

COPERNICUS: A multinational pragmatic phase 2 trial of subcutaneous amivantamab in common *EGFR*-mutated NSCLC

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Summary



COPERNICUS is an open-label, phase 2b study evaluating the efficacy and safety of subcutaneous (SC) amivantamab regimens combined with supportive care management of adverse events (AEs) in locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (*EGFR*) exon 19 deletion or exon 21 L858R substitution mutations

This study is using pragmatic design elements and broadening eligibility criteria to make the study more representative across multiple regions and aims to reduce the overall treatment burden on both patients and health care providers, while improving safety, quality of life, and treatment experience

Current Status



COPERNICUS is currently enrolling, with a planned 150 participants in Europe, the Middle East, and Africa (EMEA) and 300 participants in the United States for Cohort 1 (amivantamab SC + lazertinib). Enrolment is complete for Cohort 2 in the United States (amivantamab SC + chemotherapy)

Registration Information

This study is registered with ClinicalTrials.gov (Identifier: NCT06667076) and EudraCT (2025-520730-28-00)

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Disclosures

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Background

- For patients with common *EGFR*-mutated (exon 19 deletion/exon 21 L858R substitution) advanced NSCLC, intravenous (IV) amivantamab is US Food and Drug Administration- and European Medicines Agency (EMA)-approved in combination with lazertinib for first-line (1L) treatment and in combination with carboplatin-pemetrexed chemotherapy for second-line (2L) treatment^{1,2}
- 1L approval was based on the phase 3 MARIPOSA trial where amivantamab + lazertinib significantly prolonged progression-free survival (hazard ratio [HR], 0.70; $P < 0.001$) and overall survival (median follow-up, 37.8 months; HR, 0.75; $P < 0.005$), with a projected median survival benefit of >1 year versus osimertinib^{3,4}
- 2L approval was based on the phase 3 MARIPOSA-2 trial where amivantamab + chemotherapy significantly prolonged progression-free survival (HR, 0.48; $P < 0.001$), with a trend towards improving overall survival (median follow-up, 18.1 months; HR, 0.73; $P = 0.039$) versus chemotherapy^{5,6}

- EMA approval of amivantamab SC, co-formulated with hyaluronidase (rHuPH20) and in combination with lazertinib, for the 1L treatment of advanced NSCLC was based on the phase 3 PALOMA-3 study^{7,8}
- Amivantamab SC every 2 weeks and prophylactic anticoagulation reduced the incidence of venous thromboembolism (VTE) by 1.7-fold and reduced the rate of administration-related reactions by 5-fold versus amivantamab IV⁹
- In the phase 2 SKIPPirr trial, prophylactic dexamethasone (8 mg twice daily for 2 days and 1 day prior, and 8 mg on the day of the first dose [5 doses]) combined with standard premedication demonstrated a ~3-fold decrease in infusion-related reactions versus historical data (22.5% vs 67.4% in participants who received amivantamab IV + lazertinib⁹
- In the phase 2 COCOON trial, an enhanced prophylactic dermatologic regimen reduced the incidence of grade ≥ 2 dermatologic AEs by 50% versus standard-of-care dermatologic management in participants who received amivantamab IV + lazertinib¹⁰

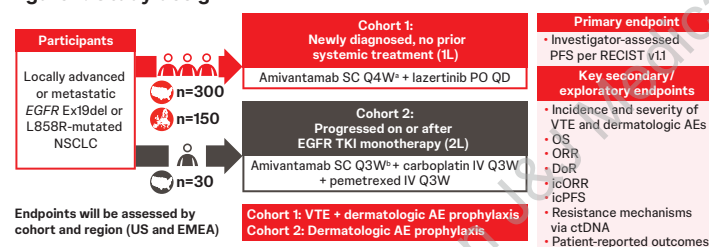
Objective

- The open-label, phase 2b COPERNICUS study will evaluate the efficacy and safety of amivantamab SC every 4 weeks in combination with lazertinib (Cohort 1) or every 3 weeks in combination with chemotherapy (Cohort 2) while participants receive mandatory VTE (Cohort 1 only) and dermatologic AE prophylaxis in a multinational, clinically representative population, with inclusion criteria reflecting clinical practice

Methods

- The study design is presented in Figure 1, with key eligibility criteria presented in Figure 2

Figure 1: Study design



Real-world data strategy*

Compare PFS between participants receiving amivantamab SC + lazertinib (Cohort 1; US participants only) and patients in a real-world clinical setting treated with osimertinib monotherapy

*In 28-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. In 21-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. The real-world comparison will be assessed under a separate protocol. 1L, first-line; 2L, second-line; AE, adverse event; ctDNA, circulating tumor DNA; DoR, duration of response; EGFR, epidermal growth factor receptor; EMEA, Europe, Middle East, and Africa; Ex19del, exon 19 deletion; iL, intravenous; IV, intravenous; L858R, exon 21 L858R substitution; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; QD, daily; Q3W, every 3 weeks; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SC, subcutaneous; TKI, tyrosine kinase inhibitor; VTE, venous thromboembolism.

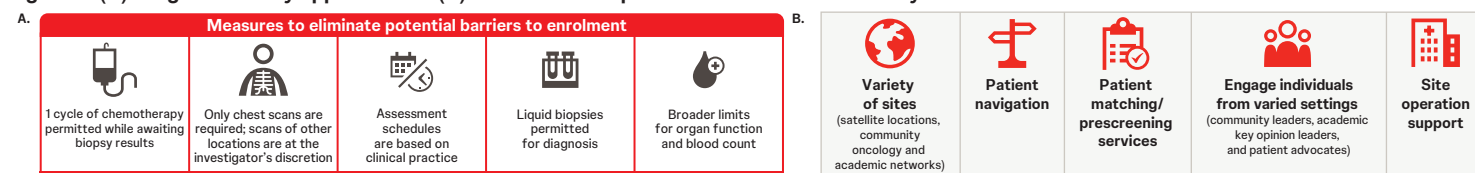
Figure 2: Key eligibility criteria

| Inclusion | Exclusion |
|--|--|
| ≥ 18 years of age | Active, untreated brain metastases* |
| ≥ 1 measurable lesion per RECIST v1.1 | Major surgery or significant traumatic injury within 4 weeks of the first dose |
| Haemoglobin ≥ 9.0 g/dL; ANC $\geq 1 \times 10^9/L$; platelet count $\geq 75 \times 10^9/L$ (without transfusion) | Uncontrolled medical conditions (eg, hypertension, diabetes, infection, impaired oxygenation, cardiovascular disease, etc) |
| eGFR: Cohort 1: ≥ 30 mL/min; Cohort 2: ≥ 45 mL/min | Medical history of active ILD, including drug-induced ILD |
| Cohort 1 only: able to receive direct oral anticoagulant or low molecular weight heparin | Cohort 1 only: targeted therapy for early-stage (resectable) disease |
| ECOG PS score of 0 or 1 | Cohort 2 only: >2 lines of prior therapy |

*Per protocol, while participants with active, untreated brain metastases are excluded, participants with previously treated, stable, or asymptomatic brain metastases are permitted in Cohort 1 and participants with any history of brain metastases (no indication for further local therapy) are permitted in Cohort 2. ANC, absolute neutrophil count; ECOG PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; ILD, interstitial lung disease; RECIST, Response Evaluation Criteria in Solid Tumors.

- The pragmatic study approach will address potential barriers to enrolment (Figure 3A), while additional measures are designed to enhance clinical trial accessibility (Figure 3B)

Figure 3: (A) Pragmatic study approach and (B) measures to improve clinical trial accessibility



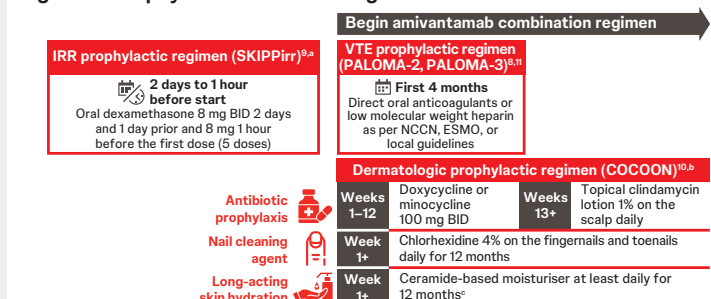
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- Prophylactic measures for preventing dermatologic AEs and VTE with amivantamab are presented in Figure 4

Figure 4: Prophylaxis for dermatologic AEs and VTE



*Includes standard premedication (antihistamines, antipyretics, and glucocorticoids). ⁹Prophylactic 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 moisturiser of the body and face at least daily. ¹⁰La Roche-Posay Lipikar AP+M moisturiser was used in COCOON. AE, adverse event; BID, twice daily; ESMO, European Society for Medical Oncology; IRR, infusion-related reaction; NCCN, National Comprehensive Cancer Network; VTE, venous thromboembolism.

- COPERNICUS will leverage a broad geographic network and incorporate satellite locations and community clinics for enrolment (Figure 5)

Figure 5: Site distribution and enrolment maximisation

