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PALOMA-2: Subcutaneous Amivantamab Administered Every 4 Weeks Plus Lazertinib in First-Line *EGFR*-Mutated Advanced NSCLC

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Background

PALOMA-2 (MARIPOSA population)

- Amivantamab + lazertinib, a third-generation EGFR TKI, is approved in the US, Europe, and other regions for 1L *EGFR*-mutated advanced NSCLC[1–5]
- In MARIPOSA (NCT04487080), amivantamab IV Q2W + lazertinib significantly prolonged PFS[a] (HR, 0.70; *P*<0.001) and OS[b] (HR, 0.75; *P*<0.005) versus osimertinib[5,6]
  - In the amivantamab + lazertinib arm:
    - BICR-assessed ORR was 86% (95% CI, 83–89) among all participants[5]
    - At a median follow-up of 37.8 months, median OS was not reached; however, the OS benefit vs osimertinib is projected to be >1 year, assuming exponential distribution in both arms[6]
- In Cohorts 1 and 6 of PALOMA-2 (NCT05498428), 1L amivantamab SC Q2W + lazertinib showed a response rate consistent with historical amivantamab IV Q2W + lazertinib[7]

Here we report the efficacy, safety, and PK of 1L amivantamab SC Q4W + lazertinib in *EGFR*-mutated advanced NSCLC

[a]Median follow-up, 22.0 months. [b]Median follow-up, 37.8 months.

1. Moores SL, et al. *Cancer Res*. 2016;76(13):3942-3953. 2. Dhillon S. *Drugs*. 2021;81(9):1107-1113. 3. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]. Janssen Biotech, Inc; 2025. 4. RYBREVANT®: EPAR [product information]. Janssen-Cilag International NV; 2025.
5. Cho BC, et al. *N Engl J Med*. 2024;391(16):1486-1498. 6. Yang J C-H, et al. Presented at: European Lung Cancer Congress (ELCC); March 26-29, 2025; Paris, France. 7. Lim SM, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA.

PALOMA-2 Cohort 5 Study Design

PALOMA-2 (MARIPOSA population)

Key eligibility criteria for Cohort 5 (N=77)

- Treatment-naïve, locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R mutations
- If brain metastases are present, they must be stable[a]
- ECOG PS score of 0 or 1

Amivantamab SC Q4W
+
lazertinib

Prophylactic anticoagulation *recommended* for the first 4 months of treatment

Dosing (in 28-day cycles)

Amivantamab SC[b]:
Subcutaneous abdominal injection with a Q4W dosing regimen of 1600 mg (2240 mg if ≥80 kg) weekly for the first 4 weeks, and 3520 mg (4640 mg if ≥80 kg) Q4W thereafter

Lazertinib: 240 mg orally daily

Primary endpoint:
- ORR by INV[c]

Secondary endpoints:
- ORR by ICR[c]
- Duration of response
- Time to response
- Clinical benefit rate[d]
- Progression-free survival
- Overall survival
- Safety
- PK

[a]Includes asymptomatic or previously treated participants with stable brain metastases. [b]Coformulated with recombinant human hyaluronidase PH20. [c]Tumor response was assessed according to RECIST v1.1. [d]Clinical benefit rate was defined as confirmed response or stable disease for ≥11 weeks.

Baseline Demographics and Clinical Characteristics

PALOMA-2 (MARIPOSA population)

- Cohort 5 enrolled a total of 77 participants
  - Median age was 63 years; 68% were female and 62% were Asian
  - Brain metastases were present in 43% of participants
- As of October 24, 2024, median follow-up was 6.5 months, and 67 (87%) participants were ongoing treatment

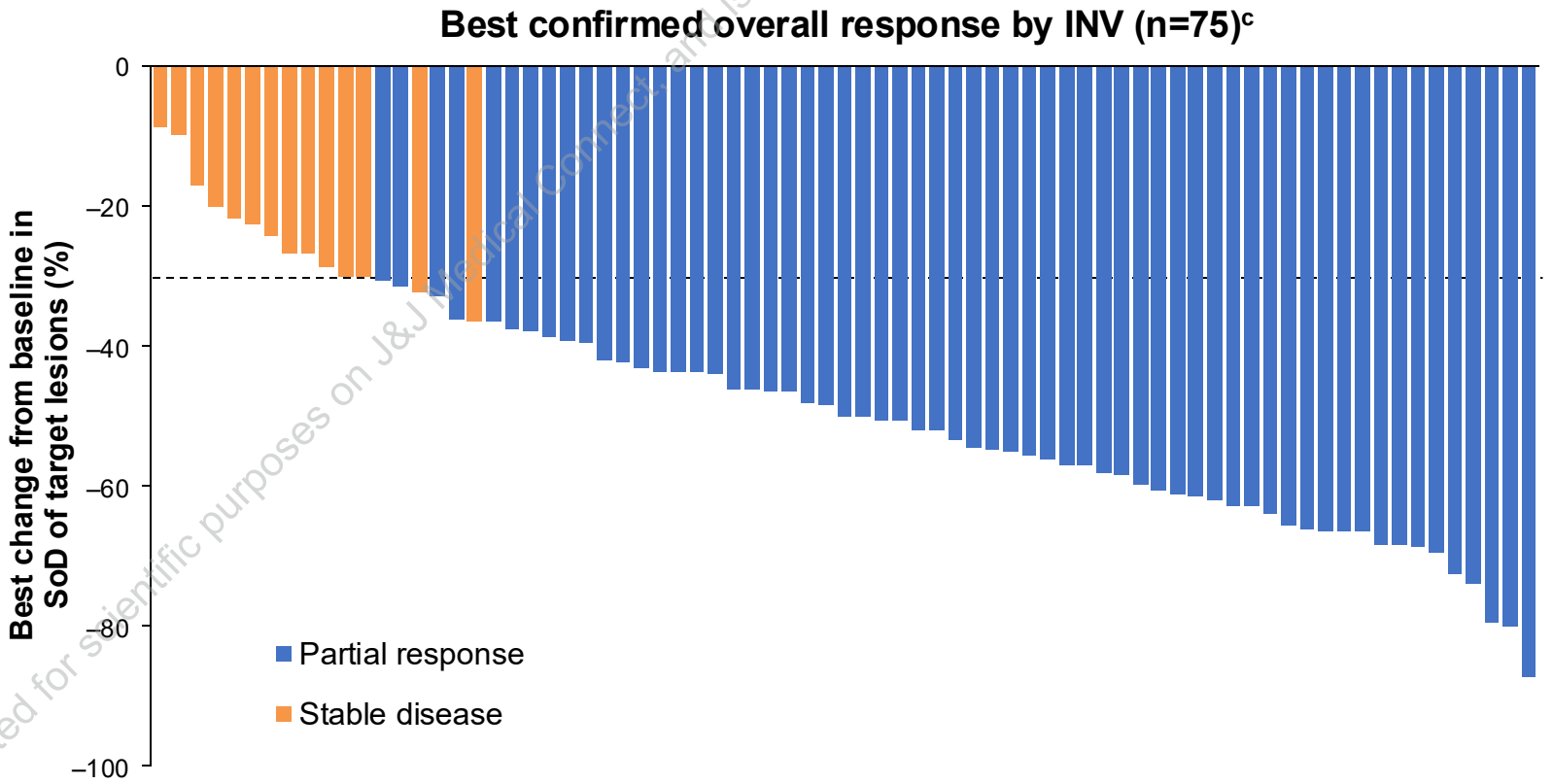
Characteristic, n (%)	Cohort 5 (N=77)
Median age, years (range)	63 (31–80)
Female	52 (68)
Race	
Asian	48 (62)
White	27 (35)
Other[a]	2 (3)
ECOG PS score of 1	52 (68)
History of smoking	25 (32)
Brain metastases	33 (43)
EGFR mutation type[b]	
Exon 19 deletion	46 (60)
L858R	31 (40)
Adenocarcinoma histology	77 (100)

[a]Other includes Black or African American and multiple. [b]Participants could be included in more than 1 category.

ORR and Best Response

PALOMA-2 (MARIPOSA population)

- Among all participants, ORR was 82% (95% CI, 71–90) by INV[a] and 87% (95% CI, 77–94) by ICR
  - Results are consistent with the primary analysis of MARIPOSA, which demonstrated an ORR of 86% (95% CI, 83–89) by BICR with amivantamab IV Q2W + lazertinib[1]
- Confirmed ORR was 79% (95% CI, 69–88) by INV and 83% (95% CI, 73–91) by ICR[b]
- Confirmed CBR was 97% (95% CI, 91–100) by INV and 96% (95% CI, 89–99) by ICR



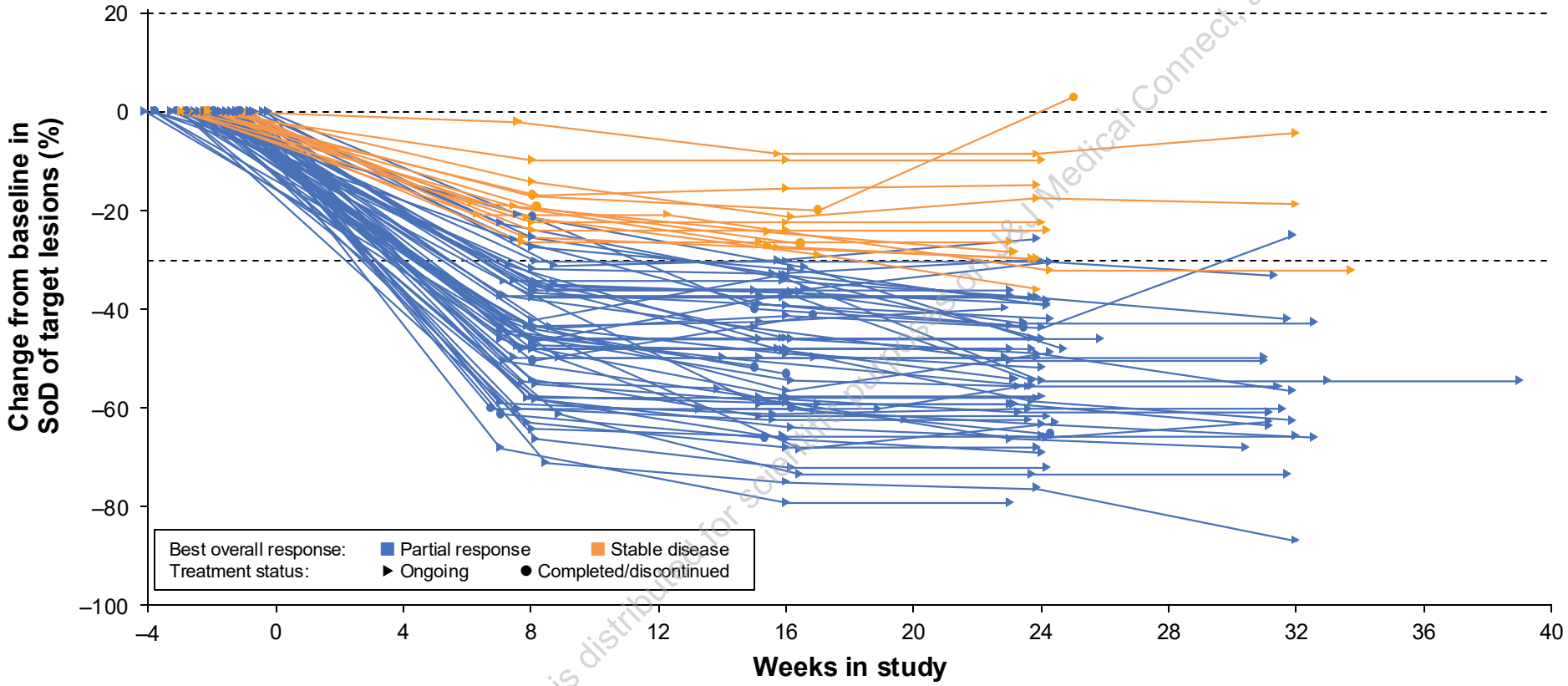
[a]The primary endpoint was met: the null hypothesis of ORR <50% by INV was rejected. [b]Confirmation of responses by repeat assessments were performed ≥4 weeks after the criteria for PR or CR were met. [c]Among participants with measurable disease at baseline.
CBR, dinical benefit rate (defined as confirmed response or stable disease for ≥11 weeks); SoD, sum of diameters.

1. Cho BC, et al. *N Engl J Med*. 2024;391(16):1486-1498.

Antitumor Activity and Secondary Endpoints

PALOMA-2 (MARIPOSA population)

Antitumor activity in participants with measurable disease[a] at baseline (n=75)



- Among confirmed responders:
  - Median time to response was 8.1 weeks (range, 7.0–16.5)
  - Median DoR was not reached for estimation, and the majority of responses were ongoing (93% [57/61])
- Median PFS and OS were not reached for estimation

[a]By INV.
SoD, sum of diameters.

Safety Profile

PALOMA-2 (MARIPOSA population)

- EGFR/MET-related TEAEs were the most common, with no new safety signals identified[1]
  - Discontinuation of all study treatment due to treatment-related AEs occurred in 8% of participants
  - No prophylactic measures for dermatologic AEs were recommended in PALOMA-2
- ARRs[a] occurred in 9 (12%) participants (grade ≥3, 1 [1%]), with the majority occurring at first injection (7/9; 78%)[b]
  - Rate of ARRs was ~5-fold lower compared with amivantamab IV Q2W administration in MARIPOSA (63%)[1]

Pharmacokinetics

- Consistent with historical amivantamab IV and SC Q2W data,[2,c] mean (%CV) amivantamab concentration on Cycle 2 Day 1 was 366 (31) µg/mL (n=56)

Most common TEAEs (≥20%), n (%)	Cohort 5 (N=77)	
	All grades	Grade ≥3
Associated with EGFR inhibition		
Paronychia	56 (73)	4 (5)
Rash	45 (58)	9 (12)
Dermatitis acneiform	31 (40)	6 (8)
Stomatitis	29 (38)	3 (4)
Pruritus	26 (34)	1 (1)
Diarrhea	22 (29)	2 (3)
Associated with MET inhibition		
Hypoalbuminemia	49 (64)	4 (5)
Peripheral edema	28 (36)	0
Other		
Increased ALT	25 (32)	3 (4)
Increased AST	21 (27)	1 (1)
Dry skin	18 (23)	0

[a]ARRs were defined as *Medical Dictionary for Regulatory Activities* preferred term "Administration Related Reaction" (referred to as IRRs in prior studies).[b]On or after Cycle 1 Day 1 but before the next dose. [c]Mean (%CV) concentration on Cycle 2 Day 1 was 317 (32) µg/mL (n=285) for amivantamab IV, 328 (32) µg/mL (n=50) for amivantamab SC in Cohort 1, and 373 (27) µg/mL (n=42) for amivantamab SC in Cohort 6.[2]

1. Cho BC, et al. *N Engl J Med*. 2024;391(16):1486-1498. 2. Lim SM, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA.

VTEs by Prophylactic Anticoagulation Use

PALOMA-2 (MARIPOSA population)

- Incidence of VTE with amivantamab SC Q4W was consistent with the baseline incidence of VTE in NSCLC (14%–30%)[1,2]
- Overall, VTE was reported in 10 (13%) participants (none grade ≥3)
  - There were no dose reductions, discontinuations, or deaths due to VTE
- Majority of participants (87%; 67/77) received prophylactic anticoagulation
- Grade ≥3 bleeding rates were low (1%)

	Prophylactic anticoagulation (n=67)	No prophylactic anticoagulation (n=10)	Overall (N=77)
Any VTE, n (%)	7 (10)	3 (30)	10 (13)
Grade ≥3	0	0	0
Grade 5	0	0	0
Any VTE leading to any discontinuation, n (%)	0	0	0
Grade ≥3 bleeding, n (%)	1 (1)	0	1 (1)

1. Khorana AA, et al. *J Immunother Cancer*. 2023;11(1):e006072. 2. Tagalakis V, et al. *J Thorac Oncol*. 2007;2(8):729-734.

Conclusions

PALOMA-2 (MARIPOSA population)

- Participants receiving 1L amivantamab SC Q4W + lazertinib demonstrated a response rate consistent with those who received amivantamab IV Q2W + lazertinib in MARIPOSA[1]
- No new safety signals were identified with amivantamab SC Q4W + lazertinib[1]
  - ARRs were reduced ~5-fold with amivantamab SC versus amivantamab IV (12% vs 63%)[1]
  - Incidence of VTE was low (13%) and consistent with baseline VTE rates observed in NSCLC[2,3]
- Consistent PK profiles with historical amivantamab IV further support the use of amivantamab SC Q4W + lazertinib[4]
- The Q4W dosing regimen for amivantamab SC + lazertinib is projected to further improve patient convenience

The efficacy of amivantamab SC Q4W + lazertinib is consistent with that of amivantamab IV Q2W + lazertinib,[1] with the added tolerability and convenience benefits of an SC formulation, further supporting it as a new SoC option for patients with *EGFR*-mutated NSCLC

1. Cho BC, et al. *N Engl J Med*. 2024;391(16):1486-1498. 2. Khorana AA, et al. *J Immunother Cancer*. 2023;11(1):e006072. 3. Tagalakis V, et al. *J Thorac Oncol*. 2007;2(8):729-734. 4. Lim SM, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA.

Next: Cohort 7 is Evaluating 2L Amivantamab SC Q3W + Chemotherapy After 1L Amivantamab + Lazertinib

PALOMA-2

PALOMA-2 Study Design *(All Cohorts)*

Eligibility criteria

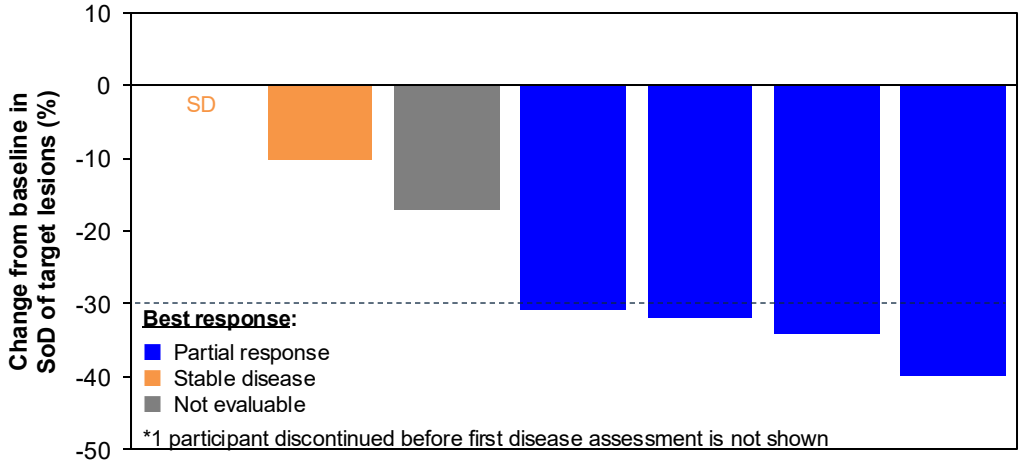
- Locally advanced or metastatic NSCLC
- Stable or asymptomatic brain metastases were allowed
- ECOG PS score of 0 or 1

	Cohort 1 Ex19del/L858R, 1L (MARIPOSA population)	Amivantamab SC Q2W + lazertinib Prophylactic anticoagulation *recommended*
	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)	Amivantamabb SC Q3W + chemotherapy
Enrolling	Cohort 4 Prior amivantamab IV	Amivantamab IV Q2W switch to amivantamab SC Q2W
	Cohort 5 Ex19del/L858R, 1L (MARIPOSA population)	Amivantamab SC Q4W + lazertinib
	Cohort 6 Ex19del/L858R 1L (MARIPOSA population)	Amivantamab SC Q2W + lazertinib Prophylactic anticoagulation *required*
Enrolling	**Cohort 7** Ex19del/L858R, 2L (Post–ami + laz)	Amivantamab SC Q3W + chemotherapy

[a]Participants who had ≥1 disease assessment or discontinued for any reason prior to first disease assessment.
SoD, sum of diameters.

1L amivantamab + lazertinib → PALOMA-2 Coh 7 → 2L amivantamab SC Q3W + chemotherapy

- As of 6 Aug 2025, 10 participants who had disease progression on 1L amivantamab + lazertinib have received 2L amivantamab SC Q3W + platinum-based chemotherapy (median follow-up, 3.6 months)
- Early safety profile consistent with prior report of amivantamab SC + chemotherapy
- Among the 8 response-evaluable participants[a], **ORR was 50%**



Acknowledgments

PALOMA-2 (MARIPOSA population)

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