

# Effect of Amivantamab Dose Interruptions on Efficacy and Safety of First-line Amivantamab Plus Lazertinib in EGFR-mutant Advanced NSCLC: Exploratory Analyses From the MARIPOSA Study

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## Key Takeaway

Amivantamab + lazertinib represents a new standard of care in patients with first-line epidermal growth factor receptor (EGFR)-mutant advanced non-small cell lung cancer (NSCLC)<sup>1</sup>

## Conclusions

Approximately half of the patients treated with amivantamab + lazertinib required dose interruptions within the first 4 months

Key skin and gastrointestinal adverse events (AEs) occurred early and diminished over time

- No grade 4 or 5 AEs were reported

Median progression-free survival (PFS) after 4 months was similar between patients with and without dose interruptions

Dose interruptions are a meaningful way to manage AEs without compromising PFS

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## Background

- Amivantamab is an EGFR-MET bispecific antibody with immune cell-directing activity<sup>2-4</sup>
- Lazertinib is a central nervous system-penetrant, third-generation EGFR tyrosine kinase inhibitor<sup>5,6</sup>
- In MARIPOSA, amivantamab + lazertinib significantly improved PFS versus osimertinib in treatment-naïve, EGFR-mutated advanced NSCLC (Figure 1)<sup>1</sup>
  - Key AEs were highest within the first 4 months<sup>7</sup>
  - The protocol recommended amivantamab dose interruptions for grade ≥2 toxicities
- We evaluated the association of amivantamab dose interruptions within the first 4 months with the efficacy and safety outcomes of amivantamab + lazertinib

## Methods

- Patients with treatment-naïve, EGFR-mutant advanced NSCLC were randomized 2:2:1 to amivantamab + lazertinib (n=429), osimertinib (n=429), or lazertinib (n=216; Figure 2)
- The primary endpoint was PFS by blinded independent central review per RECIST v1.1 for amivantamab + lazertinib versus osimertinib

## Results

### Descriptive analysis of amivantamab dose interruptions

- Among the 421 patients who received ≥1 dose of amivantamab, 206 (49%) patients had a dose interruption within the first 4 months
- Dose interruption is defined as a skipped dose that is not made up; this population may also include patients who had a dose reduction or drug discontinuation
- Outcomes were similar among patients with and without dose interruptions (Table 1)

**Table 1: Outcomes in patients with and without dose interruptions<sup>a</sup>**

Endpoint, median (95% CI)	Dose interruptions within the first 4 months (n=206)	No interruptions within the first 4 months (n=215)	All randomized patients (n=429)
PFS	23.9 mo (18.5-NE)	23.7 mo (18.4-NE)	23.7 mo (19.1-27.7)
ORR	87% (81-91)	89% (84-93)	86% (83-89)
DoR among confirmed responders	25.8 mo (16.7-NE)	26.1 mo (20.1-NE)	25.8 mo (20.1-NE)

<sup>a</sup>Patients who discontinued the study, had disease progression, or died within the first 4 months were not evaluated, as they were not in the study by the cutoff time point (and the outcome event may occur prior to the dose interruption). CI, confidence interval; DoR, duration of response; NE, not estimable; ORR, objective response rate; PFS, progression-free survival.

- However, this analysis measured exposure (interruptions) and outcomes over the same time period, which could lead to bias
  - Outcomes, such as progression or death, could occur before dose interruptions, which leads to outcome-based selection bias

### Patients

- 43/421 (10%) patients either discontinued the study, had disease progression, or died prior to 4 months and were not included in this analysis
  - Removing patients who died, progressed, or discontinued within the first 4 months avoids outcome-based selection bias between dose-interruption groups
- 188 patients had a dose interruption within the first 4 months and 190 patients did not
- Baseline characteristics were similar between patients with and without dose interruptions (Table 2)
- Among the 188 patients with dose interruptions:
  - Median time to first interruption: 43 days (interquartile range [IQR], 16-72)
  - Among the 94% of patients who resumed amivantamab, the median dose-interruption duration was 22 days (IQR, 14-41)

**Table 2: Demographic and baseline characteristics**

Characteristic, n (%)	Dose interruptions within the first 4 months (n=188)	No interruptions within the first 4 months (n=190)
Median age (range), years	63 (35-86)	62 (24-88)
Female	120 (64)	120 (63)
Race		
Asian	108 (57)	114 (60)
Non-Asian	78 (41)	76 (40)
Unknown	2 (1)	0
ECOG PS score of 1	122 (65)	127 (67)
History of smoking	61 (32)	54 (28)
History of brain metastases	80 (43)	71 (37)
EGFR mutation type		
Ex19del	101 (54)	124 (65)
L858R	87 (46)	66 (35)

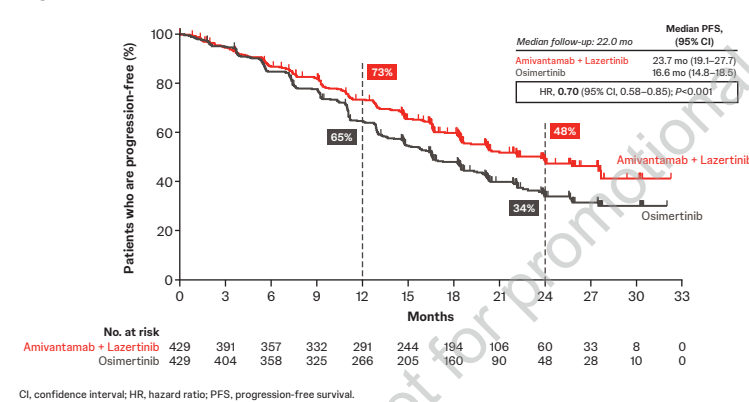
ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, Exon 19 deletion.

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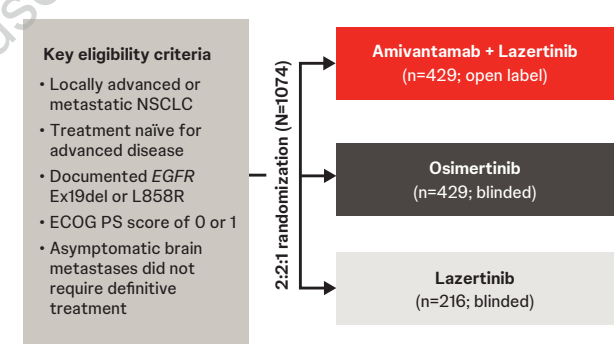
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**Figure 1: PFS from MARIPOSA<sup>1</sup>**



**Figure 2: MARIPOSA study design**

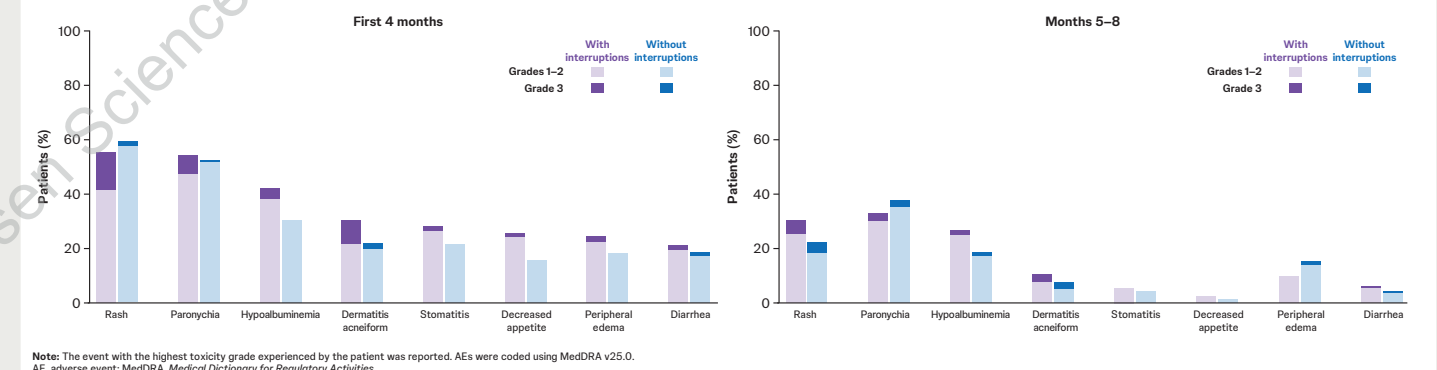


MARIPOSA (ClinicalTrials.gov Identifier: NCT04487080). EGFR, epidermal growth factor receptor; ECOG PS, Eastern Cooperative Oncology Group performance status; Ex19del, Exon 19 deletion; NSCLC, non-small cell lung cancer.

## Key AEs

- Key AEs occurred most frequently during the first 4 months and declined over the next 4 months (Figure 3)
  - The percent decrease observed in key AEs during Months 5 to 8 relative to the first 4 months was as follows: rash, 46-63%; paronychia, 29-39%; hypoalbuminemia, 36-39%; dermatitis acneiform, ~65%; stomatitis, ~80%; decreased appetite, ~89%; peripheral edema, 17-60%; diarrhea, 72-77%
- No grade 4 or 5 AEs were reported

**Figure 3: Prevalence and severity of key AEs over time**

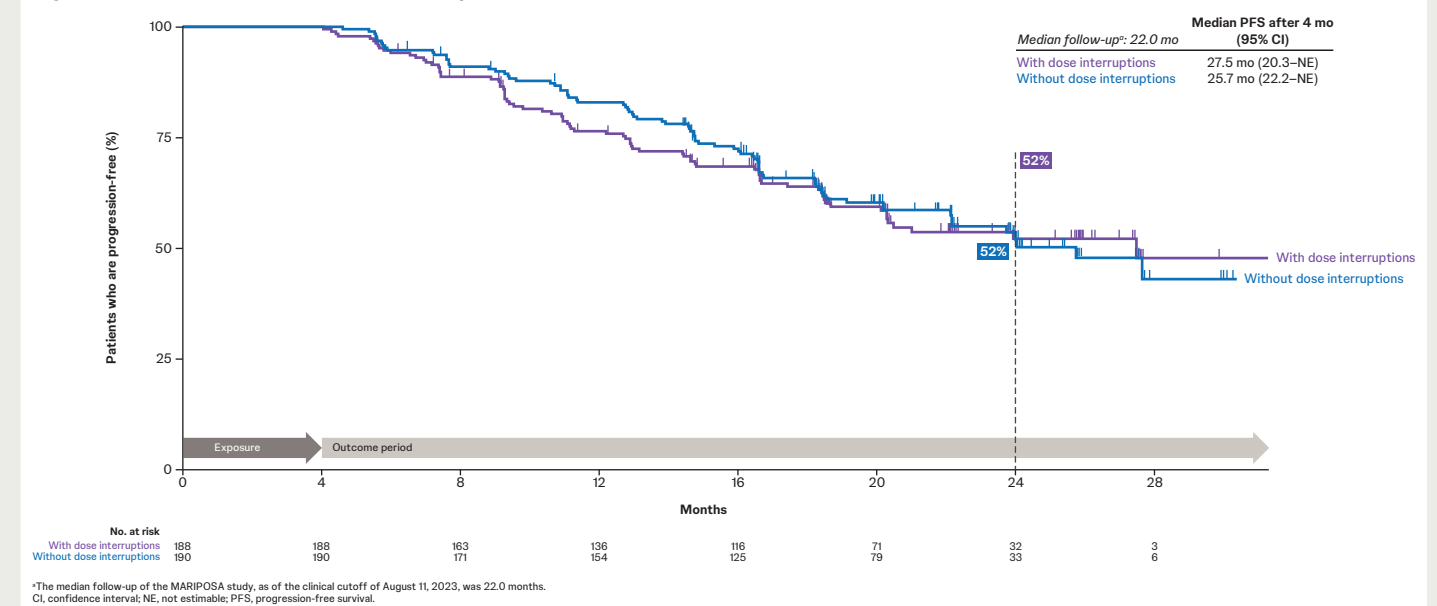


Note: The event with the highest toxicity grade experienced by the patient was reported. AEs were coded using MedDRA v25.0. AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities.

## Association of dose interruptions with PFS

- Median PFS after 4 months was similar between patients with and without dose interruptions (Figure 4)
- The PFS hazard ratio by multivariable analysis adjusting for age, Eastern Cooperative Oncology Group performance status score, EGFR mutation type, Asian race, and history of brain metastases was 1.06 (95% CI, 0.73-1.44), indicating no significant association of dose interruption with PFS after the 4-month exposure period
  - The multivariate analysis was performed via multivariate Cox proportional hazards model, only including patients who were still at risk of PFS at 4 months

**Figure 4: PFS with and without dose interruptions**



<sup>a</sup>The median follow-up of the MARIPOSA study, as of the clinical cutoff of August 11, 2023, was 22.0 months. CI, confidence interval; NE, not estimable; PFS, progression-free survival.

