Effect of Amivantamab Dose Interruptions on Efficacy and Safety in the MARIPOSA Study

MARIPOSA Overall Study Design & Exploratory Dose Interruption Analysis Summary[1-3]

Objective: Exploratory analyses from the phase 3 MARIPOSA study evaluating amivantamab and lazertinib combination therapy versus osimertinib versus lazertinib as first-line treatment in patients with *EGFR*-mutated locally advanced or metastatic non-small cell lung cancer[2,3]

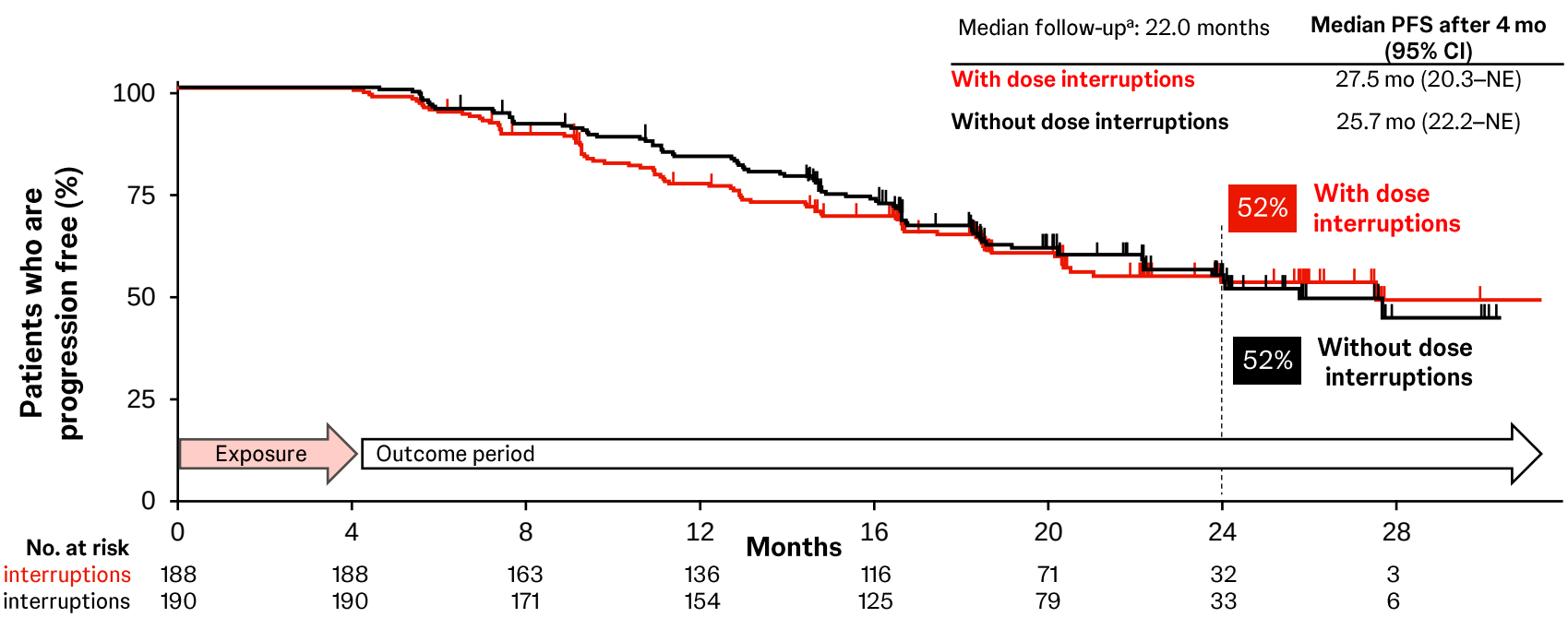
MARIPOSA Primary Endpoint: BICR-assessed PFS per RECIST v1.1. PFS was assessed using a stratified log-rank test with *EGFR* mutation type, Asian race, and history of brain metastases as stratification factors

MARIPOSA Secondary Endpoints: OS, ORR, DoR, and safety

A hierarchical hypothesis-testing approach was used: PFS then OS. Analyses of additional secondary endpoints were not part of the hypothesis testing of the trial[2,3]

Progression-Free Survival by Dose Interruptions[1]

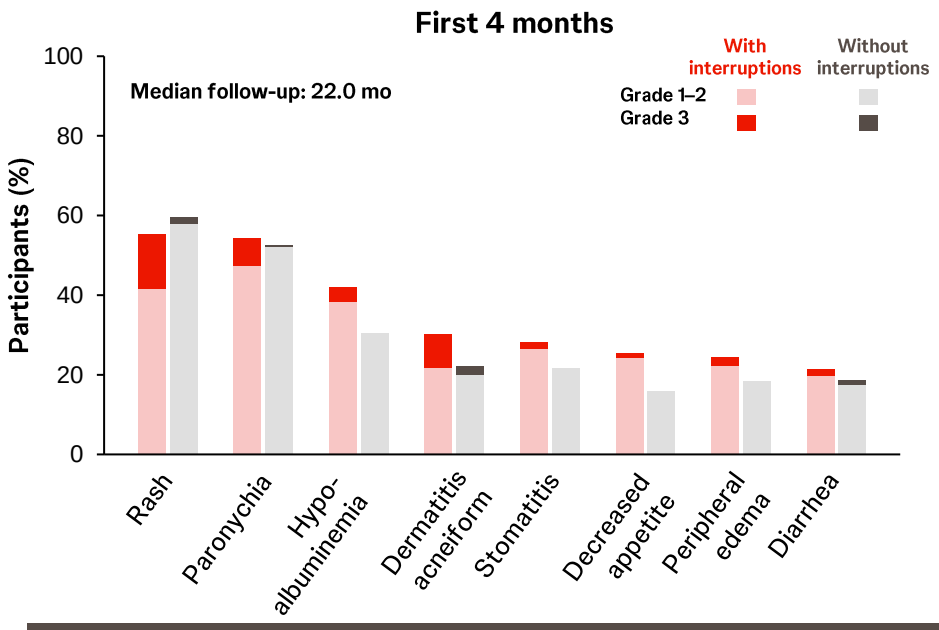
Among the 421 patients receiving ≥1 dose of amivantamab, 206 (49%) had a dose interruption within the first 4 months. Dose interruption is defined as a skipped dose that is not made up; this population may also include patients that had a dose reduction or drug discontinuation

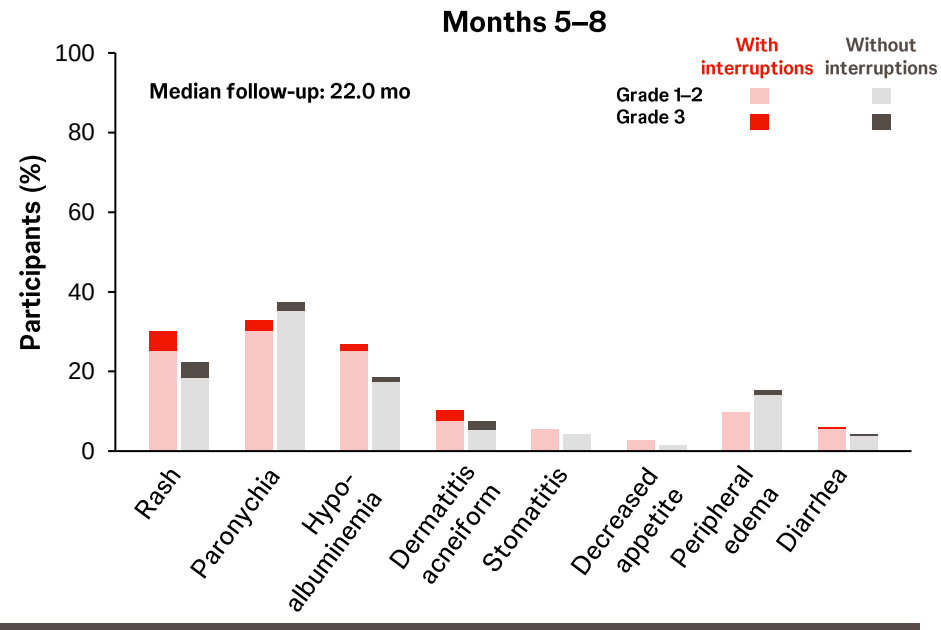


The PFS HR by multivariable analysis[b] adjusting for age, ECOG PS, *EGFR* mutation type, Asian race, and history of brain metastases was 1.06 (95% CI, 0.73–1.44)

Prevalence and Severity of Adverse Events[1,c]

Protocol recommended amivantamab dose interruptions for related grade ≥2 toxicities[1]





Study Limitations: This analysis measures outcomes and exposure (interruptions) during the same time period, which could lead to bias.[d] To minimize bias, outcomes were evaluated after the first 4 months (exposure period)[1,e]

[a]Median follow-up of the MARIPOSA study, as of the clinical cutoff of 11 August 2023, was 22.0 months.[1] [b]Via multivariate Cox proportional hazards model, only including patients still at risk of PFS at 4 months.[1] [c]The event experienced by the patient with the highest toxicity grade is reported. AEs are coded using MedDRA v25.0. Percent decrease in events during Months 5-8 relative to first 4 months: rash 46-63%; paronychia 29-39%; hypoalbuminemia 36-39%; dermatitis acneiform ~65%; stomatitis ~80%; decreased appetite ~89%; peripheral edema 17-60%; diarrhea 72-77%.[1] [d]Outcomes, such as progression events or deaths, could occur before interruptions leading to outcomes-based selection bias or immortal time bias.[1] [e]Patients who discontinued study, had disease progression, or died in the first 4 months were not evaluated, as they were not in the study by the cutoff timepoint (and the outcome event may occur prior to the interruption).[1]

AE, adverse event; BICR, blinded independent central review; CI, confidence ratio; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; HR, hazard ratio; NE, not estimable; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

1. Campelo MRG, et al. ELCC 2024. Oral presentation #5MO. 2. Cho BC, et al. *N Engl J Med.* 2024;391(16):1486-1498. 3. Yang JC-H, et al. *N Engl J Med.* 2025. Published online September 7, 2025. doi: 10.1056/NEJMoa2503001.

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Dose Modification Guide for Amivantamab and Lazertinib

The information provided in this section summarizes dose modification guidance as described in the amivantamab[1] and lazertinib[2] prescribing information. These are not recommendations for individual patient care. Interventions should be based on patient presentation and the clinical judgment of the treating physician.

Dose Reductions of Amivantamab[1] and Lazertinib[2] for Adverse Reactions

	Initial Dose*	1st Reduction	2nd Reduction	3rd Reduction
Amivantamab	1050 mg	700 mg	350 mg	DISCONTINUE amivantamab
	1400 mg	1050 mg	700 mg	
	1750 mg	1400 mg	1050 mg	
	2100 mg	1750 mg	1400 mg	
Lazertinib	240 mg	160 mg	80 mg	DISCONTINUE lazertinib

Dose Modifications of Amivantamab[1] and Lazertinib[2] for Dermatologic AEs†

Dose Modifications of Amivantamab for Dermatologic AEs[1]

Grades 1-2

- **INITIATE** supportive care management
- **REASSESS** after 2 weeks; if rash does not improve, consider dose reduction

Grade 3

- **WITHHOLD** amivantamab and **INITIATE** supportive care management
- Upon recovery to Grade ≤2, **RESUME** amivantamab at a reduced dose
- If there is no improvement within 2 weeks, **PERMANENTLY DISCONTINUE** treatment

Grade 4 or severe bullous, blistering, or exfoliating skin conditions‡

- **PERMANENTLY DISCONTINUE** amivantamab

Dose Modifications of Lazertinib for Dermatologic AEs[2]

Grade 1

- **INITIATE** supportive care management

Grade 2

- **INITIATE** supportive care management
- If there is no improvement after 2 weeks, **REDUCE** the amivantamab dose and continue lazertinib at the same dose
- **REASSESS** every 2 weeks; if there is no improvement, **REDUCE** the lazertinib dose until Grade ≤1, then may resume previous dose at HCP discretion

Grade 3

- **WITHHOLD** amivantamab and lazertinib and **INITIATE** supportive care management
- Upon recovery to Grade ≤2, **RESUME** lazertinib at the same dose or consider dose reduction, **RESUME** amivantamab at a reduced dose
- If there is no improvement within 2 weeks, **PERMANENTLY DISCONTINUE** both amivantamab and lazertinib

Grade 4 or severe bullous, blistering, or exfoliating skin conditions

- **INITIATE** supportive care management
- **PERMANENTLY DISCONTINUE** amivantamab
- **WITHHOLD** lazertinib until recovery to Grade ≤2 or baseline
- Upon recovery to Grade ≤2, **RESUME** lazertinib at a reduced dose at HCP discretion

Considerations for Amivantamab and Lazertinib Withholding and Restarting Treatment[3]

The information provided in this section summarizes interventions investigators in the MARIPOSA[3] study were instructed to perform to monitor and manage rash. These are not recommendations for individual patient care. Interventions should be based on patient presentation and the clinical judgment of the treating physician.

- If clinical observations indicate moderate toxicity and one treatment must be withheld, it is recommended to withhold amivantamab first, unless the toxicity is strongly suspected to be caused solely by lazertinib
- If both treatments (eg, amivantamab and lazertinib) are stopped, they can be restarted once the toxicity has resolved. Generally, if both are to be continued, lazertinib should be restarted at least 7 to 14 days before the next amivantamab infusion to ensure the patient is stable on lazertinib alone

For dose modifications related to ILD/pneumonitis, IRRs, VTEs, and other adverse reactions, please refer to the full prescribing information for RYBREVANT (Section 2.6) and LAZCLUZE (Section 2.4)

AE, adverse event; HCP, health care practitioner; ILD, interstitial lung disease; IRR, infusion-related reaction; VTE, venous thromboembolism.
*Dose at which the adverse reaction occurred. †Dermatitis acneiform, pruritus, and dry skin. ‡Including toxic epidermal necrolysis.

1. RYBREVANT® [Prescribing information]. Horsham, PA: Janssen Biotech, Inc. **2.** LAZCLUZE™ [Prescribing information]. Horsham, PA: Janssen Biotech, Inc. **3.** Yang JC-H, et al. *N Engl J Med.* Published online September 7, 2025. doi:10.1056/NEJMoa2503001. (supplement).

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