

Subcutaneous amivantamab + lazertinib with supportive care in *EGFR*-mutant NSCLC: longer follow-up from the pragmatic COPENICUS study

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Key Takeaway

COPENICUS safety data show that dermatologic and venous thromboembolism (VTE) prophylaxis reduces the incidence of adverse events of special interest (AESIs) and support the broad use of subcutaneous (SC) amivantamab + lazertinib as foundational first-line (1L) therapy for patients with epidermal growth factor receptor (*EGFR*)–mutated advanced non-small cell lung cancer (NSCLC)

Conclusions

COPENICUS, with its pragmatic design, supported enrollment of a more representative real-world population

- This analysis focused on Cohort 1 participants who were enrolled ≥4 months prior to data cutoff (June 12, 2026)

Dermatologic and VTE prophylaxis with SC amivantamab + lazertinib led to a reduction in administration-related reactions (ARRs), rash, VTE, and paronychia compared with MARIPOSA¹

Amivantamab discontinuations by 1 year due to ARRs, rash, or VTE were markedly lower in COPENICUS (<1% vs 9% in MARIPOSA)

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Disclosures

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Background

- In MARIPOSA (ClinicalTrials.gov identifier: NCT04487080), intravenous (IV) amivantamab + lazertinib significantly prolonged overall survival (OS) versus osimertinib in participants with 1L common *EGFR*-mutated advanced NSCLC (hazard ratio [HR], 0.75; *P*=0.005); 34% of participants discontinued amivantamab due to treatment-emergent adverse events (TEAEs)^{2,3}
 - Infusion-related reactions (IRRs), rash, and VTE were more common within the first 4 months of amivantamab + lazertinib treatment^{1,4}
- SC amivantamab (co-formulated with recombinant human hyaluronidase PH20) and enhanced prophylactic treatment protocols have substantially reduced administration time, as well as rates and severity of TEAEs of interest seen in MARIPOSA^{5–7}
- COPENICUS (NCT06667076) Cohort 1 evaluates SC amivantamab + lazertinib in 1L *EGFR*-mutated NSCLC using a pragmatic design that closely mirrors the real-world setting in addition to VTE and dermatologic prophylaxis
 - A prior report (median follow-up, 4.9 months) among US participants demonstrated low rates of ARRs (0.9%), VTE (9%), and grade ≥3 rash (preferred term; 4%)⁸
- Here, we characterize early-onset TEAEs after longer follow-up in a subset of COPENICUS Cohort 1 participants enrolled ≥4 months prior to data cutoff (June 12, 2026; this population included those who prematurely discontinued treatment)

Results

Baseline demographic and clinical characteristics

- 274 participants were enrolled in the US
- 214 were enrolled ≥4 months prior to data cutoff (June 12, 2026; **Table 1**)
 - This population included those who prematurely discontinued treatment
- Notably, 56% and 22% of the 214 participants were ≥65 and ≥75 years of age, respectively; this is higher than MARIPOSA (45% were ≥65 years of age and 12% were ≥75 years of age)^{1,8}
- The COPENICUS pragmatic design allowed for enrollment of a population with a higher level of racial and ethnic diversity compared with other studies of *EGFR* inhibitors^{1,8}

Table 1: Baseline demographic and clinical characteristics

Characteristic, n (%)	SC amivantamab Q4W + lazertinib (n=214)
Median (range) age, years	67 (34–90)
≥65 years	120 (56)
≥75 years	47 (22)
Female	141 (66)
Race	
White	107 (50)
Asian	58 (27)
Black or African American	22 (10)
Other ^a	27 (13)
Hispanic or Latino	22 (10)
ECOG PS score of 1	117 (55)
History of smoking	67 (31)
Brain metastases at screening	80 (37)
<i>EGFR</i> mutation type	
Ex19del	124 (58)
L858R	90 (42)
Received 1 cycle of chemotherapy prior to enrollment ^b	6 (3)

^aIncludes American Indian or Alaska Native (<1%), Native Hawaiian or other Pacific Islander (<1%), unknown (5%), and not reported (7%). ^bIncludes 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.

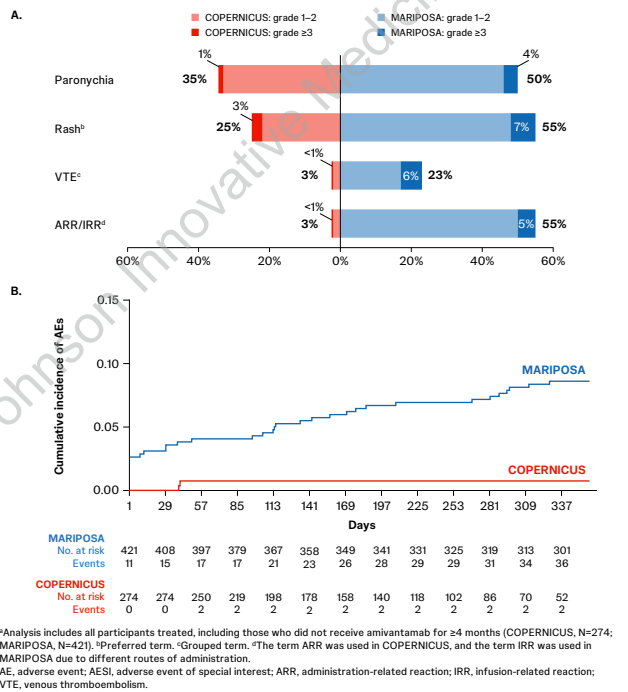
Safety

- Paronychia, rash, VTE, and ARRs/IRRs during the first 4 months of treatment were reduced in COPENICUS versus MARIPOSA (**Figure 2A**)
- In COPENICUS, 1 participant each discontinued amivantamab due to rash and VTE in the first 4 months; none discontinued due to ARRs
- 1-year cumulative incidence of amivantamab discontinuations due to selected AESIs was <1% in COPENICUS versus 9% in MARIPOSA (**Figure 2B**)

Methods

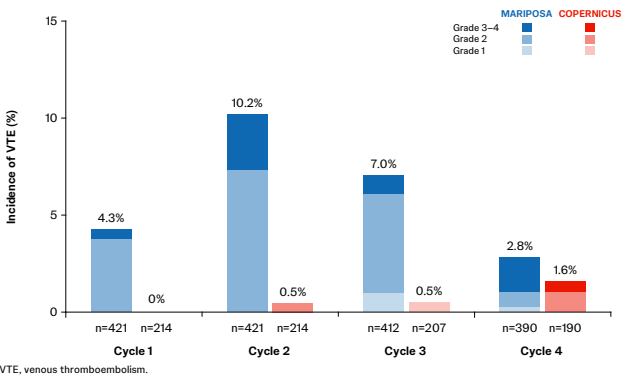
- Participants in COPENICUS Cohort 1 received SC amivantamab every 4 weeks + oral lazertinib daily as well as dermatologic adverse event (AE) and VTE prophylaxis (**Figure 1**)
- Notably, no formal, head-to-head statistical comparison was performed; because follow-up in COPENICUS is limited, results are presented for contextual reference only and should not be used for direct comparison
 - Follow-up durations were different between COPENICUS and MARIPOSA
- TEAE was defined as any new or worsening AE occurring from initial study treatment through 30 days post–last dose, or prior to subsequent systemic anticancer therapy, whichever is earlier

Figure 2: (A) Selected AESIs in the first 4 months of amivantamab + lazertinib and (B) cumulative incidence of IRR/ARR, VTE, and rash leading to amivantamab discontinuation^a



- Incidence of VTE during the first 4 months of treatment was reduced in COPENICUS versus MARIPOSA (3% vs 23%, respectively; **Figure 3**)
 - No grade ≥3 bleeding events were reported in COPENICUS⁸
- In COPENICUS, rates of VTE were similar across age subgroups (3.2% vs 2.5% in <65 vs ≥65 years, respectively)
 - These data are not based on a formal subgroup comparison

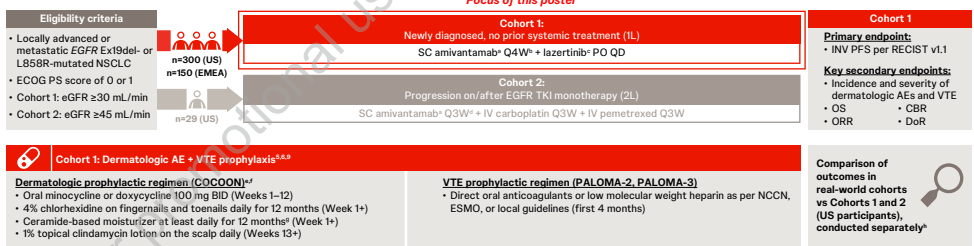
Figure 3: Incidence of VTE by cycle (28 days)



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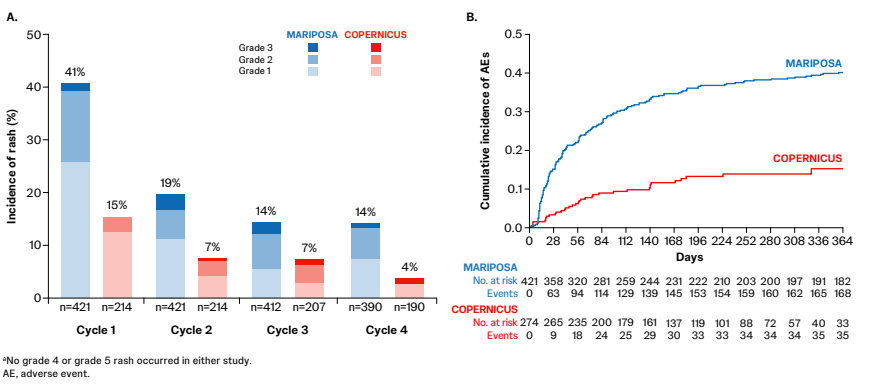
Figure 1: COPENICUS study design



COPENICUS (ClinicalTrials.gov identifier: NCT06667076). *SC abdominal injection 1800 mg (2240 mg if ≥80 kg) weekly for the first 4 weeks, and 3520 mg (4640 mg if ≥80 kg) Q4W thereafter. [†]In 28-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment; whichever comes first. [‡]Lazertinib 240 mg. [§]In 21-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. [¶]Prophylactic antibiotics: oral minocycline or doxycycline 100 mg BID and topical clemastine 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. ^{||}Tarcequa was added as a reactive management recommendation in COPENICUS based on positive results from the COCOON treatment substudy. In addition, a protocol amendment for COPENICUS recommended zinc supplementation for participants with established zinc deficiency who experienced dermatologic AEs. ^{||}La Roche-Posay Lipikar AP+M moisturizer was used in COCOON. ^{||}The comparison of clinical and health outcomes between real-world patients and participants from Cohorts 1 and 2 (US participants only) will be assessed under a separate protocol. ¹L, first-line; 2L, second-line; AE, adverse event; BID, twice daily; 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; TKI, tyrosine kinase inhibitor; VTE, venous thromboembolism.

- Incidence of rash (preferred term) during the first 4 months of treatment was lower in COPENICUS versus MARIPOSA (25% vs 55%, respectively), with lower incidence over time (**Figure 4A**)
- In COPENICUS, overall incidence of rash during the first 4 months of treatment was similar across age subgroups at 24% versus 25% in participants <65 versus ≥65 years of age, respectively
 - These data are not based on a formal subgroup comparison
- Compared with MARIPOSA, COPENICUS demonstrated a meaningful reduction in grade ≥2 rash (preferred term) occurring in the first 4 months, with a lower cumulative incidence by 1 year (**Figure 4B**)

Figure 4: (A) Incidence of rash by cycle (28 days)^a and (B) cumulative incidence of grade ≥2 rash



- Majority of TEAEs were grade 1–2, with no new safety signals compared with previous reports (**Table 2**)^{1,3}
- Incidence of grade ≥3 dermatologic TEAEs was low (dermatitis acneiform, 4%; rash, 3%; maculopapular rash, 3%; paronychia, 1%; pruritus, <1%)
- Incidence of any TEAE with onset during the first 4 months and leading to discontinuation of both amivantamab + lazertinib was 8%
 - TEAEs leading to dose reduction and dose interruption of any study drug occurred in 20% and 46% of participants, respectively

Table 2: Safety profile

TEAEs by preferred term (≥20%), n (%)	Cohort 1 (n=214)	
	All grades	Grade ≥3
EGFR-related		
Dermatitis acneiform	85 (40)	8 (4)
Stomatitis	82 (38)	6 (3)
Paronychia	74 (35)	3 (1)
Rash	53 (25)	6 (3)
Pruritus	50 (23)	1 (<1)
Maculopapular rash	46 (21)	6 (3)
MET-related		
Peripheral edema	80 (37)	3 (1)
Hypoalbuminemia	69 (32)	5 (2)
Other		
Fatigue	101 (47)	10 (5)
Nausea	93 (43)	2 (1)
Diarrhea	64 (30)	5 (2)
Constipation	59 (28)	0
Increased ALT	55 (26)	9 (4)
Decreased appetite	50 (23)	1 (<1)
Myalgia	48 (22)	0
Vomiting	46 (21)	2 (1)

ALT, alanine aminotransferase; *EGFR*, epidermal growth factor receptor; TEAE, treatment-emergent adverse event.

Solid Tumors