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First-Line Subcutaneous Amivantamab Plus Lazertinib in *EGFR*-Mutated Advanced NSCLC: Updated Results From the PALOMA-2 Study

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PALOMA-2
(MARIPOSA population)

Disclosures

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PALOMA-2 (MARIPOSA population)

Background

- Amivantamab, an EGFR-MET bispecific antibody, is approved for IV and SC (co-formulated with recombinant human hyaluronidase PH20) administration for the treatment of multiple indications in *EGFR*-mutated advanced NSCLC[1,2]
- With a median follow-up of 37.8 months in MARIPOSA, 1L IV amivantamab + lazertinib demonstrated a clinically meaningful and statistically significant OS benefit versus osimertinib (HR, 0.75; *P*=0.005) in the protocol-specified final OS analysis[3]
  - 75% of participants were alive at 2 years, and 60% were alive at 3 years[3]
- In PALOMA-3, SC amivantamab showed noninferior pharmacokinetics and efficacy, while substantially reducing IRRs (13% vs 66%) and administration time (≤5 minutes vs 2–5 hours) versus IV amivantamab after progression on/after osimertinib and chemotherapy[4]
- In the phase 2 PALOMA-2 study, 1L SC amivantamab + lazertinib previously showed a response rate and safety profile consistent with historical IV amivantamab + lazertinib, with improved tolerability[5–7]

Here, we present pooled, longer follow-up results from participants who received 1L SC amivantamab + lazertinib in PALOMA-2

IRR, infusion-related reaction.

1. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [package insert]. Janssen Biotech, Inc. 2025. 2. RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) injection, for subcutaneous use [package insert]. Janssen Biotech, Inc. 2026. 3. Yang JCH, et al. *N Engl J Med*. 2025;393(17):1681–1693. 4. Leighl NB, et al. *J Clin Oncol*. 2024;42(30):3593–3605. 5. Scott SC, et al. Presented at: World Conference on Lung Cancer (WCLC); September 6–9, 2025; Barcelona, Spain. 6. Lim SM, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA. 7. Girard N, et al. Presented at: European Lung Cancer Congress (ELCC); March 25–28, 2026; Copenhagen, Denmark.

PALOMA-2 (MARIPOSA population)

PALOMA-2 Study Design

Eligibility criteria

- Locally advanced or metastatic NSCLC
- Stable or asymptomatic brain metastases were allowed
- ECOG PS score of 0 or 1

Prophylaxis for dermatologic AEs was not mandated

Cohort 1 Ex19del/L858R, 1L (MARIPOSA population)	**Amivantamab SC Q2W + lazertinib; *prophylactic anticoagulation recommended*** *Previously presented at ASCO 2024 & ELCC 2026[1,2]*
Cohort 2 Ex20ins, 1L (PAPILLON population)	Amivantamab SC Q3W + chemotherapy
Cohort 3 Ex19del/L858R, 2L (post-osi; MARIPOSA-2 population)	Amivantamab SC Q3W + chemotherapy + lazertinib
Cohort 3b Ex19del/L858R, 2L (post-osi; MARIPOSA-2 population)	Amivantamab SC Q3W + chemotherapy
Cohort 4 Prior amivantamab IV	Amivantamab IV Q2W switch to amivantamab SC Q2W
Cohort 5 Ex19del/L858R, 1L (MARIPOSA population)	**Amivantamab SC Q4W + lazertinib; *prophylactic anticoagulation recommended*** *Previously presented at WCLC 2025[3]*
Cohort 6 Ex19del/L858R, 1L (MARIPOSA population)	**Amivantamab SC Q2W + lazertinib; *prophylactic anticoagulation required*** *Previously presented at ASCO 2024[1]*
Cohort 7 Ex19del/L858R, 2L (post-amivantamab + lazertinib)	Amivantamab SC Q3W + chemotherapy

Enrolling

- A post-hoc ITC was conducted for PALOMA-2 and MARIPOSA using IPTW-ATE to balance baseline characteristics across study populations and estimate comparative treatment outcomes

PALOMA-2 (ClinicalTrials.gov identifier: NCT05498428). Clinical cut-off: July 3, 2026. **Note:** Amivantamab was coformulated with recombinant human hyaluronidase PH20 for subcutaneous administration at 1600 mg (≥80 kg, 2240 mg) weekly for the first 4 weeks. Thereafter, participants in Cohorts 1 and 6 received the same dose of amivantamab Q2W, while participants in Cohort 5 received amivantamab Q4W at 3520 mg (≥80 kg, 4640 mg). Lazertinib was dosed orally at 240 mg daily.

Ex19del, exon 19 deletion; IPTW-ATE, inverse probability of treatment weighting average treatment effect; ITC, indirect treatment comparison. 1. Lim SM, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA. 2. Girard N, et al. Presented at: European Lung Cancer Congress (ELCC); March 25–28, 2026; Copenhagen, Denmark. 3. Scott SC, et al. Presented at: World Conference on Lung Cancer (WCLC); September 6–9, 2025; Barcelona, Spain.

PALOMA-2 (MARIPOSA population)

Baseline Demographic and Clinical Characteristics

- In the overall pooled population (N=212), 135 participants received amivantamab Q2W in Cohorts 1 and 6 and 77 participants received amivantamab Q4W in Cohort 5
- As of July 3, 2026, median follow-up was 33.1 months (range, 2.4–41.9) and median treatment duration was 25.8 months (range, 0.1–42.0)

Characteristic, n (%)	Overall (N=212)
Median (range) age, years	61 (28–85)
Female	136 (64)
Race	
Asian	139 (66)
White	64 (30)
Black or African American	7 (3)
Other[a]	2 (1)
ECOG PS score of 1	149 (70)
History of smoking	59 (28)
History of brain metastases	75 (35)
EGFR mutation type[b]	
Exon 19 deletion	129 (61)
L858R	84 (40)
Adenocarcinoma histology	208 (98)

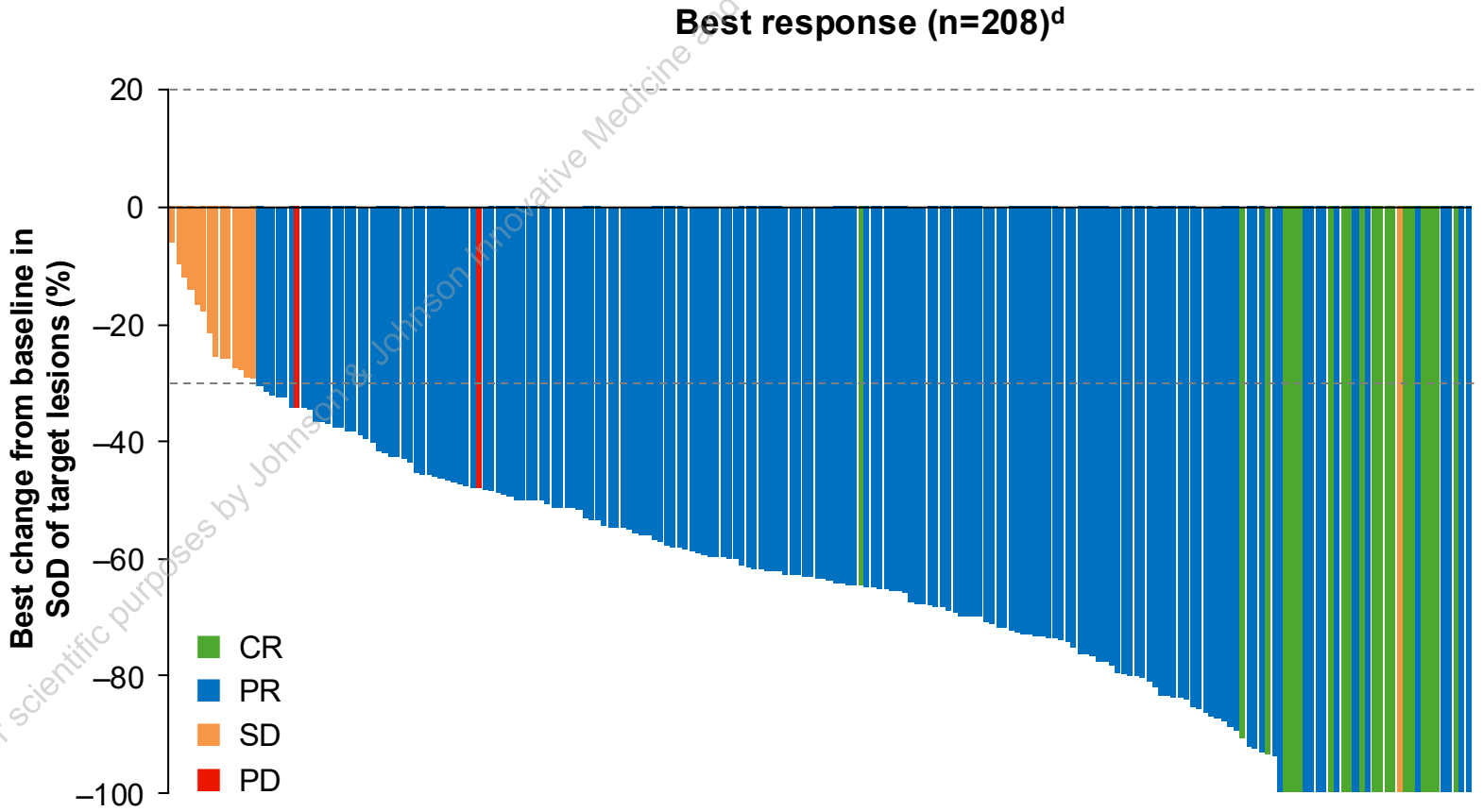
Note: Percentages may not sum to 100% due to rounding. [a]Other included Native Hawaiian or other Pacific Islander (n=1) and multiple (n=1). [b]One participant had both an exon 19 deletion and L858R substitution.

PALOMA-2 (MARIPOSA population)

ORR and Best Response

ICR-assessed response	Overall (N=212)
ORR	**90%** (95% CI, 85–94)
Best response,[a] n (%)	
CR	20 (9)
PR	171 (81)
SD[b]	15 (7)
PD	2 (1)
NE/UNK	4 (2)

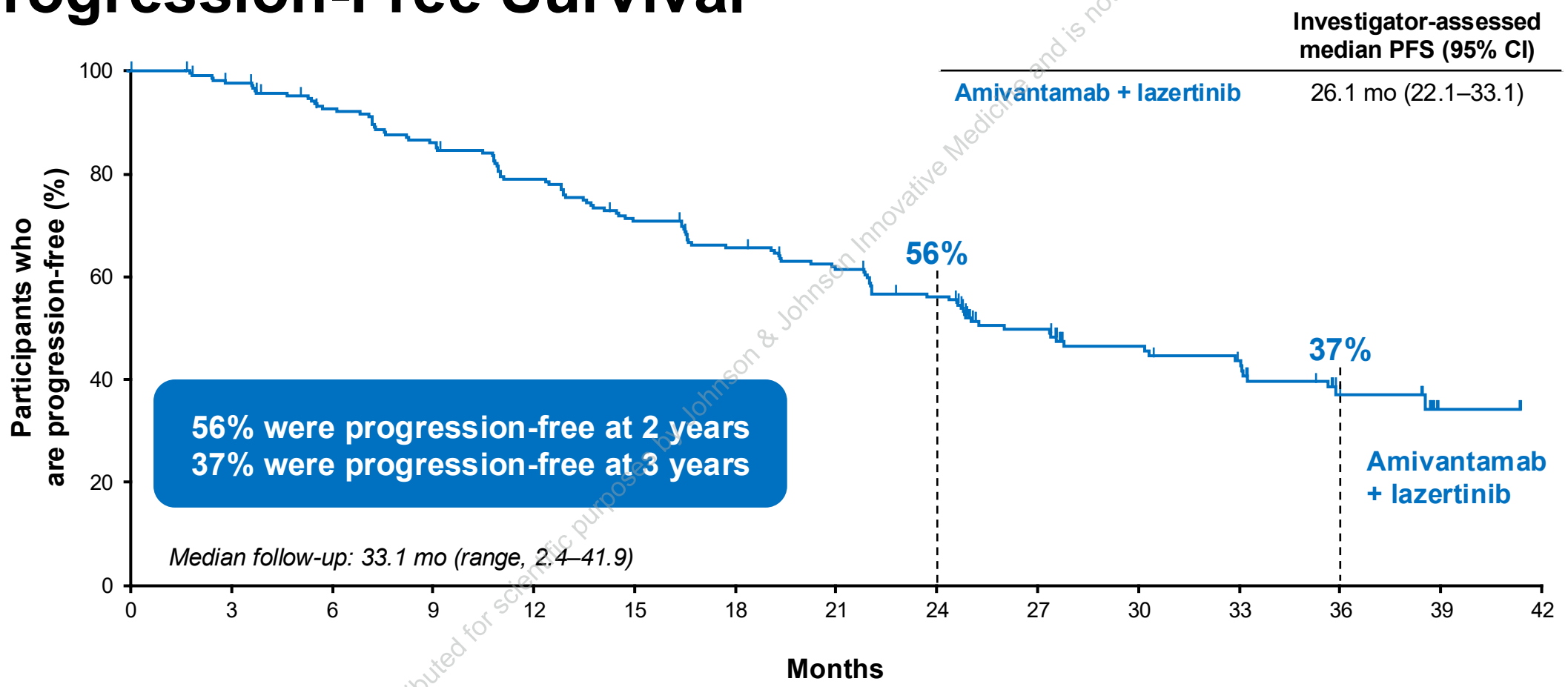
- All participants with measurable disease had tumor shrinkage of their target lesions
- Among confirmed responders (n=163):
  - Median DoR[c] was 25.6 months (95% CI, 21.1–33.8)
  - 50% (81/163) of responses were ongoing as of the data cut-off



[a]Percentages may not sum to 100% due to rounding. [b]Includes non-CR/non-PD in participants with nontarget lesions at baseline. [c]Duration of response (DoR) was assessed by the investigator. [d]Participants without a postbaseline tumor assessment were excluded.

PALOMA-2
(MARIPOSA population)

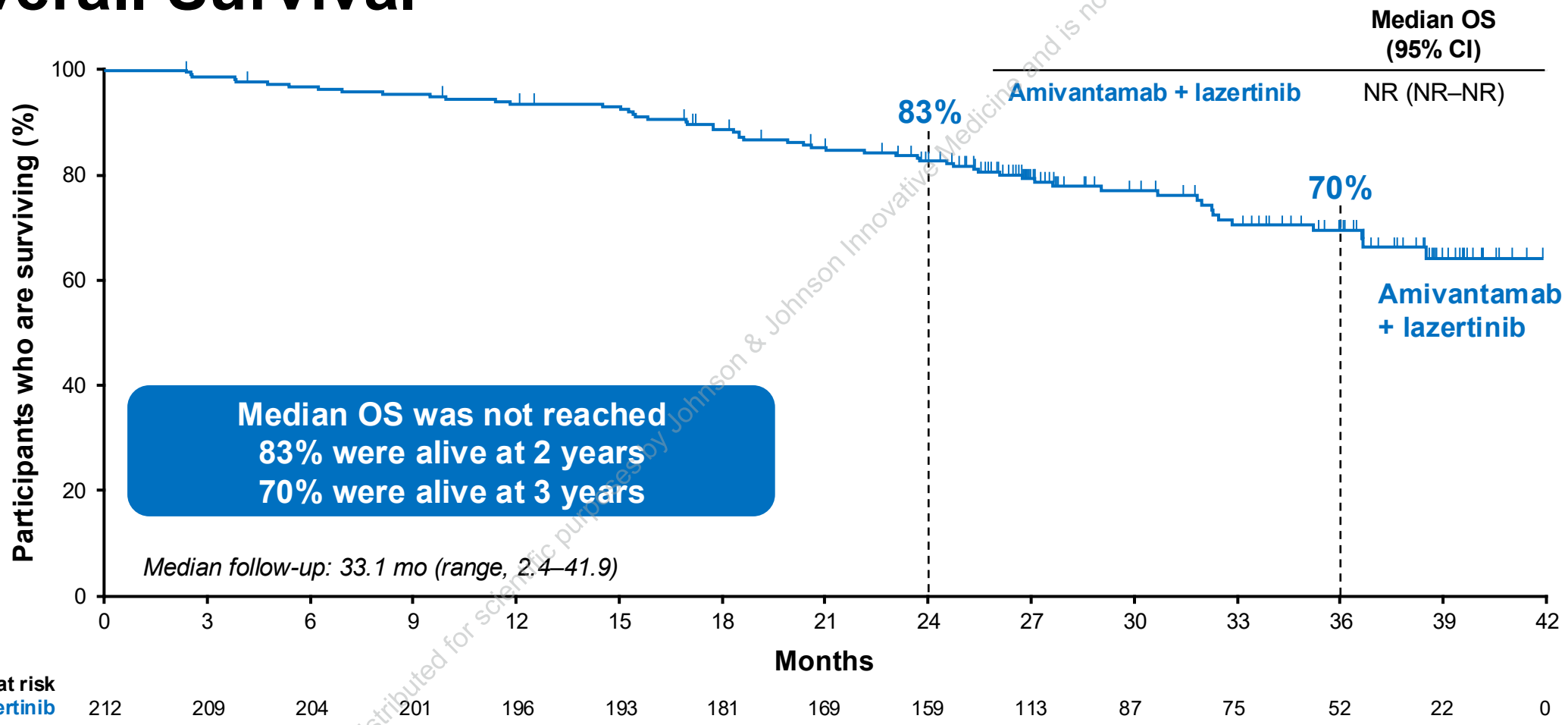
Progression-Free Survival



No. at risk															
Amivantamab + lazertinib	212	199	183	170	155	139	126	117	104	66	50	44	19	2	0

PALOMA-2 (MARIPOSA population)

Overall Survival



- SC amivantamab + lazertinib demonstrated favorable OS relative to IV amivantamab + lazertinib (HR 0.75; 95% CI, 0.56–1.02) and reduced the risk of death by 43% versus osimertinib (HR 0.57; 95% CI 0.42–0.77) in a post-hoc ITC to MARIPOSA

ITC, indirect treatment comparison.

PALOMA-2 (MARIPOSA population)

Safety Profile

- Safety profile was generally consistent with prior reports, with no new safety signals identified[1–3]
  - Primary reason for treatment discontinuation of all study agents due to treatment-related AEs occurred in **8%** (18/212) of participants
- ARRs[a] occurred in 16% of participants (grade ≥3, 0.5%)
  - The majority (76%) occurred at the first injection

Most common TEAEs (≥30%), n (%)	Overall (N=212)	
	All grades	Grade ≥3
Associated with EGFR inhibition		
Paronychia	178 (84)	26 (12)
Rash	149 (70)	38 (18)
Dermatitis acneiform	99 (47)	25 (12)
Stomatitis	94 (44)	9 (4)
Pruritus	80 (38)	2 (1)
Diarrhea	76 (36)	6 (3)
Associated with MET inhibition		
Hypoalbuminemia	136 (64)	12 (6)
Peripheral edema	89 (42)	3 (1)
Other		
Increased ALT	117 (55)	16 (8)
Increased AST	109 (51)	6 (3)

[a]ARRs are defined as Medical Dictionary for Regulatory Activities preferred term "Administration Related Reaction" (referred to as infusion-related reaction in prior studies).

ALT, alanine aminotransferase; ARR, administration related reaction; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.

1. Scott SC, et al. Presented at: World Conference on Lung Cancer (WCLC); September 6–9, 2025; Barcelona, Spain. 2. Girard N, et al. Presented at: European Lung Cancer Congress (ELCC); March 25–28, 2026; Copenhagen, Denmark. 3. Lim SM, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA.

PALOMA-2 (MARIPOSA population)

Conclusions

- Participants who received 1L SC amivantamab + lazertinib demonstrated long-term durable outcomes, with a median PFS of 26.1 months
- Median OS was not reached, and 70% of participants were alive at 3 years, which compares favorably with historical OS landmark data from MARIPOSA[1,a]
- The safety profile of SC amivantamab + lazertinib was generally consistent with prior reports before prophylactic AE management,[2–4] with no new safety signals identified
- SC administration, along with prophylactic AE management, can further improve the overall treatment experience and allow patients to remain on treatment longer

COPERNICUS MO12.09 (Halmos) *Tue Sept 15 @ 12PM*

1L treatment of *EGFR*-mutated advanced NSCLC with SC amivantamab + lazertinib continues to demonstrate clinically meaningful and durable antitumor efficacy

[a]In MARIPOSA, 1L IV amivantamab + lazertinib demonstrated a clinically meaningful OS benefit versus osimertinib with 60% of participants alive at 3 years.[1]

1. Yang JCH, et al. *N Engl J Med*. 2025;393(17):1681–1693. 2. Leighl NB, et al. *J Clin Oncol*. 2024;42(30):3593–3605. 3. Scott SC, et al. Presented at: World Conference on Lung Cancer (WCLC); September 6–9, 2025; Barcelona, Spain. 4. Girard N, et al. Presented at: European Lung Cancer Congress (ELCC); March 25–28, 2026; Copenhagen, Denmark.

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Thank You.