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COPERNICUS

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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Key Takeaways

- COPERNICUS early safety data support wide use of subcutaneous (SC) amivantamab every 4 weeks (Q4W) + lazertinib in patients with first-line (1L) epidermal growth factor receptor (*EGFR*)–mutated advanced non-small cell lung cancer (NSCLC)
- COPERNICUS has enrolled rapidly in the US, demonstrating the feasibility of treating a more representative real-world population

Conclusions

- Enhanced dermatologic and venous thromboembolism (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 administration-related reactions (ARRs) was very low (<1%) with SC amivantamab

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Disclosure

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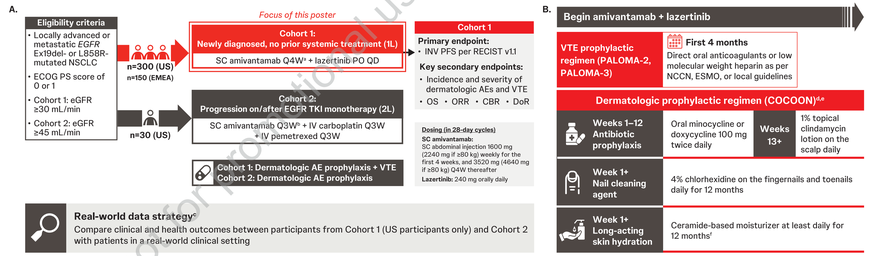
Background

- In MARIPOSA (NCT04487080), 34% of participants with 1L common *EGFR*-mutated advanced NSCLC discontinued IV amivantamab due to AEs, including infusion-related reactions (IRR), VTE, and dermatologic AEs[1,2]
- Despite these discontinuations, IV amivantamab + lazertinib significantly improved median overall survival (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 US, Europe, Japan, and China[6–9]
  - In COCOON (NCT06120140), an enhanced prophylactic dermatologic regimen significantly reduced grade ≥2 dermatologic AEs vs 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

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
- 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

Figure 1: (A) COPERNICUS study design and (B) prophylaxis for dermatologic AEs and VTE[4,10,11]



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.[12] 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.

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

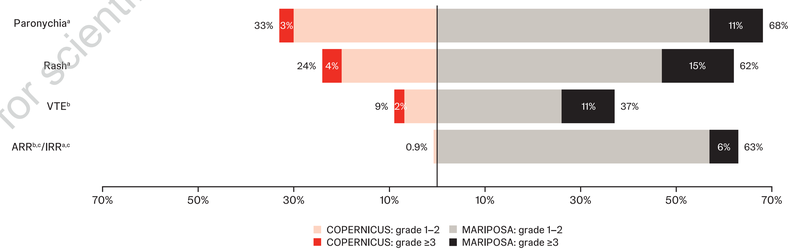
Table 1: Baseline demographic and clinical characteristics

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.

Safety

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



Note: No formal, head-to-head statistical comparison was performed. Because follow-up in COPERNICUS is limited, 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.
ARR, administration-related reaction; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

- 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 vs MARIPOSA (**Figure 2**)[1]
- Incidence of ARR was 0.9% (none grade ≥3) in COPERNICUS, which was substantially reduced versus 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

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

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

- 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 COPERNICUS (**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**)

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

EGFR, epidermal growth factor receptor; Q4W, every 4 weeks; SC, subcutaneous; TEAE, treatment-emergent adverse event.

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Lung Cancer

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