COPERNICUS

1L SC ami + laz in common *EGFR* NSCLC

COPERNICUS, a Pragmatic Phase 2b Study of First-Line Subcutaneous Amivantamab + Lazertinib With Supportive Care in *EGFR*-Mutated Advanced NSCLC: Early Safety Results

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Background

- In MARIPOSA (NCT04487080), 34% of participants with 1L common *EGFR*-mutated advanced NSCLC discontinued IV amivantamab due to AEs, including IRRs, VTE, and dermatologic AEs[1,2]
- Despite these discontinuations, IV amivantamab + lazertinib significantly improved median OS vs osimertinib (HR, 0.75; *P*=0.005), with the median OS benefit projected to exceed 1 year (not estimable at time of last data cutoff)[3]
- Several studies have evaluated different approaches to improve treatment administration and the patient experience with amivantamab + lazertinib
  - In PALOMA-3 (NCT05388669) and PALOMA-2 (NCT05498428), SC amivantamab (co-formulated with recombinant human hyaluronidase PH20) reduced ARRs, treatment administration time (≤5 minutes vs 2–5 hours), and VTE, which was further reduced with prophylactic anticoagulation, compared with IV amivantamab[4,5]
  - In Cohort 5 of PALOMA-2, SC amivantamab Q4W was evaluated, showing an overall response rate of 82% and a clinical benefit rate of 97%[5]
    - Based on PALOMA, PALOMA-2, and PALOMA-3 data, SC amivantamab has been approved in several markets, including the United States, Europe, Japan, and China[6–9]
  - In COCOON (NCT06120140), an enhanced prophylactic dermatologic regimen significantly reduced grade ≥2 dermatologic AEs versus standard of care (42% vs 75%; *P*<0.0001)[10]
- In COPERNICUS (NCT06667076), we present early results on participant demographics and safety of SC amivantamab administered Q4W + lazertinib in participants from the US with 1L common *EGFR*-mutated advanced NSCLC who also received VTE and dermatologic AE prophylaxis

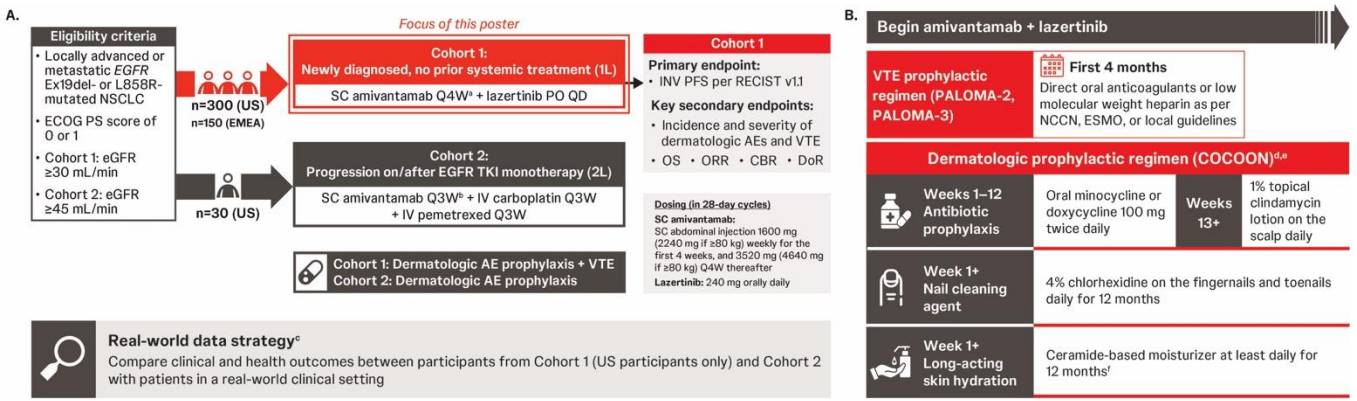
1L, first-line; AE, adverse event; ARR, administration-related reaction; EGFR, epidermal growth factor receptor; HR, hazard ratio; IRR, infusion-related reaction; IV, intravenous; NSCLC, non-small cell lung cancer; OS, overall survival; Q4W, every 4 weeks; SC, subcutaneous; VTE, venous thromboembolism.

1. Cho BC, et al. *N Engl J Med*. 2024;391(16):1486–1498. 2. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [package insert]. Janssen Biotech, Inc.; 2025. 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: International Association for the Study of Lung Cancer (IASLC) World Conference on Lung Cancer (WCLC); September 6–9, 2025; Barcelona, Spain. 6. RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) injection, for subcutaneous use [package insert]. Janssen Biotech, Inc.; 2026. 7. RYBREVANT® EPAR [product information]. Janssen-Cilag International NV; 2025. 8. RYBROFAZ® combination subcutaneous injection [package insert]. Janssen Pharmaceutical K.K.; 2025. 9. RYBREVANT FASPRO is for subcutaneous use only [package insert]. Janssen-Cilag AG; 2025.
10. Cho BC, et al. *J Thorac Oncol*. 2025;20(10):1517–1530.

Methods

- COPERNICUS is one of the largest studies enrolling in the US to evaluate common *EGFR*-mutated advanced NSCLC (**Figure 1A**)
- The pragmatic design included partnering with academic/community sites, reducing the stringency of inclusion criteria, allowing 1 cycle of 1L chemotherapy, streamlining schedule of assessments to mirror local practices in the US, and using SC amivantamab monthly to reduce visit frequency
- Participants received prophylactic anticoagulation for the first 4 months of treatment; enhanced dermatologic prophylaxis aligned with the regimen described in COCOON (**Figure 1B**)
- This early safety analysis included incidence and severity of VTE, ARRs, and dermatologic AEs in the US population

Figure 1: (A) COPERNICUS study design and (B) prophylaxis for dermatologic AEs and VTE[1–3]



- To further characterize these findings, a descriptive comparison with data from MARIPOSA was included
- Safety and efficacy in the COPERNICUS study will continue to be evaluated as data mature

COPERNICUS (ClinicalTrials.gov Identifier: NCT06667076).
[a]In 28-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. [b]In 21-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. [c]The real-world comparison will be assessed under a separate protocol. [d]Prophylactic antibiotics: oral doxycycline or minocycline 100 mg BID and topical clindamycin lotion 1% on the scalp daily before bedtime. Paronychia prophylaxis: chlorhexidine 4% on the fingernails and toenails daily. Skin moisturization of the body and face at least daily. [e]Tacrolimus was added as a reactive management recommendation in COPERNICUS based on positive results from the COCOON treatment substudy.[4] In addition, a protocol amendment for COPERNICUS recommended zinc supplementation for participants with established zinc deficiency who experienced dermatologic AEs. [f]La Roche-Posay Lipikar AP+M moisturizer was used in COCOON.
1L, first-line; 2L, second-line; AE, adverse event; ARR, administration-related reaction; CBR, clinical benefit rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; EGFR, epidermal growth factor receptor; EMEA, Europe, the Middle East, and Africa; ESMO, European Society for Medical Oncology; Ex19del, exon 19 deletion; INV, investigator-assessed; IV, intravenous; L858R, exon 21 L858R substitution; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PO, orally; Q3W, every 3 weeks; Q4W, every 4 weeks; QD, once a day; RECIST, Response Evaluation Criteria in Solid Tumors; SC, subcutaneous, VTE, venous thromboembolism.
1. Leighl NB, et al. *J Clin Oncol*. 2024;42(30):3593–3605. 2. Cho BC, et al. *J Thorac Oncol*. 2025;20(10):1517–1530. 3. Lim SM, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA. 4. Spira AI, et al. Presented at: International Association for the Study of Lung Cancer (IASLC) | American Society of Clinical Oncology (ASCO) North America Conference on Lung Cancer (NACLC); December 5–7, 2025; Chicago, IL, USA.

Results: Baseline demographic and clinical characteristics

- As of the clinical cutoff (March 16, 2026), Cohort 1 had enrolled 235 participants in the US
  - Median (range) follow-up was 4.9 (<0.1–15.7) months, and 89% of participants were still ongoing in the study
- The pragmatic design supported broad participant enrollment (**Table 1**)
  - Median age was 66 years, with 56% of participants ≥65 and 21% ≥75 years of age, which is higher than the amivantamab + lazertinib arm from MARIPOSA (45% were ≥65 and 12% were ≥75 years of age)[1]
  - 26% were Asian, 9% were Black or African American, and 12% were Hispanic or Latino
  - 6 (3%) participants had received 1 chemotherapy cycle

Table 1: Baseline demographic and clinical characteristics

Characteristic, n (%)	SC amivantamab Q4W + lazertinib (n=235)
Median (range) age, years	66 (34–90)
≥65 years	131 (56)
≥75 years	50 (21)
Female	153 (65)
Race	
White	122 (52)
Asian	62 (26)
Black or African American	22 (9)
Other[a]	29 (12)
Hispanic or Latino	29 (12)
ECOG PS score	
0	109 (46)
1	126 (54)
History of smoking	74 (31)
Brain metastases at screening	90 (38)
***EGFR* mutation type[b]**	
Ex19del	141 (60)
L858R	94 (40)
Received 1 cycle of chemotherapy prior to study enrollment[c]	6 (3)

[a]Includes American Indian or Alaska Native (<1%), Native Hawaiian or other Pacific Islander (<1%), unknown (5%), and not reported (6%). [b]Participants may have both Ex19del and L858R. [c]Includes adjuvant (17%), curative/palliative/any other intent (50%), and neoadjuvant (33%).
ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; L858R, exon 21 L858R substitution; Q4W, every 4 weeks; SC, subcutaneous.
1. Cho BC, et al. *N Engl J Med*. 2024;391(16):1486–1498.

Results: Safety

- With enhanced dermatologic prophylaxis, paronychia and rash (preferred terms) occurred in 33% (grade ≥3, 3%) and 24% (grade ≥3, 4%) of participants, respectively, showing numerical reductions versus MARIPOSA (**Figure 2**)[1]
- Incidence of ARR was 0.9% (none grade ≥3), which was substantially reduced vs MARIPOSA (**Figure 2**)[1]
- Additionally, VTE (grouped term) was numerically lower at 9% (grade ≥3, 2%; **Figure 2**)
  - No grade ≥3 bleeding event was reported in COPERNICUS
- In an additional descriptive comparison of COPERNICUS with data from the first 4 months of treatment in MARIPOSA, consistent numerical reductions were seen for TEAEs of interest in COPENICUS (**Table 2**)
- 18 (8%) participants discontinued amivantamab due to AEs; of those, 14 (6% of the total cohort) discontinued due to treatment-related AEs
- AEs were mostly grade 1 to 2, with no new safety signals identified (**Table 3**)

Figure 2: Prevalence of TEAEs of interest in COPERNICUS (n=235) and MARIPOSA (n=421; median follow-up, 22.0 months)[1]

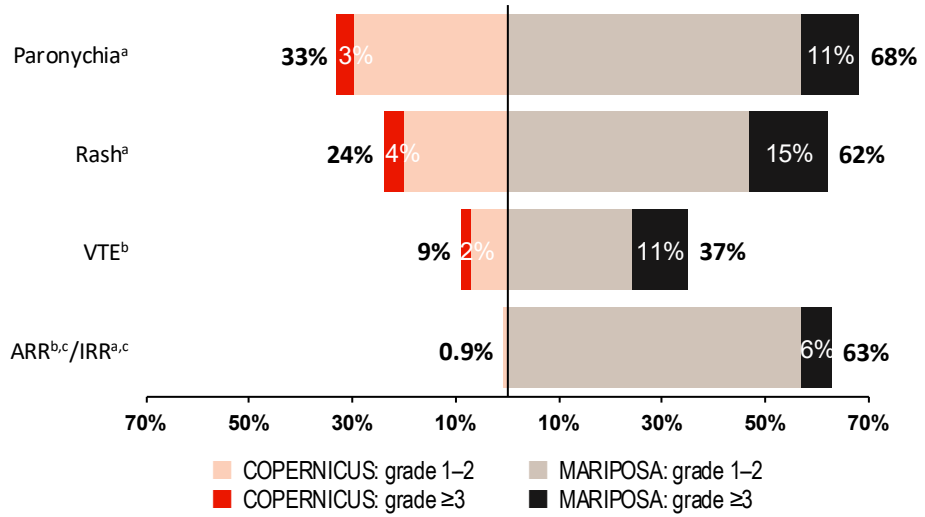


Table 2: Prevalence of TEAEs of interest in COPERNICUS and MARIPOSA (within 4 months of treatment)

TEAEs of interest, %	COPERNICUS (n=159)		MARIPOSA (n=421)	
	All grades	Grade ≥3	All grades	Grade ≥3
Paronychia[a]	37	1	50	4
Rash[a]	25	3	55	7
VTE[b]	3	1	23	6
ARR[b,c]/IRR[a,c]	1	0	55	5

Table 3: TEAEs

TEAEs by preferred term (≥20%), n (%)	SC amivantamab Q4W + lazertinib (n=235)	
	All grades	Grade ≥3
EGFR-related		
Fatigue	98 (42)	9 (4)
Dermatitis acneiform	82 (35)	9 (4)
Stomatitis	79 (34)	7 (3)
Paronychia	77 (33)	6 (3)
Diarrhea	68 (29)	4 (2)
Rash	56 (24)	10 (4)
Pruritus	51 (22)	1 (<1)
MET-related		
Peripheral edema	79 (34)	4 (2)
Hypoalbuminemia	69 (29)	10 (4)
Other		
Nausea	94 (40)	2 (<1)
Constipation	60 (26)	0
Increased alanine aminotransferase	55 (23)	11 (5)
Decreased appetite	49 (21)	1 (<1)
Myalgia	48 (20)	0

Note: No formal, head-to-head statistical comparison was performed. These results are presented for contextual reference only and should not be used for direct comparison.

[a]Preferred term. [b]Grouped term. [c]The term ARR was used in COPERNICUS and the term IRR was used in MARIPOSA.

AE, adverse event; ARR, administration-related reaction; EGFR, epidermal growth factor receptor; IRR, infusion-related reaction; Q4W, every 4 weeks; SC, subcutaneous; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

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

Conclusions

- Enhanced dermatologic and VTE prophylaxis led to a low incidence of grade ≥3 rash (<5%) and any grade VTE (<10%); however, inference is limited due to shorter and more heterogeneous follow-up than in MARIPOSA[1]
- The frequency of ARRs was very low (<1%) with SC amivantamab

Key Takeaways

- COPERNICUS early safety data support wide use of SC amivantamab Q4W + lazertinib in patients with 1L *EGFR*-mutated advanced NSCLC
- COPERNICUS has enrolled rapidly in the US, demonstrating the feasibility of treating a more representative real-world population

1L, first-line; ARR, administration-related reaction; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; Q4W, every 4 weeks; SC, subcutaneous; VTE, venous thromboembolism.

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