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PALOMA-2 (MARIPOSA population)

First-line subcutaneous amivantamab plus lazertinib in *EGFR*-mutated advanced NSCLC: Updated results from the PALOMA-2 study

Misako Nagasaka[1,*], Josiane Mourão Dias[2], Jiunn Liang Tan[3], Pei Jye Voon[4], Carlos Henrique Andrade Teixeira[5], Ke-Jing Tang[6], Susan C Scott[7], Enriqueta Felip[8], Bartomeu Massuti[9], Louise Medley[10], Nicolas Girard[11], Achim Rittmeyer[12], Saugata Das[13], John Xie[14], Miao Wang[15], Jie Zhang[16], Aria S Rhee[16], Justin N Malinou[16], Sun Min Lim[17]

[1]University of California–Irvine, School of Medicine, and UCI Health Chao Family Comprehensive Cancer Center, Orange, CA, USA; [2]Department of Medical Oncology, Barretos Cancer Hospital, Barretos, Brazil; [3]Department of Medicine, University of Malaya Medical Centre, Kuala Lumpur, Malaysia; [4]Department of Radiotherapy and Oncology, Hospital Umum Sarawak, Kuching, Sarawak, Malaysia; [5]Hospital Alemão Oswaldo Cruz, São Paulo, Brazil; [6]Division of Pulmonary and Critical Care Medicine, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [7]The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [8]Medical Oncology Service, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron Barcelona Hospital Campus, Universitat Autonoma de Barcelona, Barcelona, Spain; [9]Alicante University Dr Balmis Hospital, ISABIAL, Alicante, Spain; [10]Torbay and South Devon NHS Foundation Trust, Torquay, UK; [11]Institut du Thorax Curie-Montsouris, Paris, France, and Paris Saclay University, Université de Versailles Saint-Quentin-en-Yvelines, Versailles, France; [12]Department of Thoracic Oncology, LKI Lungenfachklinik Immenhausen, Immenhausen, Germany; [13]Johnson & Johnson, Kolkata, India; [14]Johnson & Johnson, Raritan, NJ, USA; [15]Johnson & Johnson, San Diego, CA, USA; [16]Johnson & Johnson, Spring House, PA, USA; [17]Division of Medical Oncology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea.

*Presenting author: nagasakm@hs.uci.edu

Key Takeaway

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

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

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Disclosures

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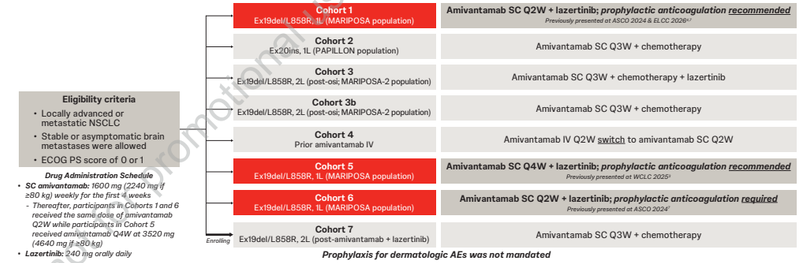
Background

- Amivantamab, an epidermal growth factor receptor (EGFR)–MET bispecific antibody, is approved for intravenous (IV) and subcutaneous (SC; co-formulated with recombinant human hyaluronidase PH20) administration for the treatment of multiple indications in *EGFR*-mutated advanced non-small cell lung cancer (NSCLC)[5,6]
- With a median follow-up of 37.8 months in MARIPOSA, first-line (1L) IV amivantamab + lazertinib demonstrated a clinically meaningful and statistically significant overall survival (OS) benefit versus osimertinib (hazard ratio, 0.75; *P*=0.005) in the protocol-specified final OS analysis[1]
  - 75% of participants were alive at 2 years, and 60% were alive at 3 years[1]
- In PALOMA-3, SC amivantamab showed noninferior pharmacokinetics and efficacy, while substantially reducing infusion-related reactions (IRRs; 13% vs 66%) and administration time (≤5 minutes vs 2–5 hours) versus IV amivantamab after progression on/after osimertinib and chemotherapy[2]
- 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[3,4,7]
- Here, we present pooled, longer follow-up results from participants who received 1L SC amivantamab + lazertinib in PALOMA-2

Methods

- PALOMA-2 (ClinicalTrials.gov identifier: NCT05498428) Cohorts 1, 5, and 6 enrolled participants with previously untreated *EGFR*-mutated (exon 19 deletion/exon 21 L858R substitution) advanced NSCLC (**Figure 1**)
- Amivantamab was co-formulated with recombinant human hyaluronidase PH20 for SC administration
- A post-hoc indirect treatment comparison (ITC) was conducted for PALOMA-2 and MARIPOSA using inverse probability of treatment weighting average treatment effect to balance baseline characteristics across study populations and estimate comparative treatment outcomes

Figure 1: PALOMA-2 study design



PALOMA-2 (ClinicalTrials.gov identifier: NCT05498428). Clinical cut-off: July 3, 2026.
1L, first-line; 2L, second-line; AE, adverse event; ASCO, American Society of Clinical Oncology; ECOG PS, Eastern Cooperative Oncology Group performance status; ELCC, European Lung Cancer Congress; Ex19del, exon 19 deletion; Ex20ins, exon 20 insertion; IV, intravenous; L858R, exon 21 L858R substitution; NSCLC, non-small cell lung cancer; osi, osimertinib; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; SC, subcutaneous; WCLC, World Conference on Lung Cancer.

Results

Baseline demographic and clinical characteristics

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

Table 1: Baseline demographic and clinical characteristics

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]**	
Ex19del	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 Ex19del and L858R substitution.
ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; L858R, exon 21 L858R substitution.

Efficacy

- In the overall pooled population, independent central review–assessed objective response rate was 90%, with a complete response rate of 9% (**Table 2**)

Table 2: ICR-assessed 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)

[a]Percentages may not sum to 100% due to rounding.
[b]Includes non-CR/non-PD in participants with nontarget lesions at baseline.
CI, confidence interval; CR, complete response; ICR, independent central review; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; UNK, unknown.

- All participants with measurable disease had tumor shrinkage of their target lesions (**Figure 2**)
- Among confirmed responders (n=163), median investigator-assessed duration of response was 25.6 months (95% confidence interval [CI], 21.1–33.8)
  - 50% (81/163) of responses were ongoing as of the data cut-off
- Investigator-assessed median progression-free survival (PFS) was 26.1 months (95% CI, 22.1–33.1); 37% were progression-free at 3 years (**Figure 3A**)
- Median OS was not reached; 70% were alive at 3 years (**Figure 3B**)

Indirect treatment comparison of OS

- 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

Safety

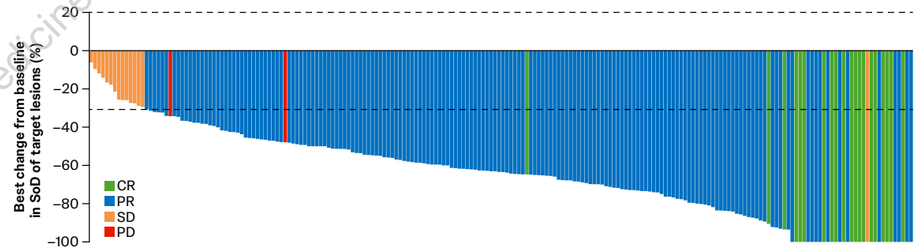
- The safety profile was generally consistent with prior reports, with no new safety signals identified (**Table 3**)[3,4,7]
  - The primary reason for treatment discontinuation of all study agents due to treatment-related adverse events (AEs) occurred in 8% (18/212) of participants
- Administration related reactions occurred in 16% of participants (grade ≥3, 0.5%)
  - Majority (76%) occurred at the first injection

Table 3: Safety profile

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)

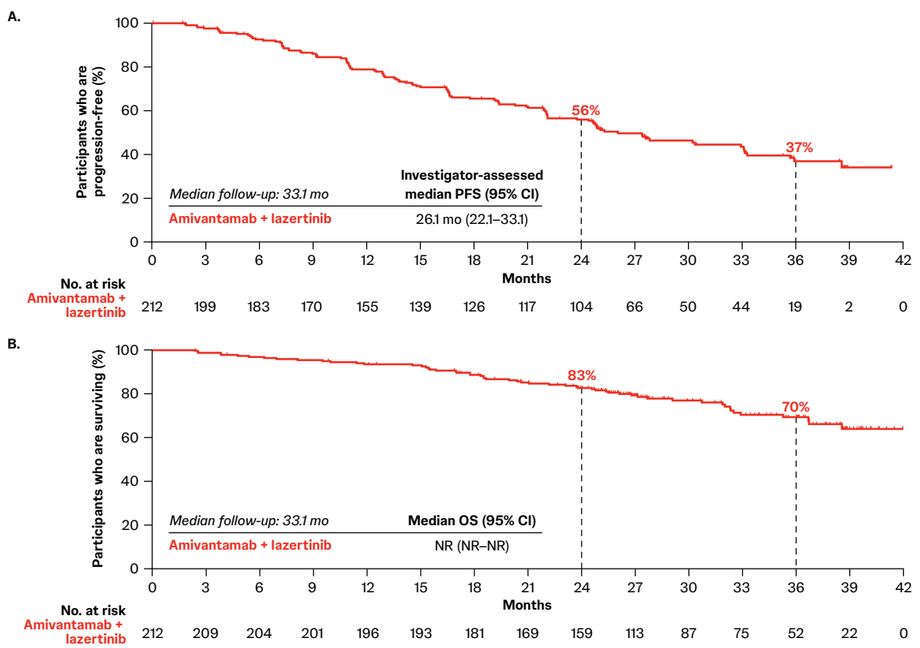
Note: ARRs are defined as *Medical Dictionary for Regulatory Activities* preferred term "Administration Related Reaction" (referred to as IRR in prior studies).
ALT, alanine aminotransferase; ARR, administration-related reaction; AST, aspartate aminotransferase; EGFR, epidermal growth factor receptor; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event.

Figure 2: Best response (n=208)[a]



[a]Participants without a postbaseline tumor assessment were excluded.
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameters.

Figure 3: (A) PFS and (B) OS



CI, confidence interval; NR, not reached; OS, overall survival; PFS, progression-free survival.

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Lung Cancer

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