PALOMA-3: Subcutaneous Amivantamab in Combination With Lazertinib

PALOMA-3: Phase 3 Study of Subcutaneous Amivantamab Compared with Intravenous Amivantamab, Both in Combination with Lazertinib, in Refractory *EGFR*-mutated NSCLC[1]

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Disease had progressed on or after osimertinib and platinum-based chemotherapy, irrespective of order
- Documented *EGFR* Ex19del or L858R
- ECOG PS 0–1

1:1 Randomization (N=418)

- **SC Amivantamab + Lazertinib (n=206)**
- **IV Amivantamab + Lazertinib (n=212)**

Prophylactic anticoagulation recommended for the first 4 months of treatment

Dosing (in 28-day cycles)

SC amivantamab*,† (co-formulated with rHuPH20 and administered by manual injection): 1600 mg (2240 mg if ≥80 kg) weekly for the first 4 weeks, then every 2 weeks thereafter

IV amivantamab†: 1050 mg weekly (1400 mg if ≥80 kg) for the first 4 weeks, then every 2 weeks thereafter

Lazertinib: 240 mg PO daily

Co-Primary Endpoints:

- C_{trough} (noninferiority)
- C2 AUC (noninferiority)

Key Secondary Endpoints:

- ORR (noninferiority)
- PFS (superiority)
- Patient-reported outcomes
- Safety
- Health care resource utilization

Predefined Exploratory Endpoint:

- OS

SC Amivantamab Demonstrated PK Non-inferiority and Sustained Amivantamab Exposure Compared with IV Amivantamab, While Reducing ARRs and Improving Patient Convenience[1,2]

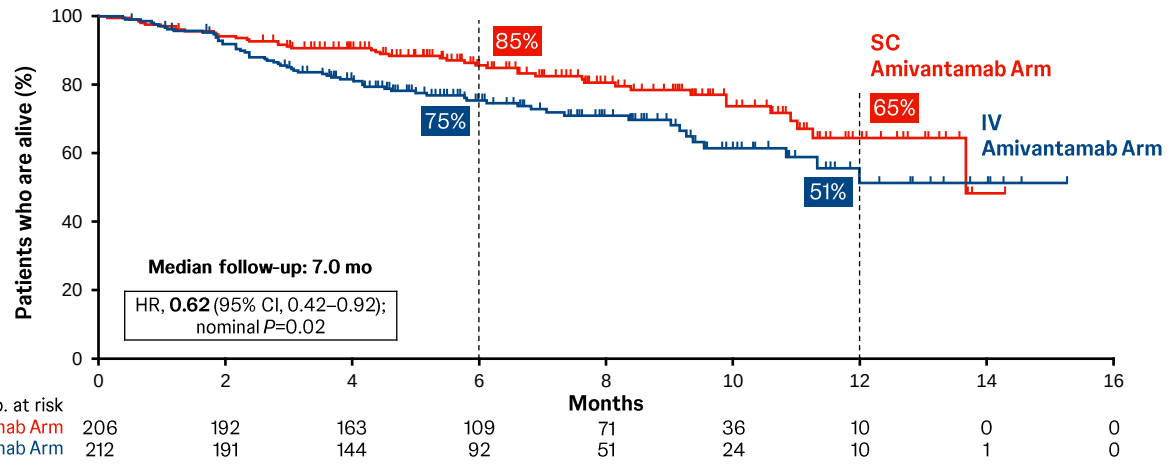
Compared with IV amivantamab plus lazertinib, SC amivantamab plus lazertinib demonstrated:

- Noninferior PK and sustained amivantamab exposure
- Comparable antitumor response and survival outcomes
- Shorter administration time
- Enhanced patient convenience
- Reduced ARRs and VTEs

Key Primary and Secondary Endpoints

Endpoint	SC Amivantamab Arm (n=206)	IV Amivantamab Arm (n=212)
Co-primary Endpoints		
C_{trough} at C2D1, GMR (90% CI)	1.15 (1.04–1.26)	
C2 $AUC_{D1–D15}$, GMR (90% CI)	1.03 (0.98–1.09)	
C_{trough} at steady state (C4D1), GMR (90% CI)	1.43 (1.27–1.61)	
Secondary Endpoints		
ORR, % (95% CI)	30 (24–37)	33 (26–39)
PFS, median (95% CI)	6.1 mo (4.3–8.1)	4.3 mo (4.1–5.7)
	HR, 0.84 (95% CI, 0.64-1.10) *P*=0.20	

Exploratory Endpoint: Overall Survival†



P value was nominal; the prespecified endpoint was exploratory and not part of hierarchical hypothesis testing.

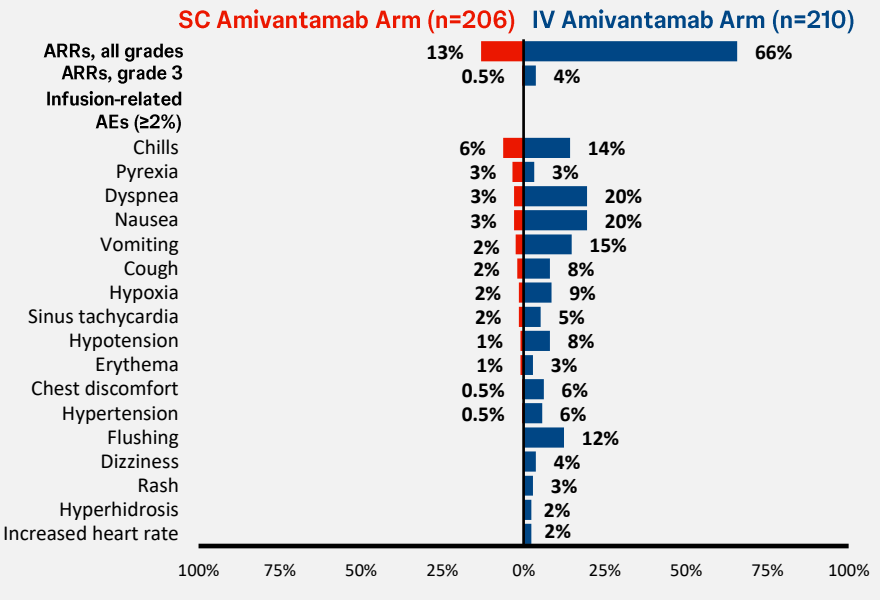
Compared to IV Amivantamab, SC Amivantamab Demonstrated a 5-fold Reduction in ARRs[1]

Consistent TEAEs Between Arms‡

	SC Amivantamab Arm (n=206)	IV Amivantamab Arm (n=210)
Paronychia	54% (Grade ≥3: 4%)	51% (Grade ≥3: 1%)
Rash	46% (Grade ≥3: 4%)	43% (Grade ≥3: 4%)
Dermatitis acneiform	31% (Grade ≥3: 9%)	33% (Grade ≥3: 6%)
Venous thromboembolism	9% (Grade ≥3: 2%)	14% (Grade ≥3: 0.6%)

Prophylactic anticoagulation was recommended for the first 4 months of treatment, with 80% and 81% of patients in the SC and IV arms, respectively, receiving prophylactic anticoagulation.

Fewer ARRs in the SC Arm



Shorter Administration Times and Enhanced Patient Convenience were Observed with SC Compared to IV Amivantamab[1,2]

- Administration time <5 minutes vs 5 hours
- **>80%** of SC patients found the injection convenient
  C1D1: 85% vs 52% EOT: 85% vs 35%
- **>75%** of SC patients preferred SC administration as a way to receive cancer treatment
  C1D1: 77% C3D1: 81%

*SC amivantamab was co-formulated with rHuPH20 at a concentration of 160 mg/mL. †C1 for IV: Days 1 to 2 (Day 2 applies to IV split dose only [350 mg on Day 1 and the remainder on Day 2]), 8, 15, and 22; C1 for SC: Days 1, 8 , 15, and 22; after C1 for all: Days 1 and 15 (28-day cycles). ‡Select TEAEs of interest are being displayed.

AE, adverse event; ARR, administration-related reaction; AUC, area under the curve; C, Cycle; CI, confidence interval; C_{trough}, observed serum concentration of amivantamab at steady state; D, Day; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; EOT, end of treatment; GMR, geometric mean ratio; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; PO, oral; rHuPH20, hyaluronidase; SC, subcutaneous; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

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1. Leighl NB, et al. *J Clin Oncol*. 2024;42(30):3593-3605. 2. Alexander M, et al. *Eur J Cancer*. 2025;227:115624.