IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

wclc.iaslc.org #WCLC25

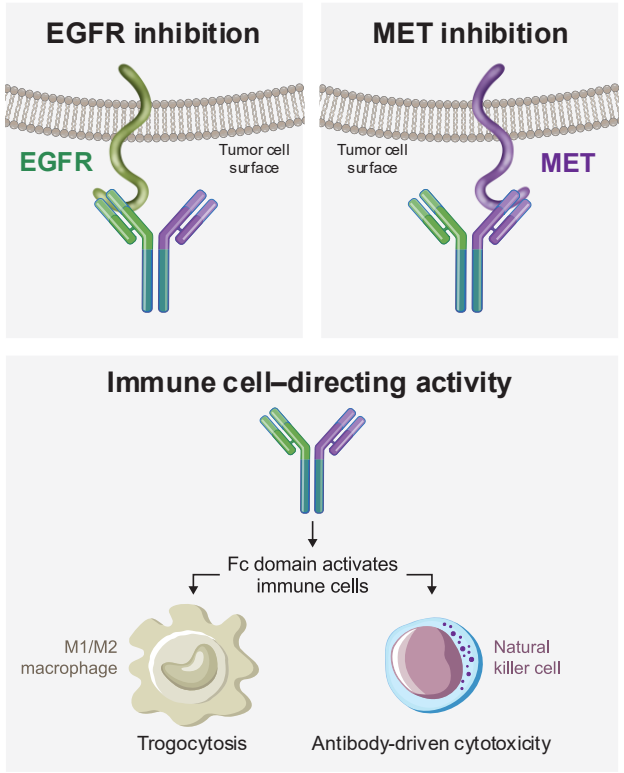
First-Line Subcutaneous Amivantamab Plus Chemotherapy in *EGFR* Exon 20 Insertion-Mutated Advanced NSCLC: Results From PALOMA-2

Sun Min Lim[1], Jiunn Liang Tan[2], Jialei Wang[3], Luis Paz-Ares[4], Noriko Yanagitani[5], Ke-Jing Tang[6], Damien Urban[7], Susan C Scott[8], Achim Rittmeyer[9], Sandrine Hiret[10], Louise C Medley[11], Diego Signorelli[12], Saugata Das[13], Ali Alhadab[14], Miao Wang[14], Janine M Mahoney[15], Jie Zhang[15], Sujay Shah[15], Mahadi Baig[16], Josiane Mourão Dias[17]

[1]Division of Medical Oncology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea; [2]Department of Medicine, University of Malaya Medical Centre, Kuala Lumpur, Malaysia; [3]Department of Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; [4]Hospital Universitario 12 de Octubre, Madrid, Spain; [5]Department of Thoracic Medical Oncology, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; [6]Division of Pulmonary and Critical Care Medicine, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [7]Institute of Oncology, Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel; Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [8]The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [9]Department of Thoracic Oncology, LKI Lungenfachklinik Immenhausen, Immenhausen, Germany; [10]Institut de Cancérologie de l'Ouest, Saint Herblain, France; [11]Torbay and South Devon NHS Foundation Trust, Torquay, UK; [12]Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, Milan, Italy; [13]Johnson & Johnson, Kolkata, India; [14]Johnson & Johnson, San Diego, CA, USA; [15]Johnson & Johnson, Spring House, PA, USA; [16]Johnson & Johnson, Raritan, NJ, USA; [17]Department of Medical Oncology, Barretos Cancer Hospital, Barretos, Brazil

PALOMA-2
(PAPILLON population)

Background



- IV amivantamab combined with chemotherapy is approved for 1L *EGFR* Ex20ins-mutated advanced NSCLC[1–5]
- In PAPILLON[a] (NCT04538664), amivantamab IV Q3W + chemotherapy significantly prolonged median PFS versus chemotherapy (11.4 vs 6.7 months; HR, 0.40; *P*<0.001) with a BICR-assessed ORR of 73%[6]
- In PALOMA-3, amivantamab SC Q2W demonstrated noninferior PK and ORR, fewer IRRs, shorter administration time (<5 min), and higher patient convenience versus amivantamab IV, leading to its approval by the European Commission[7–9]
- PALOMA-2 (NCT05498428) is a phase 2 bridging study evaluating amivantamab-based SC regimens in various *EGFR*-mutated advanced NSCLC settings

Here we report the efficacy, safety, and PK of 1L amivantamab SC Q3W + chemotherapy in *EGFR* Ex20ins-mutated advanced NSCLC

[a]Median follow-up, 14.9 months.

1. Moores SL, et al. *Cancer Res*. 2016;76(13):3942-3953. 2. Vijayaraghavan S, et al. *Mol Cancer Ther*. 2020;19(10):2044-2056. 3. Yun J, et al. *Cancer Discov*. 2020;10(8):1194-1209. 4. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]: Janssen Biotech, Inc; 2025.
5. RYBREVANT®: EPAR [product information]. Janssen-Cilag International NV; 2024. 6. Zhou C, et al. *N Engl J Med*. 2023;389(22):2039-2051. 7. Leighl NB, et al. *J Clin Oncol*. 2024;42(30):3593-3605. 8. Alexander M, et al. *Eur J Cancer*, 2025;227:115624. Online ahead of print.
9. Johnson & Johnson. European Commission approves subcutaneous RYBREVANT® (amivantamab) for the treatment of patients with advanced *EGFR*-mutated non-small cell lung cancer. April 7, 2025. Accessed June 20, 2025.

PALOMA-2 Cohort 2 Study Design

PALOMA-2
(PAPILLON population)

Key eligibility criteria for Cohort 2 (N=66)

- Treatment-naïve, locally advanced or metastatic NSCLC
- Documented *EGFR* Ex20ins mutations
- If brain metastases are present, they must be stable[a]
- ECOG PS score of 0 or 1

Amivantamab SC Q3W
+
chemotherapy

Dosing (in 21-day cycles)

Amivantamab SC[b]:
Subcutaneous abdominal injection at 1600 mg (2240 mg if ≥80 kg) on Cycle 1 Day 1, then 2400 mg (3360 mg if ≥80 kg) on Days 8 and 15 of Cycle 1, and Q3W thereafter.

Chemotherapy on the first day of each cycle:
- **Carboplatin:** AUC5 for a maximum of 4 cycles
- **Pemetrexed:** 500 mg/m^2 until disease progression

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 (PAPILLON population)

- Cohort 2 enrolled a total of 66 participants
  - Median age was 63 years; 52% were male and 56% were Asian
- As of October 24, 2024, the median follow-up was 10.4 months, with a median treatment duration of 9.3 months
  - As of the data cutoff, 37 (56%) participants remained on treatment

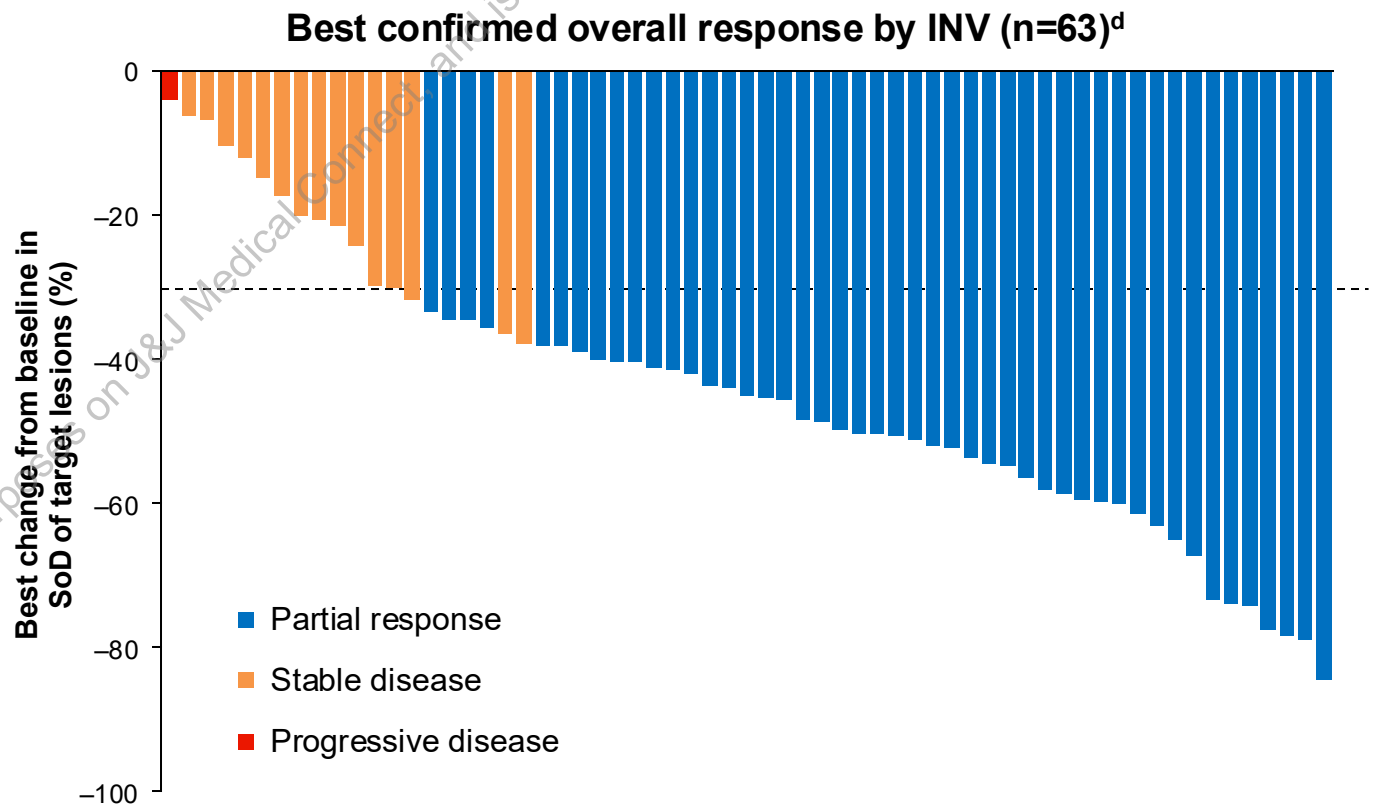
Characteristic, n (%)	Cohort 2 (N=66)
Median age, years (range)	63 (31–80)
Male	34 (52)
Race	
Asian	37 (56)
White	27 (41)
Other[a]	2 (3)
ECOG PS score of 1	42 (64)
History of smoking	24 (36)
Brain metastases	24 (36)
EGFR mutation type[b]	
Ex20ins	66 (100)
Ex19del	1 (2)
L858R	1 (2)
Adenocarcinoma histology	64 (97)

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

ORR and Best Response

PALOMA-2 (PAPILLON population)

- Among all participants, ORR was 76% (95% CI, 64–86) by INV[a] and 77% (95% CI, 65–87) by ICR[a]
  - Results are consistent with the primary analysis of PAPILLON, which demonstrated an ORR of 73% (95% CI, 65–80) by BICR[b] with amivantamab IV Q3W + chemotherapy[1]
- Confirmed ORR was 71% (95% CI, 59–82) by INV and 67% (95% CI, 54–78) by ICR[c]
- Confirmed CBR was 94% (95% CI, 85–98) by INV and 89% (95% CI, 79–96) by ICR
- Among confirmed responders:
  - Median time to response was 6.4 weeks (range, 3.5–21.7)
  - Median DoR was 10.6 months (95% CI, 8.3–NE), and the majority of responses were ongoing (66% [31/47])
  - 62% (29/47) of participants had a response duration ≥6 months



[a]The primary endpoint was met: the null hypothesis of ORR <25% by INV was rejected. [b]In PAPILLON, ORR by INV was 66% (95% CI, 58–74) for amivantamab IV Q3W + chemotherapy. [c]Confirmation of responses by repeat assessments were performed ≥4 weeks after the criteria for PR or CR were met. [d]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.

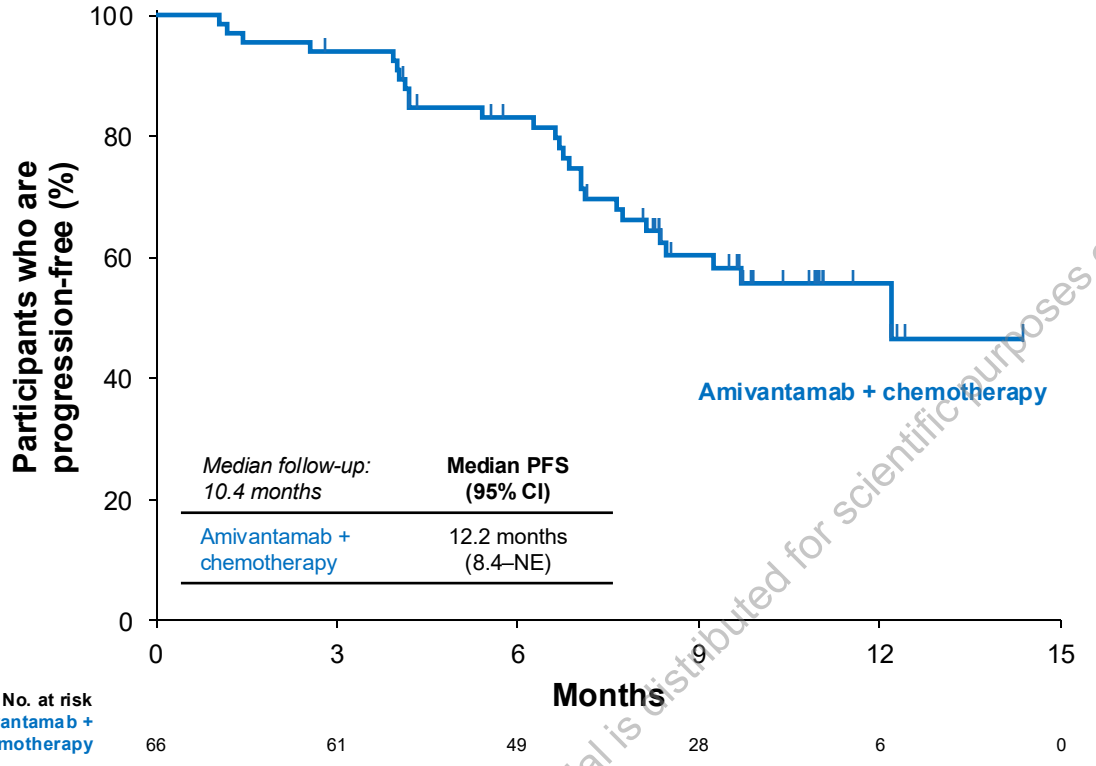
1. Zhou C, et al. *N Engl J Med.* 2023;389(22):2039-2051.

PFS and OS

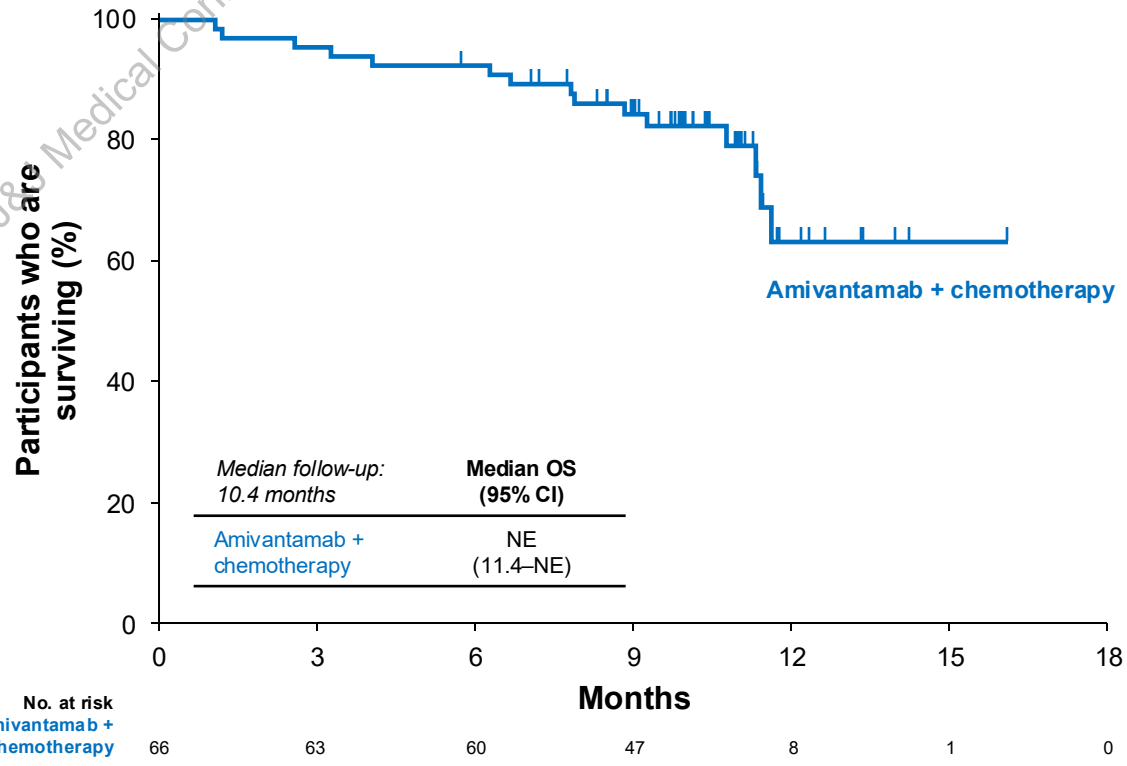
PALOMA-2 (PAPILLON population)

- At a median follow-up of 10.4 months, median PFS was 12.2 months, and OS was NE, consistent with the primary analysis of PAPILLON[a]

Progression-free survival



Overall survival



[a]In PAPILLON, INV-assessed PFS was 12.9 months (95% CI, 11.4–16.7), and OS was NE for amivantamab IV Q3W + chemotherapy, at a median follow-up of 14.9 months.[1]

1. Zhou C, et al. *N Engl J Med.* 2023;389(22):2039-2051.

Safety Profile

PALOMA-2 (PAPILLON population)

- EGFR/MET-related and hematologic TEAEs were the most common, and no new safety signals were identified[1]
  - Discontinuation of amivantamab SC due to treatment-related AEs occurred in 12% of participants
- ARRs[a] were reported in 4 (6%) participants (none grade ≥3), and all occurred at the first injection[b]
  - Median time to ARR onset was 1.6 hours (range, 0.7–2.4) and median duration of ARR was 7.2 hours (range, 0.3–14.0)
  - Rate of ARRs was 7-fold lower compared with amivantamab IV Q3W administration in PAPILLON (42%)[1]
- Consistent with historical amivantamab IV Q3W data,[2,c] mean (%CV) amivantamab plasma concentration on Cycle 2 Day 1 was 439 (27) µg/mL (n=41)

Most common TEAEs (≥25%), n (%)	Cohort 2 (N=66)	
	All grades	Grade ≥3
Associated with EGFR inhibition		
Paronychia	45 (68)	3 (5)
Rash	30 (45)	6 (9)
Dermatitis acneiform	26 (39)	3 (5)
Stomatitis	24 (36)	4 (6)
Associated with MET inhibition		
Hypoalbuminemia	36 (55)	7 (11)
Peripheral edema	27 (41)	1 (2)
Other		
Neutropenia[d]	33 (50)	19 (29)
Nausea	31 (47)	1 (2)
Anemia	30 (45)	10 (15)
Thrombocytopenia[d]	27 (41)	9 (14)
Constipation	23 (35)	0
Increased ALT	21 (32)	1 (2)
Increased AST	19 (29)	1 (2)
Leukopenia	18 (27)	4 (6)

[a]ARRs were defined as *Medical Dictionary for Regulatory Activities* preferred term (referred to as IRRs in prior IV studies). [b]On or after Cycle 1 Day 1 but before the next dose. [c]Mean (%CV) amivantamab plasma concentration on Cycle 2 Day 1 was 365 (30) µg/mL (n=140) for amivantamab IV in PAPILLON.[2] [d]Decreases in neutrophil and platelet counts were transient during Cycle 1 followed by recovery by Cycle 2 Day 1 and stabilization thereafter.

ARR, administration-related reaction; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event.

1. Zhou C, et al. *N Engl J Med*. 2023;389(22):2039-2051. 2. Data on file.

Conclusions

PALOMA-2 (PAPILLON population)

- Participants receiving 1L amivantamab SC Q3W + chemotherapy demonstrated consistent ORR, DoR, PFS, and OS with those who received amivantamab IV Q3W + chemotherapy in PAPILLON[1]
- No new safety signals were identified with amivantamab SC Q3W + chemotherapy
  - ARRs were reduced 7-fold with amivantamab SC versus historical IV data (6% vs 42%)[1]
- Consistent PK profiles with historical amivantamab IV Q3W data further support the use of amivantamab SC Q3W + chemotherapy

The efficacy of amivantamab SC Q3W + chemotherapy is consistent with that of amivantamab IV Q3W + chemotherapy,[1] with the added tolerability and convenience benefits of an SC formulation, further supporting it as a new SoC for patients with *EGFR* Ex20ins-mutated NSCLC

1. Zhou C, et al. *N Engl J Med.* 2023;389(22):2039-2051.

Acknowledgments

PALOMA-2
(PAPILLON population)

- Participants who were enrolled in the study and their families and caregivers
- Physicians and nurses who cared for participants and staff members who supported this clinical trial
- Staff members at the study sites and involved in data collection/analyses
- Medical writing assistance was provided by Lumanity Communications Inc. and funded by Johnson & Johnson