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Enhanced vs Standard Dermatologic Management with Amivantamab-Lazertinib in Advanced NSCLC: Phase 2 COCOON Study

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Background

- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity[1-4]
- Lazertinib is a CNS-penetrant, third-generation EGFR-TKI[5-6]
- In MARIPOSA (ClinicalTrials.gov Identifier: NCT04487080), first-line amivantamab + lazertinib significantly improved PFS versus osimertinib in *EGFR*-mutated advanced NSCLC[7]
- EGFR-targeted therapies are associated with dermatologic AEs, which can impact patients' quality of life and treatment adherence, and are often treated reactively with topical/systemic corticosteroids and/or systemic antibiotics[8,9]
- Previous studies have demonstrated that use of a prophylactic oral tetracycline antibiotic resulted in significantly fewer grade ≥2 dermatologic AEs among patients who were receiving EGFR inhibitors[10]
- COCOON (ClinicalTrials.gov Identifier: NCT06120140) aims to evaluate the impact of enhanced versus standard dermatologic management on the incidence of dermatologic AEs among patients receiving first-line amivantamab + lazertinib

AE, adverse event; CNS, central nervous system; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

1. Moores SL, et al. *Cancer Res*. 2016;76(13):3942-3953. 2. Vijayaraghavan S, et al. *Mol Cancer Ther*. 2020;19(10):2044-2056. 3. Yun J, et al. *Cancer Discov*. 2020;10(8):1194-1209. 4. Cho BC, et al. *Clin Lung Cancer*. 2023;24(2):89-97. 5. Ahn M-J, et al. *Lancet Oncol*. 2019;20(12):1681-1690. 6. Cho BC, et al. *J Thorac Oncol*. 2022;17(4):558-567. 7. Cho BC, et al. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614. 8. Peng Y, et al. *Biosci Trends*. 2019;12(6):537-552. 9. Basse C, et al. *Lung Cancer*. 2022;173:116-123. 10. Petrelli F, et al. *Br J Dermatol*. 2016;175(6):1166-1174.

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Study Design

- COCOON is a phase 2, open-label, randomized study currently enrolling patients with treatment-naïve *EGFR*-mutated locally advanced or metastatic NSCLC
- As background treatment, all patients will receive IV amivantamab + oral lazertinib
  - Prophylactic anticoagulation is mandatory for the first 4 months of treatment
- Patients in Arm A will use a digital health tool to monitor treatment compliance
- All patients will receive general skincare recommendations and will be eligible to receive additional dermatologic measures as per physician discretion

Key eligibility criteria

- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS score of 0 or 1

Stratification factors

- Race (Asian vs non-Asian)
- Age (<65 years vs ≥65 years)

IV amivantamab
1050 mg (1400 mg if ≥80 kg) once weekly for 4 weeks; every 2 weeks thereafter
+
Oral lazertinib
240 mg QD

1:1 randomization (N≈180[a]; US, EU, LATAM, APAC)

Arm A: amivantamab + lazertinib + enhanced dermatologic management (n=90)

	Weeks 1–12	Weeks 13–52
Prophylactic antibiotics	Oral doxycycline or minocycline 100 mg BID	Topical clindamycin lotion 1% on scalp QD before bedtime
Paronychia prophylaxis	Chlorhexidine 4% on the fingernails and toenails QD	
Skin moisturization	La Roche Posay Lipikar AP+M Moisturizer on the body and face at least QD	

Arm B: amivantamab + lazertinib + standard dermatologic management (n=90)

COCOON (ClinicalTrials.gov Identifier: NCT06120140).

[a]Planned enrollment is 180 patients, which is estimated to provide a power of 90%, with a 2-sided alpha of 0.05, to detect a treatment difference between Arms A and B in the incidence of grade ≥2 dermatologic AEs.

AE, adverse event; APAC, Asia-Pacific; BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; IV, intravenous; LATAM, Latin America; NSCLC, non-small cell lung cancer; QD, once daily.

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Additional Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
• ≥18 years of age • Disease is not amenable to curative therapy • May have brain metastases if: all lesions were treated as clinically indicated, any definitive local therapy was completed ≥2 weeks prior to randomization, and patients are receiving no more than prednisone 10 mg (or equivalent) for treatment • Moderate renal impairment (eGFR >45 mL/min) is allowed	• History of uncontrolled illness[a] or significant drug allergy[b] • History of ILD/pneumonitis • History of clinically significant cardiovascular disease[c] • Received any prior systemic treatment at any time for locally advanced stage III or metastatic stage IV disease[d] • Received any prior treatment with an EGFR-TKI for metastatic or unresectable disease[e] • Active or history of leptomeningeal disease • Active hepatitis B or C virus infection or other clinically active liver disease of infectious origin

[a]Including, but not limited to, uncontrolled diabetes, ongoing/active infection, active bleeding diathesis, impaired oxygenation requiring continuous oxygen supplementation, and psychiatric illness or other circumstances that would limit compliance with study requirements. [b]Known allergy, hypersensitivity, or intolerance to the excipients of amivantamab or lazertinib; to tetracyclines, doxycycline, minocycline, or their excipients; or to any component of the enhanced dermatologic management. [c]Including, but not limited to, deep vein thrombosis or pulmonary embolism within 1 month prior to administration of the first dose of background anticancer treatment or any of the following within 6 months prior to administration of the first dose: myocardial infarction, unstable angina, stroke, transient ischemic attack, coronary/peripheral artery bypass graft, or any acute coronary syndrome; prolonged QTc interval >480 msec or clinically significant cardiac arrhythmia or electrophysiologic disease; uncontrolled hypertension; congestive heart failure within 6 months of administration of the first dose of study treatment; pericarditis/clinically significant pericardial effusion; left ventricular ejection fraction outside of normal institutional limits during screening; and myocarditis. [d]Adjuvant/neoadjuvant therapy for stage I/II disease is allowed if administered >12 months prior to the development of locally advanced or metastatic disease. [e]Adjuvant treatment with osimertinib is allowed if administered >12 months prior to the development of locally advanced or metastatic disease and all osimertinib toxicities are resolved prior to enrollment.

eGFR, estimated glomerular filtration rate; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; FDA, US Food and Drug Administration; ILD, interstitial lung disease; NSCLC, non-small cell lung cancer; QTc, corrected QT interval; TKI, tyrosine kinase inhibitor.

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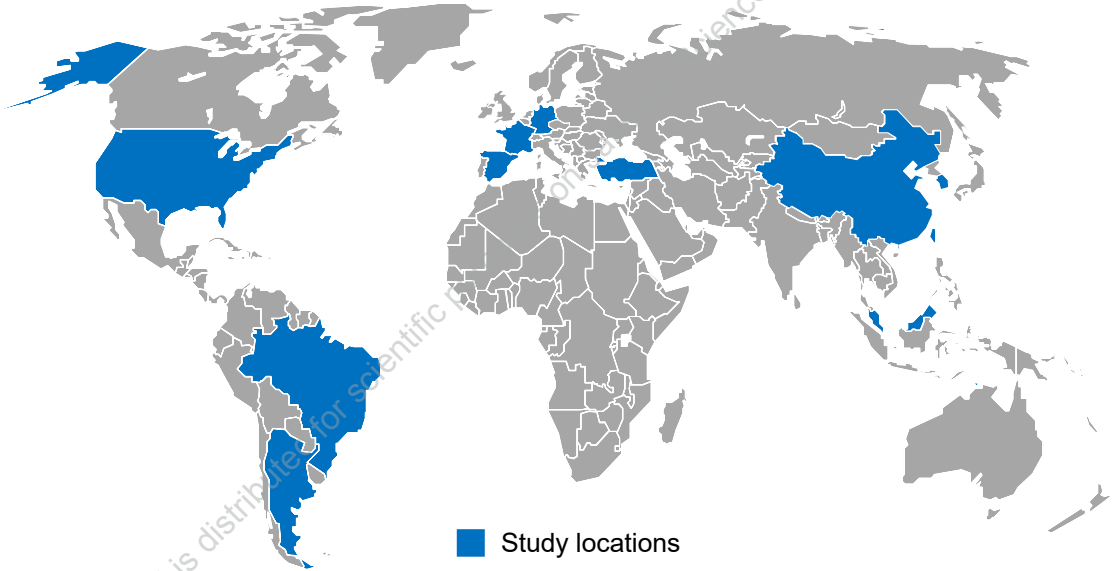
COCOON Enrollment Sites

- Patients are being enrolled at 78 sites across 11 locations



Study Objectives and Endpoints

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Primary objective	Primary endpoint
• Evaluate the incidence of grade ≥2 DAEIs with enhanced versus standard dermatologic management in patients with locally advanced or metastatic stages IIIB/C to IV *EGFR*-mutated NSCLC who were treated with first-line amivantamab + lazertinib ○ DAEIs included rash, dermatitis, paronychia, skin fissures, acne, erythema, skin exfoliation, skin lesion, skin irritation, and eczema[a]	• Incidence of grade ≥2 DAEIs in the first 12 weeks after initiation of amivantamab + lazertinib treatment in Arm A versus Arm B[b]
Key secondary objectives	**Key secondary endpoints**
• Characterize dermatologic toxicity in patients who were treated with enhanced versus standard dermatologic management	• Incidence and severity of any DAEIs[b] • Incidence and severity of grade ≥2 DAEIs in the first 6 months[b] • Time to first grade ≥2[b] DAEI • Incidence and severity of paronychia[b] • Incidence and severity of scalp rash[b]
• Assess the impact of enhanced versus standard dermatologic management on patients' health-related quality of life	• Change from baseline up to 12 months in PROs
• Evaluate the impact of enhanced dermatologic management on amivantamab + lazertinib treatment compliance	• Frequency of dose reductions, interruptions, and discontinuations due to DAEIs • Relative dose intensity of amivantamab + lazertinib

[a]Preferred terms included rash, dermatitis acneiform, pruritus, skin fissures, acne, folliculitis, erythema, eczema, maculopapular rash, skin exfoliation, skin lesion, skin irritation, dermatitis, rash erythematous, rash macular, rash papular, rash pruritic, rash pustular, dermatitis contact, dermatitis exfoliative generalized, drug eruption, dyshidrotic eczema, eczema asteatotic, and paronychia. [b]AE severity per NCI CTCAE v5.0.

AE, adverse event; DAEI, dermatologic adverse event of interest; EGFR, epidermal growth factor receptor; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NSCLC, non-small cell lung cancer; PRO, patient-reported outcome.

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Summary

- COCOON is a phase 2, open-label, randomized study evaluating the impact of enhanced versus standard dermatologic management in patients with *EGFR*-mutated locally advanced or metastatic NSCLC who were treated with first-line amivantamab + lazertinib
- **Current status:** The study is currently recruiting, with a goal of 180 patients
- **Registration information:** This study is registered with ClinicalTrials.gov (Identifier: NCT06120140)

EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer.

Other Amivantamab Presentations at WCLC 2024

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MARIPOSA

Longer follow-up of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 10:47-10:57am
(OA02.03; Gadgeel)

MARIPOSA

Patient-relevant outcomes of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Tuesday, Sep 10 1:55-2:00pm
(MA12.07; Nguyen)

MARIPOSA

Lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 11:07-11:17am
(OA02.05; Lee)

PAPILLON

High-risk biomarker subpopulations from patients with *EGFR* Ex20ins in PAPILLON

Tuesday, Sep 10 1:50-1:55pm
(MA12.06; Goldman)

PALOMA-3

Subcutaneous vs intravenous amivantamab: patient satisfaction and resource utilization results

Monday, Sep 9 11:07-11:17am
(OA09.05; Alexander)

SKIPPirr

Preventing infusion-related reactions with intravenous amivantamab: primary results

Tuesday, Sep 10 2:00-2:05pm
(MA12.08; Lopes)

EGFResisters

Development of a **patient-friendly lung cancer lexicon**:
Sunday, Sep 8 6:15-7:45pm
(P2.16F.03; Feldman)

Poster tour: Monday, Sep 9 6:45-6:53pm

Additional posters:

- **PolyDamas TiP:** Amivantamab + cetrelimab in advanced NSCLC: Virtual ePoster (EP.12H.02; Voon)
- 5-year survival estimates with 1L osimertinib for *EGFR*-mutant advanced NSCLC in the US: Virtual ePoster (EP.12A.03; Sabari)

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