elcc European Lung Cancer Congress 2024

# Amivantamab Plus Chemotherapy vs Chemotherapy in *EGFR*–mutant Advanced NSCLC After Progression on Osimertinib: A Post-progression Analysis of MARIPOSA-2

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# DECLARATION OF INTERESTS



## Ryan D. Gentzler

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# Phase 3 MARIPOSA-2 Study (NCT04988295)

- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity[1-3]
- Lazertinib is a highly selective, CNS-penetrant, 3rd-generation EGFR TKI with efficacy in both activating *EGFR* mutations and T790M[4-6]

**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)

*Dosing schedule of the amivantamab-lazertinib-chemotherapy arm was modified during the study. Results will be reported after additional follow-up.*

- **Amivantamab-Lazertinib-Chemotherapy (n=263)**
- **Chemotherapy (n=263)**
- **Amivantamab-Chemotherapy (n=131)**

***Focus of this presentation***

**Secondary Endpoints[b]:**

- Objective response rate (ORR)
- Duration of response (DoR)
- Overall survival (OS)
- Intracranial PFS
- Safety
- Time to symptomatic progression (TTSP)
- Time to subsequent therapy (TTST)
- PFS after first subsequent therapy (PFS2)

**Exploratory Endpoint[b]:**

- Time to treatment discontinuation (TTD)

[a]Analyses were further stratified based on osimertinib line of therapy, history of brain metastases, and race (Asian vs non-Asian).
[b]A graphical testing strategy was used to control for Type 1 errors. PFS, ORR, and then OS were included in the hierarchical testing. *P* values are nominal for all other secondary and exploratory endpoints.

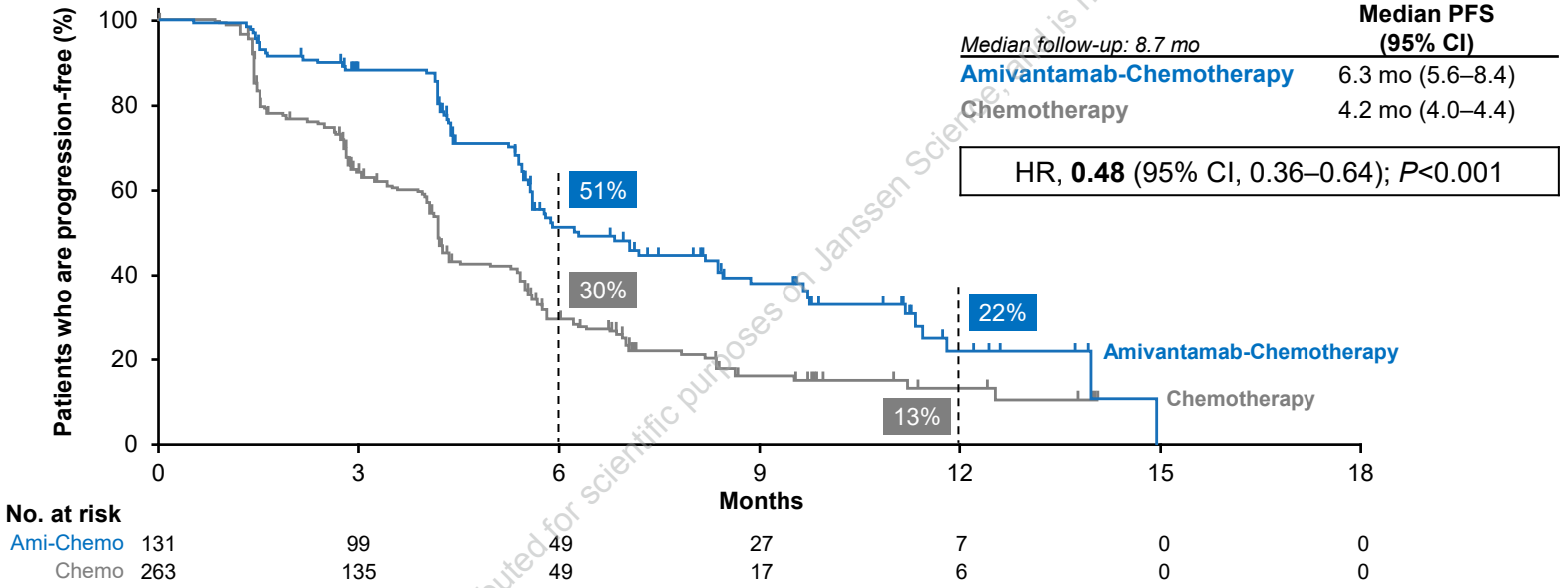
CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

1. Moores SL, et al. *Cancer Res*. 2016;76(13):3942-3953. 2. Vijayaraghavan S, et al. *Mol Cancer Ther*. 2020;19(10):2044-2056. 3. Yun J, et al. *Cancer Discov*. 2020;10(8):1194-1209. 4. Ahn M-J, et al. *Lancet Oncol*. 2019;20(12):1681-1690. 5. Cho BC, et al. *J Thorac Oncol*. 2022;17(4):558-567. 6. Soo RA, et al. *J Thorac Oncol*. 2023;18(12):1756-1766.

MARIPOSA-2

# Primary Endpoint: Progression-free Survival by BICR

*At a median follow-up of 8.7 months, amivantamab-chemotherapy reduced the risk of progression or death by 52%*




| *Median follow-up: 8.7 mo* | Median PFS (95% CI) |
|---|---|
| Amivantamab-Chemotherapy | 6.3 mo (5.6–8.4) |
| Chemotherapy | 4.2 mo (4.0–4.4) |

HR, **0.48** (95% CI, 0.36–0.64); *P*<0.001

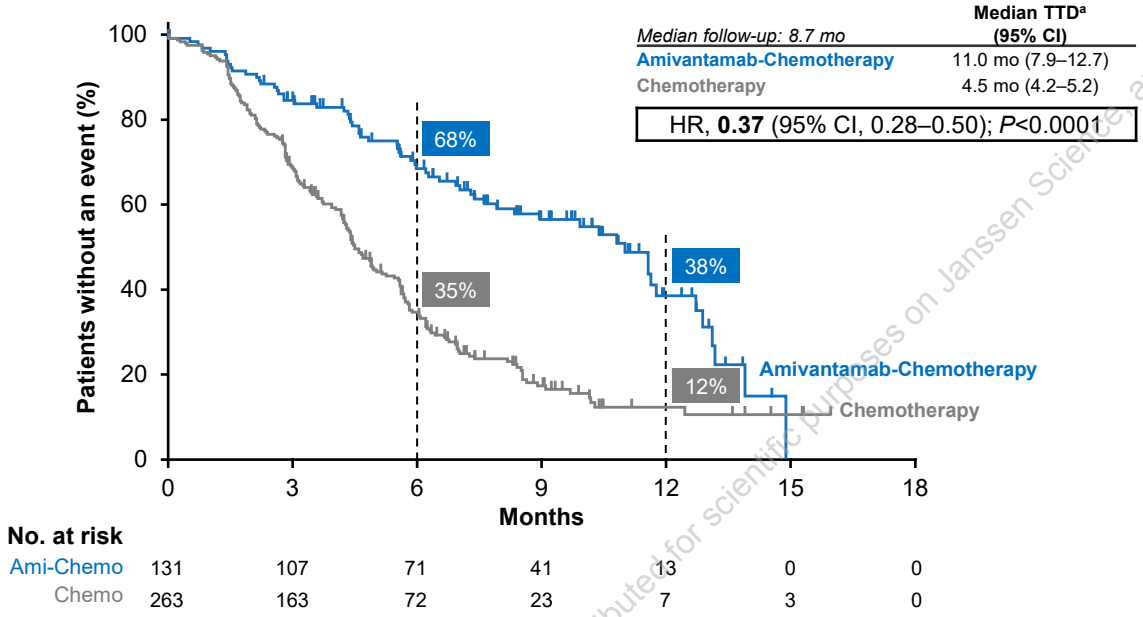
**Consistent PFS benefit by investigator: HR, 0.41 (8.2 vs 4.2 mo; *P*<0.001)**

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; mo, months; PFS, progression-free survival.

1. Passaro A, et al. *Ann Oncol*. 2023;S0923-7534(23)04281-3.

# Time to Treatment Discontinuation

*Median TTD was longer with amivantamab-chemotherapy compared to chemotherapy*



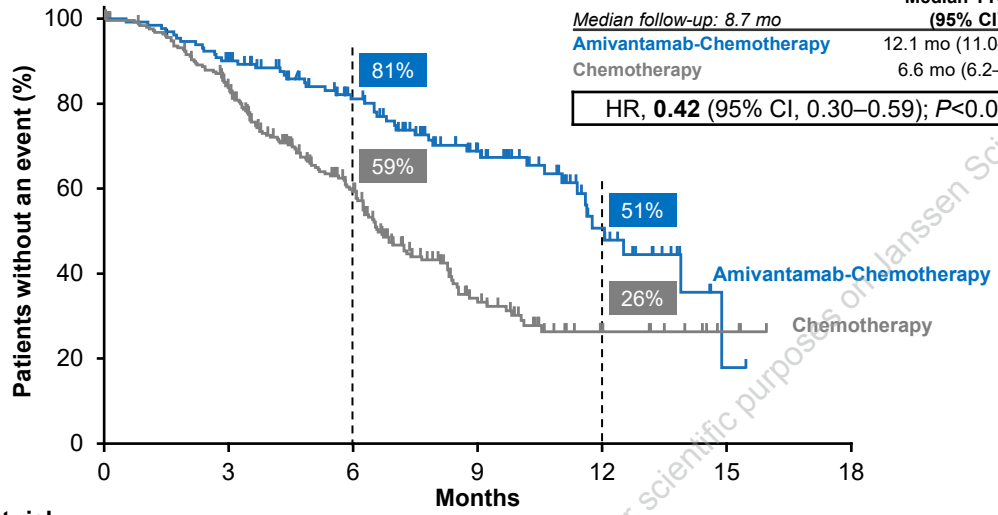

- In the amivantamab-chemotherapy arm, **42% (55/130)** of patients versus **71% (173/243)** of patients in the chemotherapy arm had progressive disease
- Among those with disease progression, **35% (19/55)** and **16% (28/173)** of patients, respectively, continued treatment beyond progression
- Median duration of treatment post-progression was:
  - **18.3 weeks (95% CI, 9.0–NE)** for amivantamab-chemotherapy
  - **9.0 weeks (95% CI, 6.0–16.4)** for chemotherapy

[a]TTD was defined as the time from randomization to discontinuation of all study treatments for any reason.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; mo, months; NE, not estimable; TTD, time to treatment discontinuation.

# Time to Subsequent Therapy

*Median TTST was longer with amivantamab-chemotherapy compared to chemotherapy*




| *Median follow-up: 8.7 mo* | Median TTST[a] (95% CI) |
|---|---|
| Amivantamab-Chemotherapy | 12.1 mo (11.0–14.9) |
| Chemotherapy | 6.6 mo (6.2–8.1) |

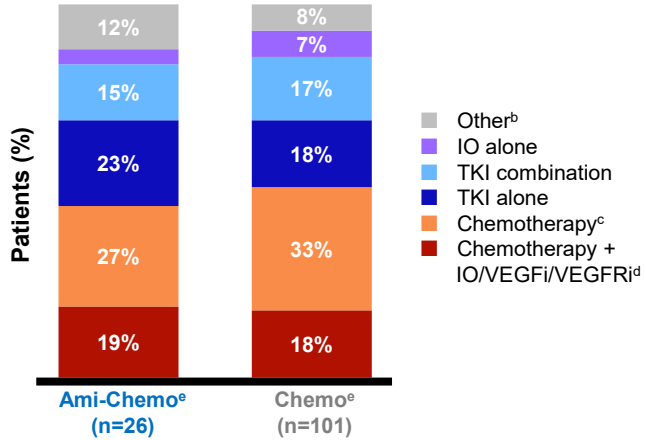
HR, **0.42** (95% CI, 0.30–0.59); *P*<0.0001

**No. at risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Ami-Chemo | 131 | 116 | 80 | 47 | 18 | 1 | 0 |
| Chemo | 263 | 200 | 112 | 36 | 11 | 3 | 0 |

## Most Common First Subsequent Therapy Classes

- In both arms, 63% of patients with disease progression and discontinuation of study treatment received a subsequent therapy
- Most common therapies were docetaxel and osimertinib

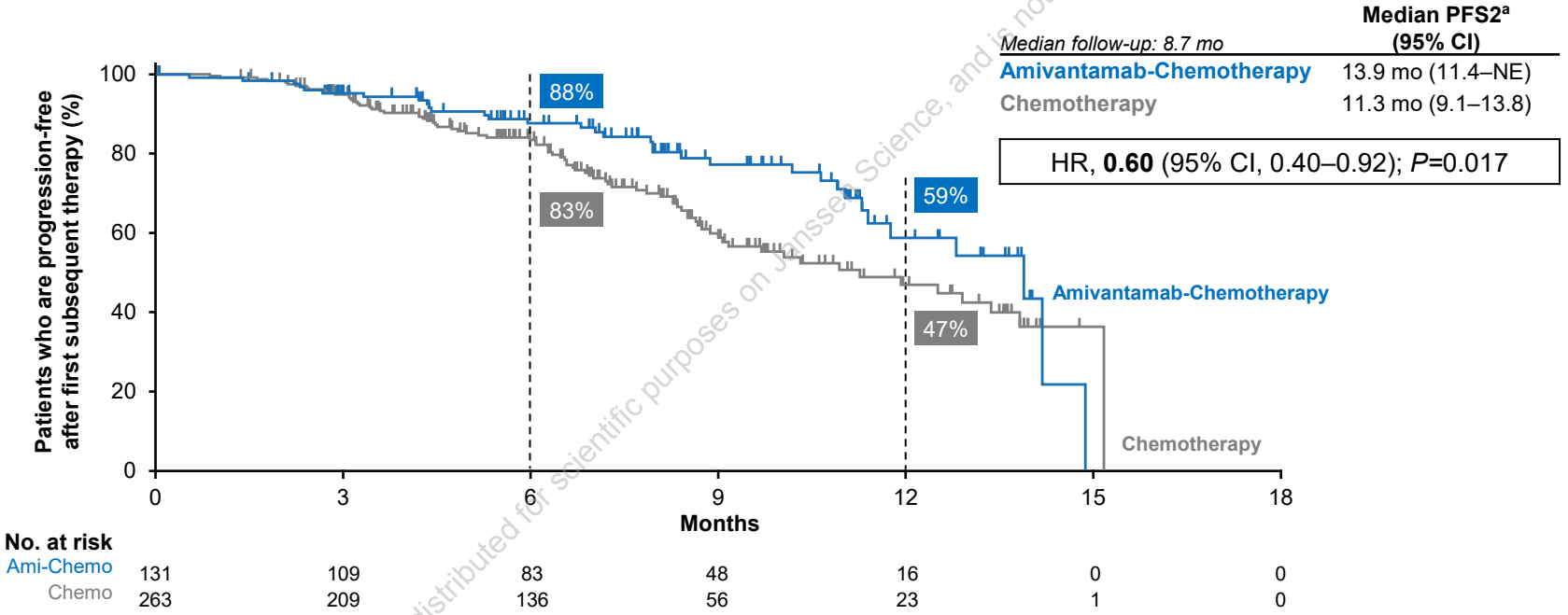



[a]TTST was defined as the time from the date of randomization to the start date of the first subsequent anticancer therapy following study treatment discontinuation, or death, whichever occurred first. [b]The other category included bispecific monoclonal antibodies, antibody-drug conjugate–based regimens, ALK TKIs, herbal, and other investigational agents. [c]In the Ami-Chemo and Chemo arms, 19% and 23% of patients received single-agent chemotherapy, respectively, and 8% and 10% of patients received doublet chemotherapy. In the Ami-Chemo and Chemo arms, the most common chemotherapy was docetaxel (12% and 15%, respectively). [d]The most common chemotherapy + IO/VEGFi/VEGFRi were bevacizumab + paclitaxel, bevacizumab + pemetrexed, docetaxel + ramucirumab, and atezolizumab + bevacizumab + carboplatin + paclitaxel (4% each) for the Ami-Chemo arm and docetaxel + ramucirumab (7%) for the Chemo arm. [e]In the Ami-Chemo and Chemo arms, the most common subsequent therapies overall were docetaxel (12% and 15%, respectively) and osimertinib (23% and 14%, respectively).

Ami-chemo, amivantamab-chemotherapy; ALK, anaplastic lymphoma kinase; Chemo, chemotherapy; EGFR, epithelial growth factor receptor; IO, immuno-oncology; TKI, tyrosine kinase inhibitor; VEGFi, vascular endothelial growth factor inhibitor; VEGFRi, vascular endothelial growth factor receptor inhibitor.

# PFS After First Subsequent Therapy (PFS2)

*Amivantamab-chemotherapy reduced the risk of second disease progression or death by 40%*

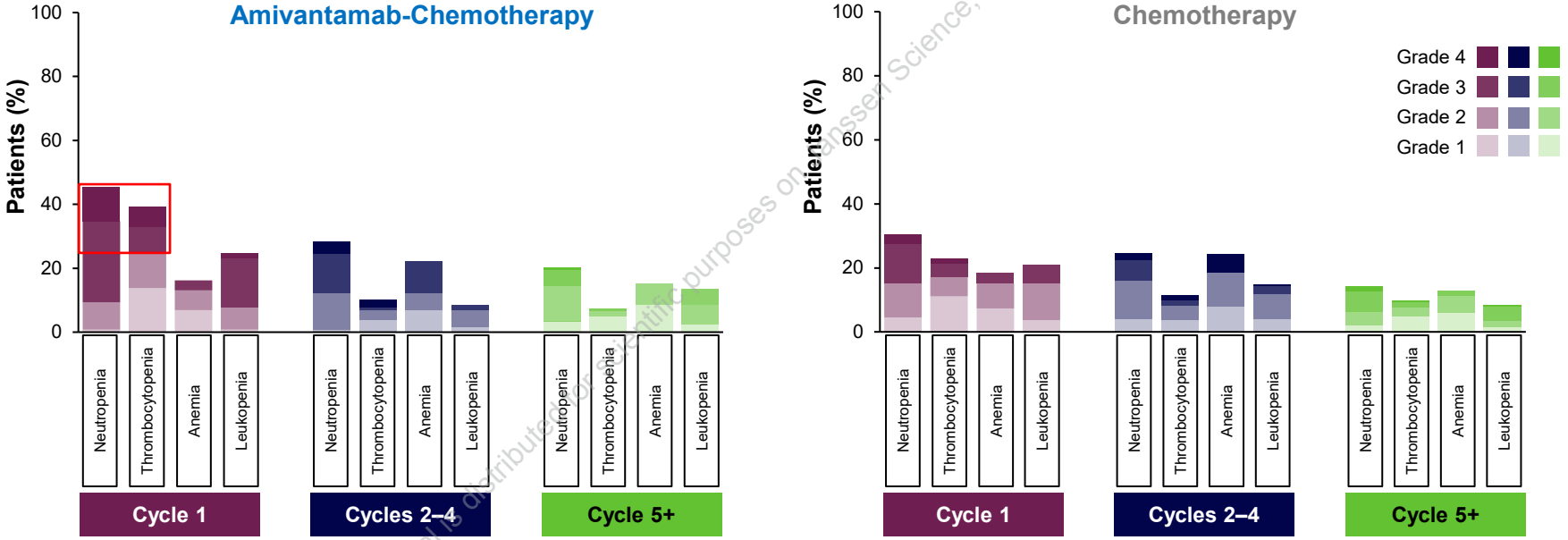



[a]PFS2 was defined as the time from randomization until the date of second objective disease progression after initiation of subsequent anticancer therapy, based on clinical progression as determined by the investigator or death, whichever occurred first.

CI, confidence interval; HR, hazard ratio; mo, months; NE, not estimable; PFS, progression-free survival.

# Hematologic AE Onset[a] and Severity Over Time

- Labs were measured weekly in Cycle 1 for both arms and less frequently for subsequent cycles
- Hematologic AEs were:
  - Highest in Cycle 1 and decreased over time
  - Similar between both arms from Cycle 2 onward




**Note**: the event experienced by the patient with the worst toxicity in each period is reported. [a]The prevalence of AEs are shown.

AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities.

# Conclusions

- Compared to chemotherapy, **amivantamab-chemotherapy** in patients with *EGFR*-mutant advanced NSCLC after disease progression on osimertinib significantly prolonged:
  - Time to treatment discontinuation (**11.0 months** vs 4.5 months; HR, 0.37; *P*<0.0001)
  - Time to subsequent therapy (**12.1 months** vs 6.6 months; HR, 0.42; *P*<0.0001)
  - Progression-free survival after first subsequent therapy (**13.9 months** vs 11.3 months; HR, 0.60; *P*=0.017)
- Subsequent therapies received were similar in both arms, with osimertinib and docetaxel being the most common
- The higher incidence and severity of hematologic AEs for amivantamab-chemotherapy was limited to Cycle 1, with profiles similar between both arms from Cycle 2 onward

**Amivantamab-chemotherapy represents the new standard of care among patients with *EGFR*-mutant advanced NSCLC after disease progression on osimertinib**



AE, adverse event; EGFR, epidermal growth factor receptor; HR, hazard ratio; NSCLC, non-small cell lung cancer.

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