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

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Conclusions

Ami-chemo significantly prolonged TTD, TTST, and PFS2 vs chemo. Ami-chemo represents the new standard of care for pts with EGFR-mutant advanced NSCLC after PD on osimertinib.

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https://www.congresshub.com/oncology/DGHO2024#product-amivantamab

Poster

Acknowledgments

- 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

Disclosures

Amanda Tufman: Consulting fees: Lilly, Boehringer Ingelheim, Pfizer, Takeda, Roche, AstraZeneca, Novartis, GSK, Merck Sharp & Dohme, Bristol-Myers Squibb, Amgen, Janssen
Payment or honoraria for lectures, presentations, speakers, bureaus, manuscript writing or educational events: Lilly, Boehringer Ingelheim, Pfizer, Takeda, Roche, AstraZeneca, Novartis, GSK, Merck Sharp & Dohme, Bristol-Myers Squibb
Participation on a Data Safety Monitoring Board or Advisory Board: AstraZeneca (COMPEL Study)
Other financial or non-financial interests: AstraZeneca

Background

- Amivantamab (ami) is an EGFR-MET bispecific antibody with immune cell-directing activity. In MARIPOSA-2 (NCT04988295), ami plus carboplatin-pemetrexed (ami-chemo) significantly prolonged progression-free survival (PFS) vs chemo in patients (pts) with EGFR-mutant advanced NSCLC after progression on osimertinib (Passaro Ann Oncol 2023). Post-progression outcomes from MARIPOSA-2 were assessed.

Methods

- 657 pts were randomized. These analyses focus on the 131 pts randomized to ami-chemo (safety: n=130) and 263 to chemo (safety: n=243). A third arm (ami-lazertinib-chemo) was modified and will be reported in the future. Post-progression endpoints were time to treatment discontinuation (TTD), time to subsequent therapy (TTST), and PFS after first subsequent therapy (PFS2).

Results

- At a median follow-up of 8.7 months (mo), 55/130 (42%) pts in the ami-chemo arm and 173/243 (71%) in the chemo arm had progressive disease (PD). Among those with PD, 19/55 (35%) in the ami-chemo arm and 28/173 (16%) in the chemo arm were treated beyond progression for >4 weeks with a median (95% CI) post-progression treatment duration of 18.3 (9.0–NE) and 9.0 (6.0–16.4) weeks, respectively.
- Compared to chemo, ami-chemo significantly prolonged TTD (median, 11.0 vs 4.5 mo for chemo; HR, 0.37 [95% CI, 0.28–0.50]; P<0.0001), TTST (median, 12.1 vs 6.6 mo for chemo; HR, 0.42 [95% CI, 0.30–0.59]; P<0.0001), and PFS2 (median, 13.9 vs 11.3 mo for chemo; HR, 0.60 [95% CI, 0.40–0.92]; P=0.017). Among pts with PD, including pts treated beyond PD, 75% (41/55) in the ami-chemo arm discontinued treatment after progression vs 93% (161/173) for chemo. 63% of pts with PD initiated subsequent systemic therapy in both arms. Most common subsequent therapies were osimertinib (ami-chemo:10%; chemo: 9%) and docetaxel (ami-chemo: 7%; chemo: 9%).

Phase 3 MARIPOSA-2 (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

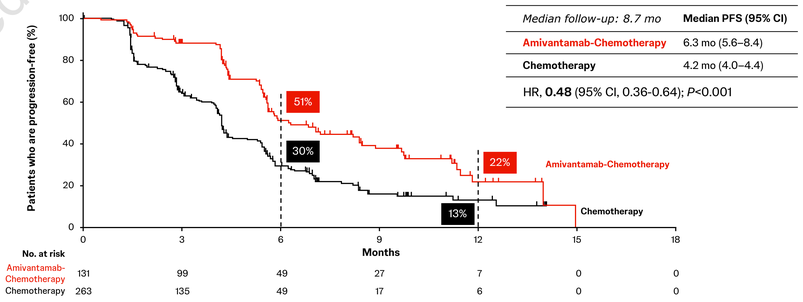
2:2:1 randomisation[a] (N=657)
- Amivantamab-Lazertinib-Chemotherapy (n=263)
- Chemotherapy (n=263)
- Amivantamab-Chemotherapy (n=131)

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)

Primary endpoint: Progression-free survival by BICR

- At 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)

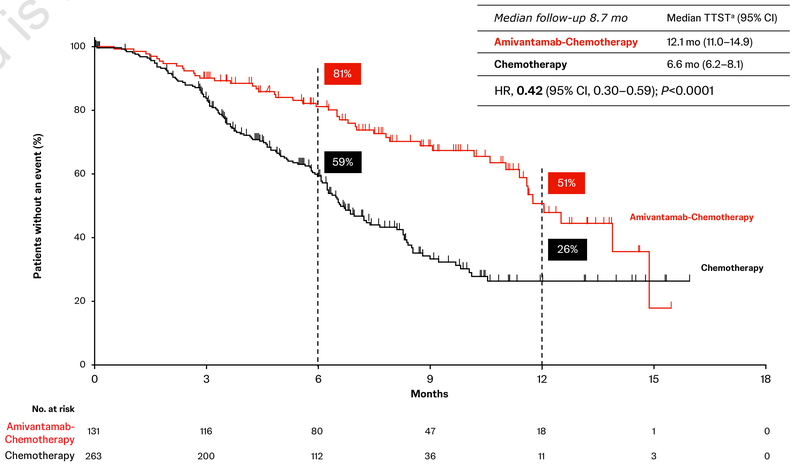
HR, **0.48** (95% CI, 0.36-0.64); *P*<0.001

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

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 subsequent therapy

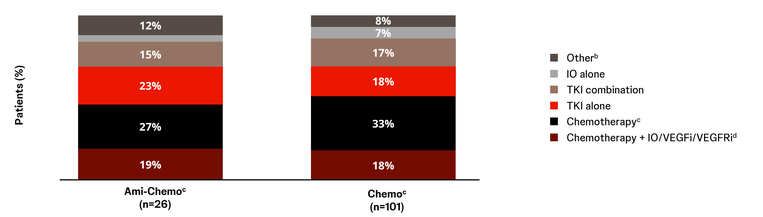
- Median TTST was longer with amivantamab-based chemotherapy compared to chemotherapy



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

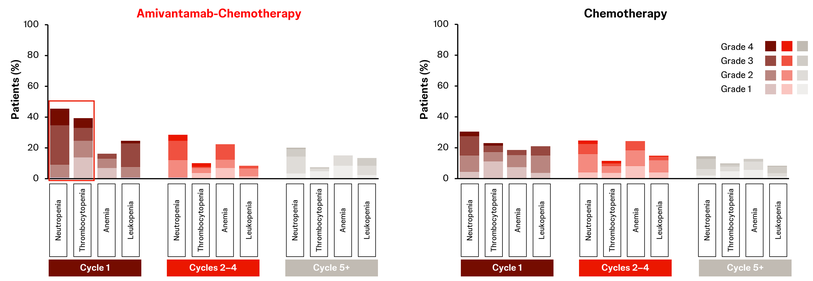
Most common first subsequent therapy classes



Among patients that discontinued study treatment and had progressive disease, 63% in both arms received a subsequent therapy

Haematologic AE onset[a] and severity were highest in Cycle 1 and decreased over time

- Haematologic AE profiles were similar between both arms from Cycle 2 onwards



Note: the event experienced by the patient with the worst toxicity in each period is reported. AEs were coded using MedDRA v25.0. In the study, labs were measured weekly in Cycle 1 for both arms. [a]The prevalence of AEs are shown. AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities.

Originally presented by R Gentzler at the European Lung Cancer Congress; March 20–23 2024; Prague, Czech Republic