

Dose modifications to manage adverse events in 1L *EGFR*-mutated advanced NSCLC: Post hoc, exploratory analyses from the phase 3 MARIPOSA trial

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Key Takeaway



Amivantamab dose modifications for grade ≥ 2 AEs are an effective approach to mitigate rash/dermatitis acneiform, paronychia, and peripheral edema

Conclusions



A high rate of AE improvement (approximately 80%) was found in participants who had their dose modified with grade ≥ 2 key AEs (rash/dermatitis acneiform, paronychia, peripheral edema)



After dose modification, most AEs improved in <1 month, with grade ≥ 3 AEs improving in approximately 2 weeks



SC amivantamab and prophylactic measures, which were not included in MARIPOSA, have now been shown to further mitigate the incidence and severity of key AEs,^{3–6} and may enable patients to stay on therapy longer



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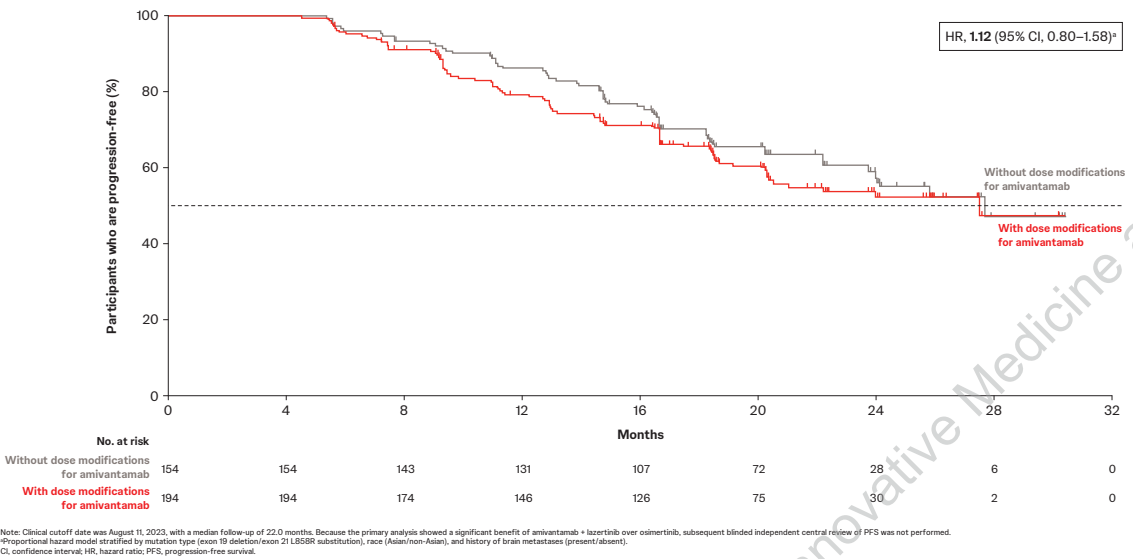
Disclosures

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Introduction

- In MARIPOSA (ClinicalTrials.gov Identifier: NCT04487080), first-line (1L) intravenous (IV) amivantamab + lazertinib significantly improved overall survival versus osimertinib (hazard ratio, 0.75; $P=0.005$) in participants with common (exon 19 deletion/exon 21 L858R substitution) epidermal growth factor receptor (*EGFR*)–mutated advanced non-small cell lung cancer (NSCLC)¹
- Key adverse events (AEs) first occurred during the first 4 months after randomization in MARIPOSA¹
 - Dose modifications, including dose interruptions and dose reductions, assisted AE management while maintaining efficacy (Figure 1)²
- Notably, MARIPOSA was conducted prior to the availability of subcutaneous (SC) amivantamab and prospective data on the effectiveness of prophylactic AE strategies^{3–6}

Figure 1: PFS by dose modification status within 4 months²



Results

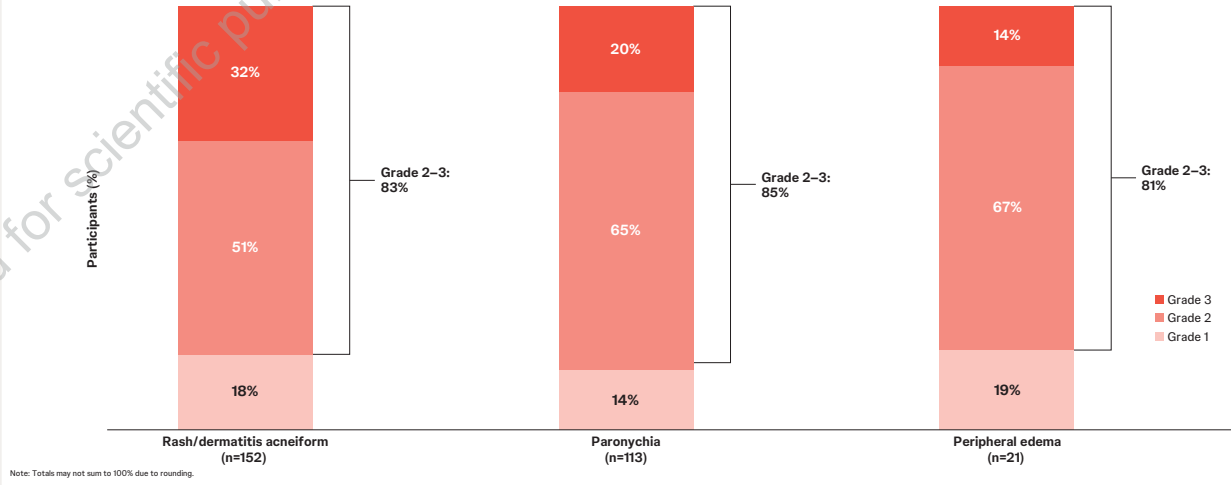
Types of dose modifications

- The majority of participants (363/421; 86%) experienced amivantamab dose modifications (interruptions and/or reductions)
 - 345 participants had dose interruptions, and 274 participants had dose reductions
- Median time to dose modification was 85 days (range, 2–925)
- By 6 months, the median relative dose intensity among treated participants, defined as the percentage of the planned total dose received, was 83%

AEs leading to first dose modifications

- The most common amivantamab-associated AEs leading to first dose modifications were paronychia (27%), rash (26%), dermatitis acneiform (13%), and peripheral edema (5%)
- Among common AEs reported (rash/dermatitis acneiform, paronychia, peripheral edema), 86% to 92% were grade 1 or 2 at first onset
- Dose modifications for AEs typically occurred at grade 2 or 3 (Figure 3)
 - Interruption was the most common first modification (82% of participants)
- Most participants who dose modified with grade ≥ 2 rash/dermatitis acneiform, paronychia, or peripheral edema experienced AE improvement (Figure 4)

Figure 3: Grade at time of first dose modification

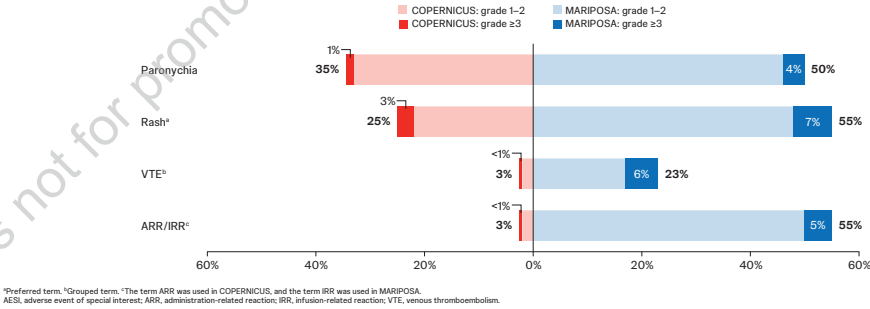


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- The COPERNICUS study, which evaluated SC amivantamab + lazertinib in 1L *EGFR*-mutated NSCLC, showed that the SC formulation with dermatologic and venous thromboembolism prophylaxis demonstrated a meaningful reduction in the incidence and severity of AEs of special interest compared with MARIPOSA (Figure 2)⁶
- Here, we report the impact of first dose modifications among key clinically observable EGFR- and MET-related AEs that were the most common reasons for IV amivantamab dose modifications in MARIPOSA

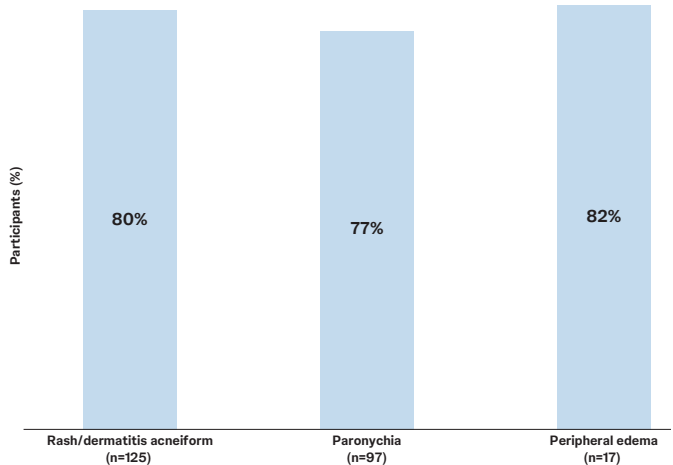
Figure 2: Incidence of selected AESIs during the first 4 months of treatment in COPERNICUS and MARIPOSA⁶



Methods

- Participants with *EGFR*-mutated advanced NSCLC were randomized 2:2:1 to receive amivantamab + lazertinib (n=429), osimertinib monotherapy (n=429), or lazertinib monotherapy (n=216)
 - The safety analysis set (amivantamab + lazertinib: n=421) included randomized participants who received ≥ 1 dose of any study treatment
- This post hoc, exploratory analysis of the amivantamab + lazertinib arm included per-protocol amivantamab dose modifications recommended for treatment-related grade ≥ 2 AEs⁷
 - For grade 1 or 2 dermatologic AEs, supportive care was initiated and dose reduction was considered if there was no improvement after 2 weeks; for grade 3, amivantamab treatment was interrupted
 - For other grade 3 AEs, amivantamab treatment was withheld until recovery to grade ≤ 1 or baseline
 - Amivantamab was to be modified prior to modifying lazertinib in participants who experienced treatment-related grade ≥ 2 AEs
- Improvement was defined as resolution of the AE, reduction in grade (eg, grade 3 to 2, grade 2 to 1, or grade 3 to 1), or both

Figure 4: Percentage of participants with improvement in grade ≥ 2 rash/dermatitis acneiform, paronychia, and peripheral edema after dose modification



Time to AE improvement after first dose modification for grade ≥ 2 AEs

- After dose modification, the median time to improvement among those who improved was <1 month for both grade ≥ 2 and grade ≥ 3 AEs (Table 1)

Table 1: Median time to improvement since dose modification for grade ≥ 2 AEs

AE	Median time to AE improvement (days)	
	Grade ≥ 2 AEs	Grade ≥ 3 AEs
Rash/dermatitis acneiform	16.5	15.0
Paronychia	22.0	15.5
Peripheral edema	27.5	15.0