Amivantamab Plus Chemotherapy vs Chemotherapy in *EGFR*-mutant Advanced NSCLC After Progression on Osimertinib: Secondary Analyses of Patient-relevant Endpoints From MARIPOSA-2

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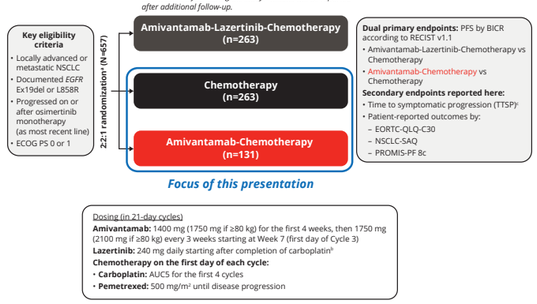
BACKGROUND

- Amivantamab is an epidermal growth factor receptor (EGFR)-MET bispecific antibody with immune cell–directing activity[1–3]
- In MARIPOSA-2 (NCT04988295), amivantamab plus carboplatin-pemetrexed (chemotherapy) significantly prolonged progression-free survival vs chemotherapy (hazard ratio [HR], 0.48; *P*<0.001) in patients with osimertinib-pretreated, *EGFR*-mutant advanced non-small cell lung cancer (NSCLC)[4]
- Here, time to symptomatic progression (TTSP) and patient-reported outcomes (PROs) of amivantamab-chemotherapy vs chemotherapy from MARIPOSA-2 were evaluated

METHODS

- MARIPOSA-2 is a global, randomized, phase 3 trial that compared amivantamab-chemotherapy and amivantamab-lazertinib-chemotherapy vs chemotherapy (**Figure 1**)
- Secondary endpoints reported here include TTSP and PROs measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30), Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ), and Patient-Reported Outcomes Measurement Information System Short Form Physical Function 8c (PROMIS-PF 8c) instruments
  - TTSP: time from randomization to onset of new/worsening symptoms related to lung cancer (per investigator) and required either a change in treatment and/or clinical intervention, or death

FIGURE 1: Phase 3 MARIPOSA-2 study design



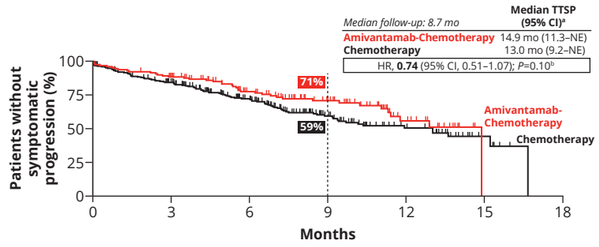
[a]Analyses were further stratified based on osimertinib line of therapy, history of brain metastases, and race (Asian vs non-Asian). [b]All patients randomized before November 7, 2022, initiated lazertinib on the first day of Cycle 1. [c]Also included death.

AUC, area under the curve; BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; Ex19del, Exon 19 deletion mutation; NSCLC, non-small cell lung cancer; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; PFS, progression-free survival; PROMIS-PF 8c, Patient-Reported Outcomes Measurement Information System Short Form Physical Function 8c; RECIST, Response Evaluation Criteria in Solid Tumors.

RESULTS

- Amivantamab-chemotherapy reduced the risk of symptomatic progression by 26% (**Figure 2**)

FIGURE 2: Time to symptomatic progression (TTSP)

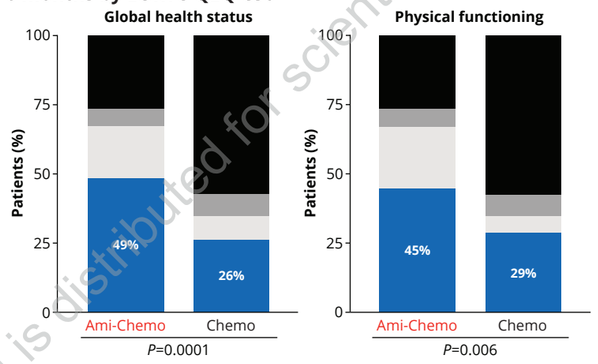


[a]Median TTSP of the ITT population with 95% CIs calculated using the Kaplan-Meier method. [b]HR with 95% CI calculated using a stratified Cox regression model; *P* value calculated using a stratified log-rank test.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; NE, not estimable; TTSP, time to symptomatic progression.

- More patients in the amivantamab-chemotherapy arm reported improved or stable global health status and physical functioning vs chemotherapy at 6 months (**Figure 3**)
  - Results were consistent for role, emotional, cognitive, and social functioning (all *P*<0.05)

FIGURE 3: Patients reporting improved/stable symptoms at 6 months by EORTC-QLQ-C30

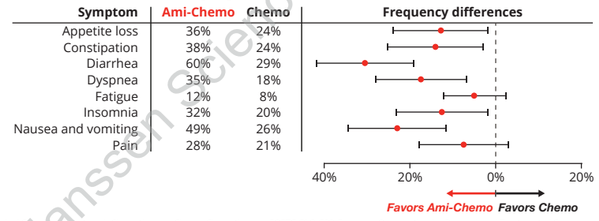


Note: percentages exclude patients with insufficient follow-up. Role functioning is measured by limitation in pursuing work or other daily activities.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; PRO, patient-reported outcome.

- More patients in the amivantamab-chemotherapy arm reported absence of key symptoms vs chemotherapy (**Figure 4**)

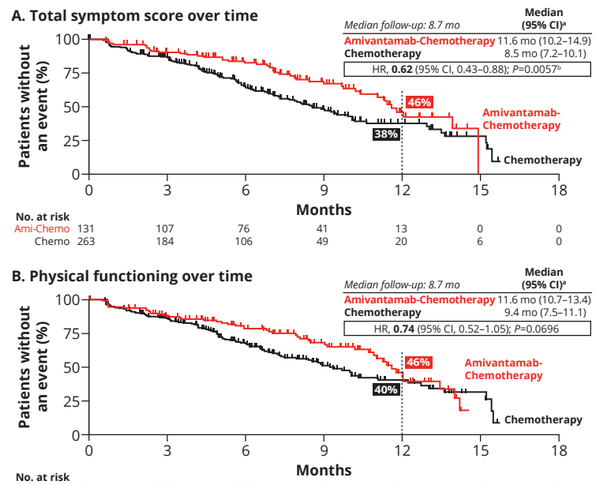
FIGURE 4: Patients reporting absence of key symptoms at 6 months by EORTC-QLQ-C30



Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire.

- Amivantamab-chemotherapy prolonged time to sustained deterioration in lung cancer symptoms (**Figure 5A**) and physical functioning (**Figure 5B**) vs chemotherapy

FIGURE 5: Time to sustained deterioration[a] by (A) NSCLC-SAQ and (B) PROMIS-PF 8c



[a]Time to sustained deterioration was defined as the time from randomization until the date of the first clinically meaningful deterioration (ie, decrease of ≥2.5 points [NSCLC-SAQ] or ≥6.5 points [PROMIS-PF 8c] relative to baseline on the total score) or death that was not subsequently followed by a score above the meaningful deterioration threshold at any later visits. [b]Kaplan-Meier analyses of PROs are influenced by disease progressions, which are not part of the definition, and patients post progression have fewer PRO data than those prior to progression.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; PRO, patient-reported outcome; PROMIS-PF 8c, Patient-Reported Outcomes Measurement Information System Short Form Physical Function 8c.

KEY TAKEAWAY

Amivantamab-chemotherapy demonstrated improvements in time to symptomatic progression and key patient-reported outcomes compared to chemotherapy among patients with *EGFR*-mutant advanced NSCLC after disease progression on osimertinib

CONCLUSIONS

Amivantamab-chemotherapy numerically prolonged time to symptomatic progression vs chemotherapy (14.9 vs 13.0 mo; HR, 0.74; *P*=0.10)

More patients in the amivantamab-chemotherapy arm reported improved/stable functioning and absence of key symptoms vs chemotherapy based on the EORTC-QLQ-C30

Amivantamab-chemotherapy substantially prolonged time to sustained deterioration in lung cancer symptoms vs chemotherapy (11.6 vs 8.5 mo) based on the NSCLC-SAQ

Amivantamab-chemotherapy numerically prolonged time to sustained deterioration in physical functioning vs chemotherapy (11.6 vs 9.4 mo) based on the PROMIS-PF 8c

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P. Tomasini: received payment or honoraria from AstraZeneca, Takeda, Bristol Myers Squibb, Roche, Janssen, and Amgen; and received support for attending meetings and/or travel from Takeda, AstraZeneca, and Bristol Myers Squibb. **A. Blasco:** received payment or honoraria from Roche, Clover Biopharmaceuticals, Sanofi, janssen-Cilag, Takeda, and GSK; and received support for attending meetings and/or travel from Roche, Bristol Myers Squibb, and Takeda. **C. Dooms:** received consulting fees from Janssen. **M. Mackean:** received consulting fees from Boehringer Ingelheim, Roche, Takeda, and AstraZeneca; received payment or honoraria from Bristol Myers Squibb and Takeda; and received support for attending meetings and/or travel from Takeda, Bristol Myers Squibb, Janssen-Cilag, Merck Sharp & Dohme, and Roche. **A. Bearz:** received consulting fees from Pfizer and Roche; received payment or honoraria from Novartis and Lilly; and participated on a data safety monitoring board or advisory board for Pfizer, Roche, and Regeneron. **O.J. Vidal:** received consulting fees from Bristol Myers Squibb, Merck Sharp & Dohme, AstraZeneca, Pfizer, Janssen, and Takeda; received payment or honoraria from Bristol Myers Squibb, Merck Sharp & Dohme, AstraZeneca, Pfizer, Janssen, Takeda, and Roche/Genentech; and received support for attending meetings and/or travel from AstraZeneca, Takeda, Merck Sharp & Dohme, Pfizer, and Roche/Genentech. **D. Kowalski:** received consulting fees from Bristol Myers Squibb, Merck Sharp & Dohme, Pfizer, AstraZeneca, Novartis, Roche, Takeda, Boehringer Ingelheim, Sanofi-Aventis, Amgen, Janssen, and Merck; and had a leadership or fiduciary role for the Polish Lung Cancer Study Group. **K. Stencel:** received consulting fees from Takeda; received payment or honoraria from Amgen, AstraZeneca, Bristol Myers Squibb, Merck Sharp & Dohme, Takeda, Roche, Janssen, and Pfizer; received support for attending meetings and/or travel from Merck Sharp & Dohme and Roche; participated on a data safety monitoring board or advisory board for Merck Sharp & Dohme and Amgen; and received equipment, materials, drugs, medical writing, gifts, or other services from Bristol Myers Squibb. **R. Califano**, **P. Hulo**, and **V. Surmont:** have no disclosures to report. **A. Zer:** received consulting fees from Merck Sharp & Dohme, Takeda, AstraZeneca, AbbVie, Roche, Oncotest-Rhenium, and Janssen; received payment or honoraria from Merck Sharp & Dohme, Takeda, AstraZeneca, Roche, Oncotest-Rhenium, and AbbVie; received support for attending meetings and/or travel from Roche and Merck Sharp & Dohme; participated on a data safety monitoring board or advisory board for Beyond Cancer; and has stock or stock options with Nixio. **J. Schuchard**, **J. Diels**, **P.-L. Chu**, **S. Shah**, **B. Diorio**, **A. Girvin**, and **J.M. Bauml:** are employees of Janssen and may hold stock in Johnson & Johnson. **E. Felip:** received research funding from Merck Healthcare KGaA and FUNDACIÓN MERCK SALUD; attended speakers bureaus for Amgen, AstraZeneca, Bristol Myers Squibb, Lilly, F. Hoffman-La Roche, Janssen, Medical Trends, Medscape, Merck Serono, Merck Sharp & Dohme, PeerVoice, Pfizer, Sanofi, Takeda, and Touch Oncology; and participated on an advisory board for Amgen, AstraZeneca, Bayer, Bristol Myers Squibb, Daiichi Sankyo, Lilly, F. Hoffman-La Roche, GSK, Janssen, Merck Serono, Merck Sharp & Dohme, Novartis, Peptomyc, Pfizer, Sanofi, Takeda, and BerGenBio.

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