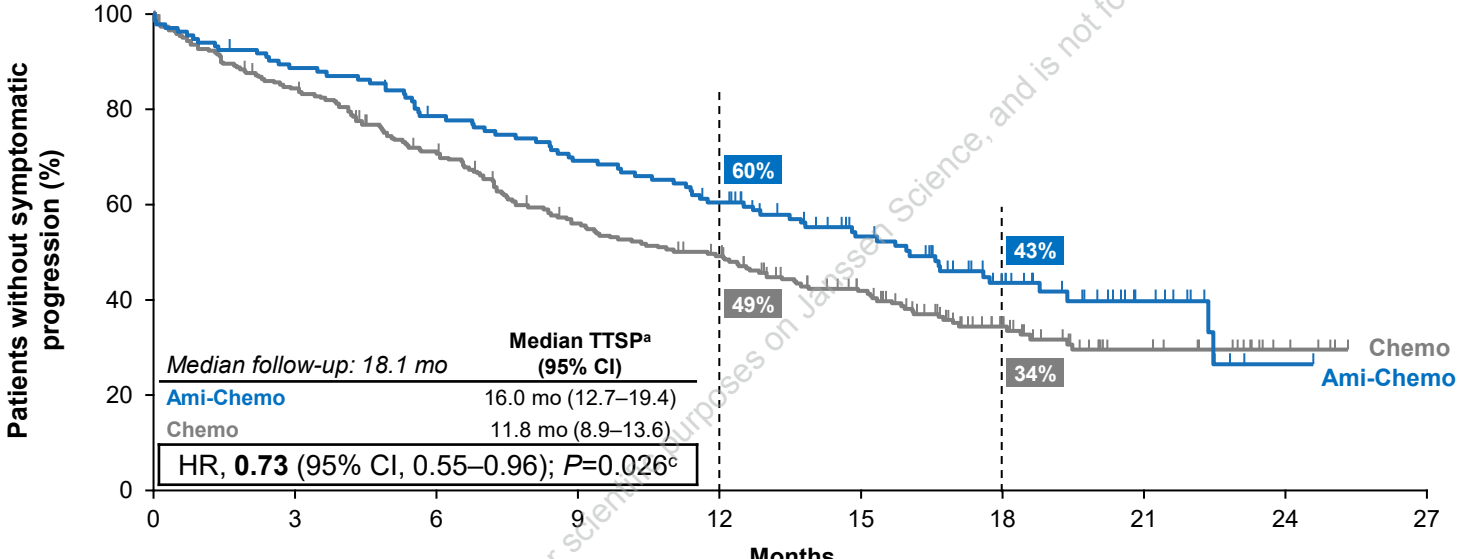
Time to Symptomatic Progression[a]

MARIPOSA-2
Ami-Chemo in 2L+ *EGFR*+ NSCLC

TTSP was significantly improved with amivantamab-chemotherapy vs chemotherapy[b]



No. at risk										
Ami-Chemo	131	115	100	88	76	54	33	12	1	0
Chemo	263	212	173	132	113	81	42	18	5	0

27% reduction in the risk of symptomatic progression with amivantamab-chemotherapy vs chemotherapy

[a]Time from randomization to onset of new symptoms or symptom worsening that was considered by the investigator to be related to lung cancer and required either a change in anticancer therapy and/or clinical intervention, or death, whichever occurred first. [b]In the primary analysis, ami-chemo numerically improved TTSP vs chemo (HR, 0.74; 95% CI, 0.51–1.07; *P*=0.10).[1] [c]*P*-value is from a log-rank test stratified by osimertinib line of therapy (first-line vs second-line), history of brain metastases (yes or no), and Asian race (yes vs no). Ami, amivantamab; chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; TTSP, time to symptomatic progression. 1. Tomasini P, et al. Presented at: European Lung Cancer Congress (ELCC) 20–23 March 2024; Prague, Czech Republic.

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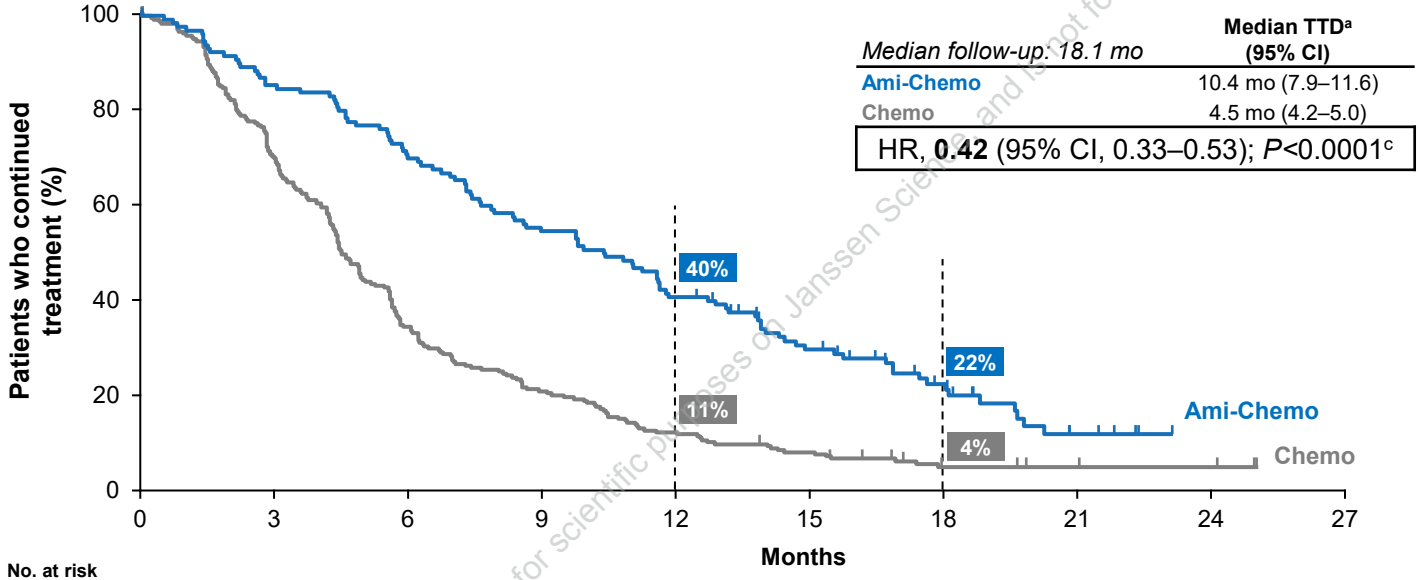
Time to Treatment Discontinuation[a]

TTD was significantly prolonged with amivantamab-chemotherapy vs chemotherapy[b]



Median follow-up: 18.1 mo	Median TTD[a] (95% CI)
Ami-Chemo	10.4 mo (7.9–11.6)
Chemo	4.5 mo (4.2–5.0)

HR, **0.42** (95% CI, 0.33–0.53); *P*<0.0001[c]

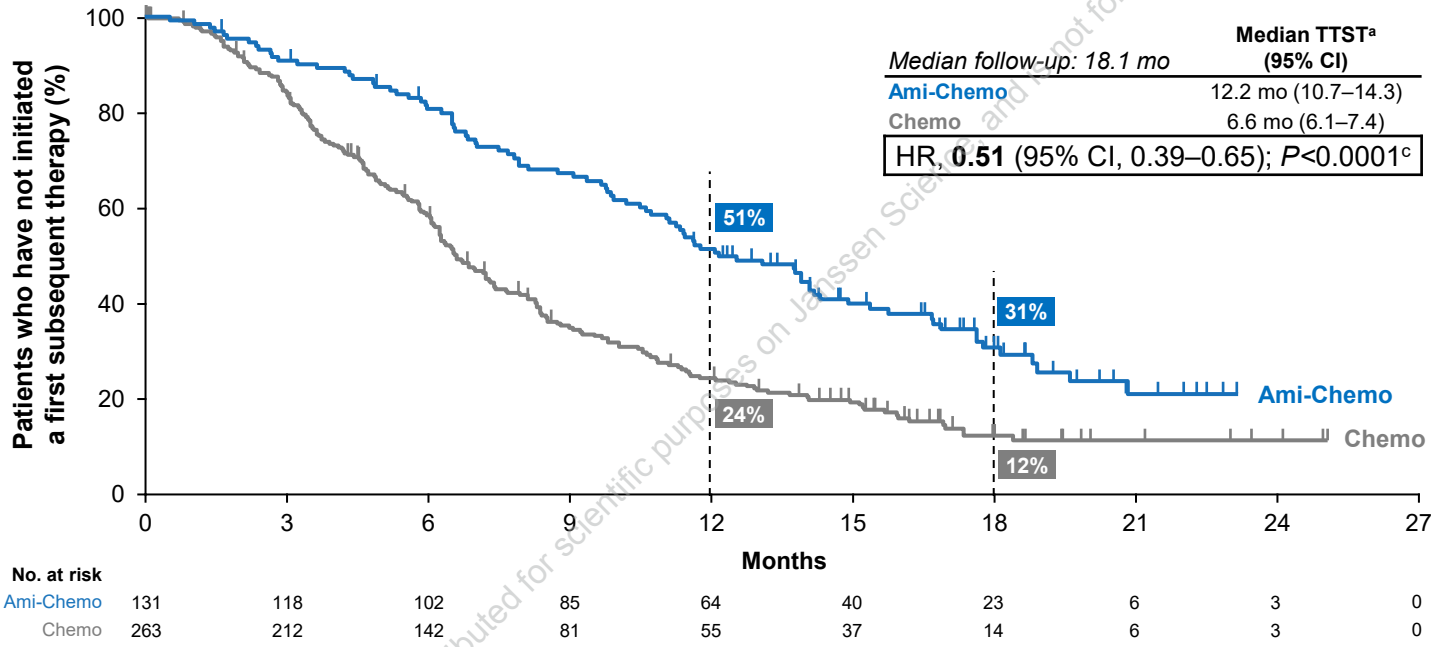
For amivantamab-chemotherapy, ~5-fold more patients remained on treatment at 18 months vs chemotherapy

[a]Time from randomization to discontinuation of all study treatments for any reason, including disease progression, treatment toxicity, or death. [b]In the primary analysis, ami-chemo significantly prolonged TTD vs chemo (HR, 0.37; 95% CI, 0.28–0.50; *P*<0.0001).[1] [c]*P*-value is from a log-rank test stratified by osimertinib line of therapy (first-line vs second-line), history of brain metastases (yes or no), and Asian race (yes vs no). Ami, amivantamab; chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; PD, progressive disease; TTD, time to treatment discontinuation.

1. Gentzler RD, et al. Presented at: European Lung Cancer Congress (ELCC) 20–23 March 2024; Prague, Czech Republic.

Time to Subsequent Therapy[a]

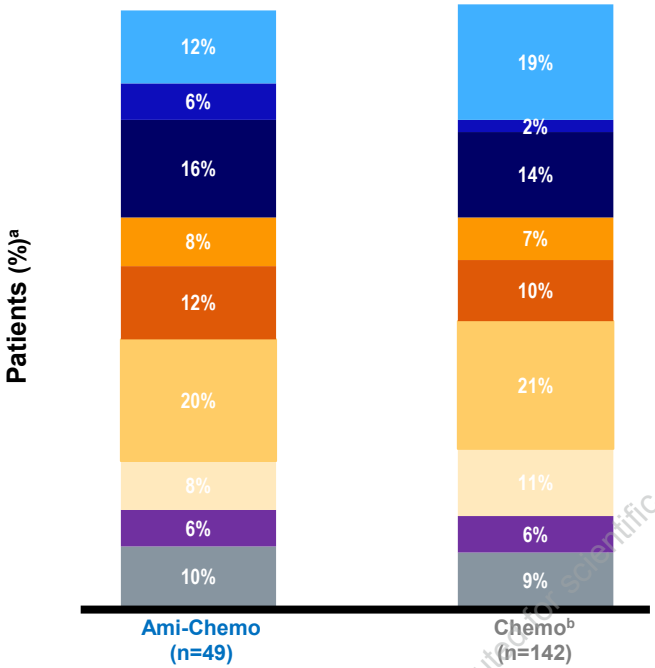
TTST was significantly prolonged with amivantamab-chemotherapy vs chemotherapy[b]



Median TTST was ~2-fold longer with amivantamab-chemotherapy vs chemotherapy (12.2 vs 6.6 mo)

[a]Time from the date of randomization to the start date of the subsequent anticancer therapy following study treatment discontinuation, or death, whichever occurred first. [b]In the primary analysis, ami-chemo significantly prolonged TTST vs chemo (HR, 0.42; 95% CI, 0.30–0.59; *P*<0.0001).[1] [c]*P*-value is from a log-rank test stratified by osimertinib line of therapy (first-line vs second-line), history of brain metastases (yes or no), and Asian race (yes vs no). Ami, amivantamab; chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; TTST, time to subsequent therapy. 1. Gentzler RD, et al. Presented at: European Lung Cancer Congress (ELCC) 20–23 March 2024; Prague, Czech Republic.

First Subsequent Therapy



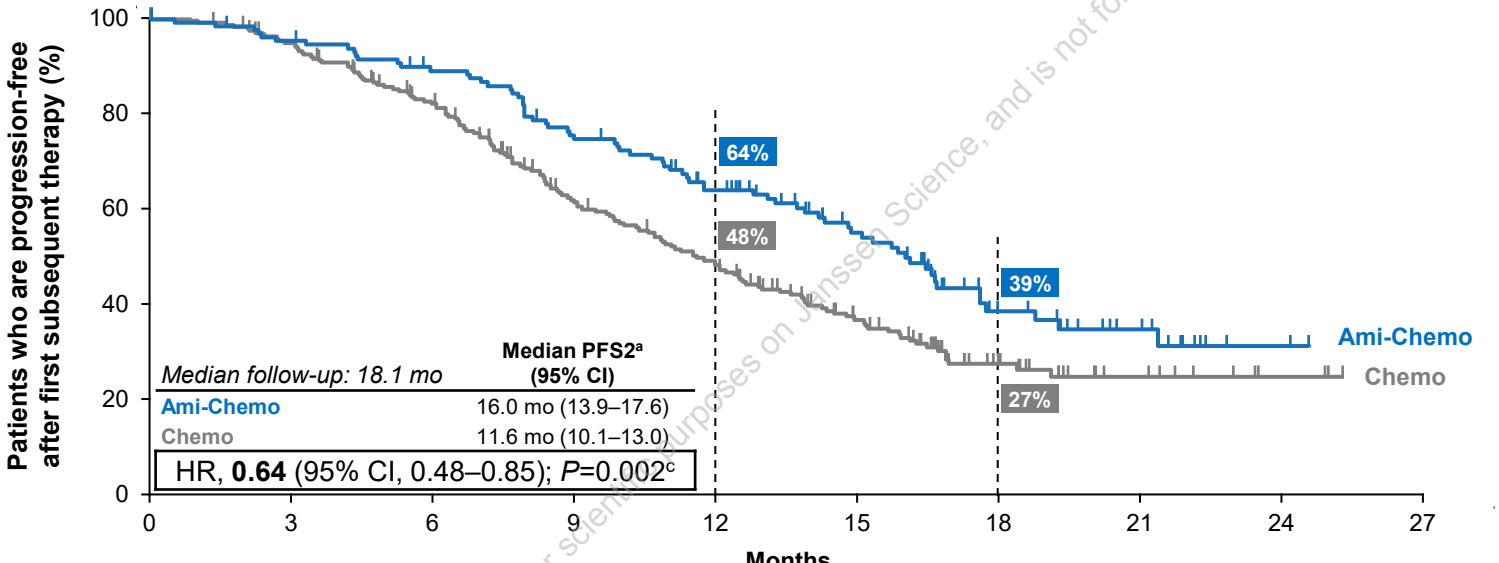
- Fewer patients in the ami-chemo arm had disease progression (**68% [88/130]** vs **83% [202/243]**) than chemo
- Majority of patients in both arms went on to receive a subsequent therapy
- No single therapy class was identified as the most prominent subsequent therapy

Patients in the third-line setting are often re-exposed to previously used therapies, highlighting the importance of maximizing second-line treatment duration

[a]Percentages may not sum to 100 due to rounding. [b]Three patients in the chemo arm received amivantamab as the first subsequent therapy (2 as monotherapy and 1 in combination with carboplatin/pemetrexed). [c]The other category included VEGFi alone, bispecific monoclonal antibodies, antibody-drug conjugate–based regimens, ALK TKIs, herbal, and other investigational agents. Ami, amivantamab; chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; IO, immuno-oncology; TKI, tyrosine kinase inhibitor; TTST, time to subsequent therapy; VEGFi, vascular endothelial growth factor inhibitor; VEGFRi, vascular endothelial growth factor receptor inhibitor.

PFS After First Subsequent Therapy[a]

PFS2 was significantly prolonged with amivantamab-chemotherapy vs chemotherapy[b]



18-month landmark PFS2 was 39% for amivantamab-chemotherapy vs 27% for chemotherapy

[a]Time from randomization until the date of second objective disease progression, after initiation of subsequent anticancer therapy, based on investigator assessment (after that used for PFS) or death, whichever occurred first. [b]In the primary analysis, ami-chemo significantly prolonged PFS2 vs chemo (HR, 0.60; 95% CI, 0.40–0.92; *P*=0.017).[1] [c]*P*-value is from a log-rank test stratified by osimertinib line of therapy (first-line vs second-line), history of brain metastases (yes or no), and Asian race (yes vs no). Ami, amivantamab; chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; PFS2, progression-free survival after first subsequent therapy. 1. Gentzler RD, et al. Presented at: European Lung Cancer Congress (ELCC) 20–23 March 2024; Prague, Czech Republic.

Conclusions

- At the second interim analysis (median follow-up: 18.1 months), data continued to favor amivantamab-chemotherapy over chemotherapy, with a promising OS trend in the post-osimertinib setting (median, 17.7 vs 15.3 mo; HR, 0.73; *P*=0.039)
  - MARIPOSA-2 is ongoing and will proceed to the final OS analysis as planned
- Post-progression endpoints showed significant and sustained improvement for amivantamab-chemotherapy vs chemotherapy:
  - Time to symptomatic progression (HR, 0.73; *P*=0.026)
  - Time to treatment discontinuation (HR, 0.42; *P*<0.0001)
  - Time to subsequent therapy (HR, 0.51; *P*<0.0001)
  - Progression-free survival after first subsequent therapy (HR, 0.64; *P*=0.002)
- Amivantamab's multi-targeted MoA and immune cell–directing activity combined with chemotherapy's antitumor effects is likely contributing to the observed durability

Longer MARIPOSA-2 follow-up results confirm the superior outcomes of amivantamab-chemotherapy vs chemotherapy in *EGFR*-mutant advanced NSCLC after disease progression on osimertinib

EGFR, epidermal growth factor receptor; HR, hazard ratio; MoA, mechanism of action; NSCLC, non-small cell lung cancer; OS, overall survival.

Also at ESMO 2024

MARIPOSA

Mechanisms of acquired resistance to first-line amivantamab + lazertinib in *EGFR*-mutant advanced NSCLC

Saturday, Sep 14 9:20-9:30am
(LBA55; Besse)

RIGAMI-1

Amivantamab + FOLFOX/FOLFIRI in metastatic colorectal cancer

Saturday, Sep 14 3:45-3:50pm
(513MO; Pietrantonio)

SKIPPirr

Preventing infusion-related reactions with intravenous amivantamab: Updated results

Saturday, Sep 14 12:00-1:00pm
(1269P; Paz-Ares)

Acknowledgements

- Patients who participated in the study and their families and caregivers
- Physicians and nurses who cared for patients 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 Janssen Global Services, LLC

A total of 776 patients from 29 countries were randomized in the MARIPOSA-2 study