Enhanced vs Standard Dermatologic Management with Amivantamab-Lazertinib in *EGFR*m Advanced NSCLC: the COCOON Global RCT

Byoung Chul Cho[1], Weimin Li[2], Alexander I Spira[3], Maxwell Sauder[4], Jill Feldman[5], Farastuk Bozorgmehr[6], Milena Mak[7], Janellen Smith[8], Pei Jye Voon[9], Panwen Tian[2], Jiunn-Liang Tan[10], Cheng-Ta Yang[11], Jin-Yuan Shih[12], Nuri Karadurmus[13], Juan Esteban Cundom[14], Glaucio Bertollo[15], Irfan Cicin[16], Jorge Nieva[17], Ana Laura Ortega-Granados[18], Pascale Tomasini[19], Danny Nguyen[20], Enriqueta Felip[21], Julia Schuchard[22], Sean P Murphy[23], Bailey G Anderson[23], Tonatiuh Romero[23], Yichuan Xia[24] Shubin Sheng[23], Joshua M Bauml[24], Parthiv J Mahadevia[23], Julian Kam[23], Mehregan Nematian-Samani[23], Jairo Simoes[23], Mark Wildgust[23], Nicolas Girard[25]

[1]Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [2]Department of Pulmonary Care and Critical Care Medicine, West China Hospital of Sichuan University, Chengdu, Sichuan, China; [3]Virginia Cancer Specialists, Fairfax, VA, USA; [4]University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, Toronto, ON, Canada; [5]EGFR Resisters, Deerfield, IL, USA; [6]Thoraxklinik Heidelberg gGmbH, University Hospital Heidelberg, Heidelberg, Germany; [7]Instituto do Cancer do Estado de São Paulo – Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; [8]University of California – Irvine, Irvine, CA, USA; [9]Department of Radiotherapy and Oncology, Sarawak General Hospital, Kuching, Sarawak, Malaysia; [10]Department of Medicine, University of Malaya, Kuala Lumpur, Malaysia; [11]Department of Internal Medicine, Division of Thoracic Medicine, Chang Gung Memorial Hospital at Linkou; College of Medicine, Chang Gung University, Taoyuan, Taiwan; [12]Department of Internal Medicine, National Taiwan University Hospital, Taipei City, Taiwan; [13]SBU Gulhane Training and Research Hospital, Ankara, Turkey; [14]Instituto Argentino de Diagnóstico y Tratamiento (IADT), Buenos Aires, Argentina; [15]AFECC/Hospital Santa Rita de Cássia, Vitória-ES, Brazil; [16]Istinye University Medical Oncology and İ.A.Ü. VM Medical Park Florya Hospital, Istanbul, Turkey; [17]University of Southern California/Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [18]Hospital Universitario de Jaén, Jaén, Spain; [19]Aix Marseille University - CNRS, INSERM, CRCM; CEPCM - AP-HM Hôpital de La Timone, Marseille, France; [20]City of Hope National Medical Center, Duarte, CA, USA; [21]Medical Oncology Service, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron Barcelona Hospital Campus, Universitat Autonoma de Barcelona, Barcelona, Spain; [22]Johnson & Johnson, Horsham, PA, USA; [23]Johnson & Johnson, Raritan, NJ, USA; [24]Johnson & Johnson, Spring House, PA, USA; [25]Institut du Thorax Curie-Montsouris, Paris, France; Paris Saclay University, UVSQ, Versailles, France

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Disclosures

Byoung Chul Cho served in a consulting or advisory role for AstraZeneca, Boehringer Ingelheim, Roche, Bristol Myers Squibb, Pfizer, Yuhan Corporation, Janssen, Takeda, Merck Sharp & Dohme, Ono Pharmaceutical, Eli Lilly, MedPacto, Blueprint Medicines, Cyrus Therapeutics, Guardant Health, Novartis, CJ Bioscience, Abion, BeiGene, CureLogen, Onegene Biotechnology, GI Cell, HK inno.N, Imnewrun Biosciences, Hanmi, RAND Bioscience, Kanaph Therapeutics, BridgeBio, and Oscotec; served in a leadership role for Interpark Bio and J INTS BIO; holds patents, royalties, or other intellectual property for Champions Oncology, Crown Bioscience, and Imagen; has other relationships with DAAN Biotherapeutics; owns stock or other ownership interests with Theravance, Gencurix, BridgeBio, Kanaph Therapeutics, Cyrus Therapeutics, Interpark Bio, and J INTS BIO; and received research funding from Novartis, Bayer, AstraZeneca, MOGAM Institute for Biomedical Research, Dong-A ST, Champions Oncology, Janssen, Yuhan Corporation, Ono Pharmaceutical, Dizal Pharma, Merck Sharp & Dohme, AbbVie, GI Innovation, Eli Lilly, Blueprint Medicines, Interpark Bio, LG Chem, Oscotec, GI Cell, Abion, Boehringer Ingelheim, CJ Bioscience, CJ Blossom Park, Cyrus Therapeutics, Genexine, Nuvalent, Oncternal Therapeutics, Regeneron, BridgeBio, ImmuneOncia, Illumina, Kanaph Therapeutics, Therapex, J INTS BIO, Hanmi, and CHA Bundang Medical Center.

Background

- Amivantamab plus lazertinib significantly improved PFS and prolonged OS versus osimertinib among participants with *EGFR*–mutant NSCLC in the MARIPOSA trial, with a projected >1-year median OS benefit[1,2]
- Consistent with EGFR-targeted therapies, amivantamab plus lazertinib is associated with dermatologic AEs, including rash, dermatitis acneiform, pruritus, and paronychia[1,2]
  - Dermatologic AEs are mostly grade 1 or 2, generally occur in the first 4 months of treatment[1,3]
- Mitigation strategies for dermatologic AEs were not evaluated in MARIPOSA; therefore, the COCOON study investigated the effect of enhanced DM versus standard of care DM on the incidence of dermatologic AEs among participants with *EGFR*-mutant NSCLC treated with first-line amivantamab plus lazertinib
  - At the preplanned interim analysis of COCOON (n=138), enhanced DM significantly reduced the incidence of grade ≥2 dermatologic AEs versus standard of care DM in the first 12 weeks[4]

Here, we present results from the fully enrolled (N=201) COCOON study

DM, dermatologic management; OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; QoL, quality of life; TKI, tyrosine kinase inhibitor.
1. Cho BC, et al. *N Engl J Med*. 2024;391(16):1486–1498. 2. Yang JC-H, et al. Presented at: European Lung Cancer Congress (ELCC); March 26–29, 2025; Paris, France. 3. Li Y, et al. *Front Oncol*. 2022;12:804212.
4. Girard N, et al. Presented at European Lung Cancer Congress (ELCC); March 26–29, 2025; Paris, France.

Methods

- COCOON enrolled adults with histologically or cytologically confirmed locally advanced or metastatic NSCLC with *EGFR* Ex19del or L858R, who were treatment naïve and had an ECOG performance status score of 0 or 1 (**Figure 1**)
- Participants were randomized 1:1 to enhanced COCOON DM or SoC DM
- VTE prophylaxis was mandatory for all participants for the first 4 months
- Efficacy endpoints presented here include the incidence of grade ≥2 DAEIs in the first 12 weeks (primary endpoint) and the change from baseline in patient-reported outcomes

DAEI, dermatologic adverse event of interest; DM, dermatologic management; ECOG, Eastern Cooperative Oncology Group; Ex19del, exon 19 deletion; L858R, exon 21 L858R substitution; SoC, standard of care; VTE, venous thromboembolism.

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Methods

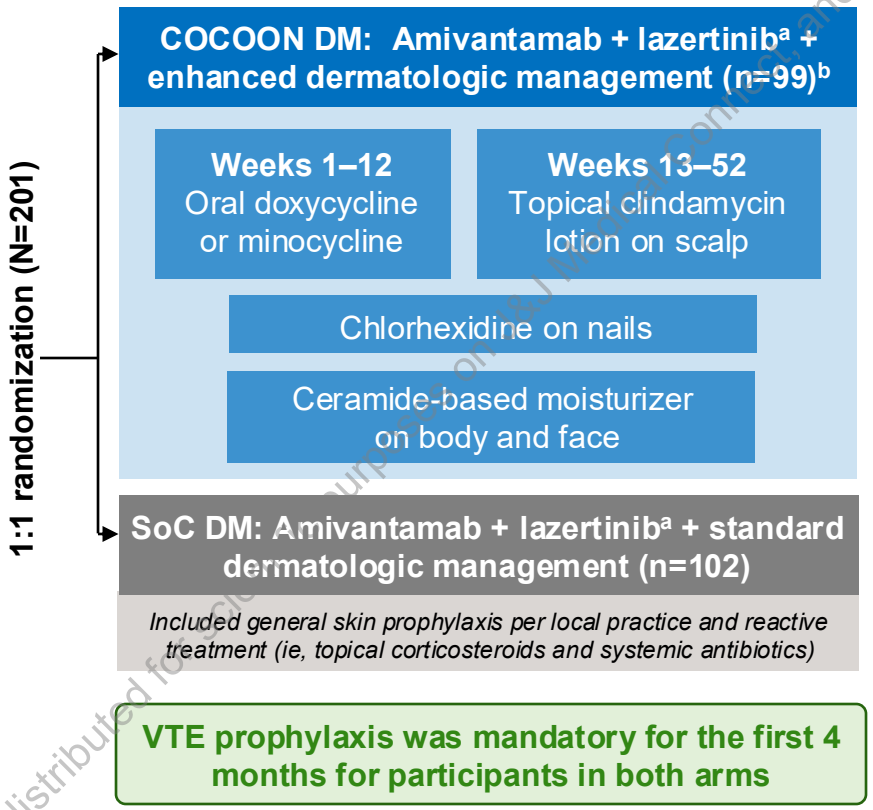
Figure 1. COCOON Study Design

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)



VTE prophylaxis was mandatory for the first 4 months for participants in both arms

Primary endpoint

- Incidence of grade ≥2 DAEIs[c] in the first 12 weeks of amivantamab + lazertinib treatment

Secondary endpoints

- Number of grade ≥2 dermatologic AEs[c] per participant
- Incidence and severity of paronychia[d]
- Incidence and severity of scalp rash[d]
- Frequency of dose reductions, interruptions, and discontinuations due to AEs

COCOON (ClinicalTrials.gov Identifier: NCT06120140).
[a]IV amivantamab was administered at 1050 mg (1400 mg if ≥80 kg) once weekly for 4 weeks and every 2 weeks thereafter; lazertinib was orally administered daily at 240 mg. [b]Prophylactic antibiotics: oral doxycycline or minocycline 100 mg BID and topical clindamycin lotion 1% on the 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. [c]DAEIs include 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. [d]AE severity per NCI CTCAE v5.0.
DM, dermatologic management; ECOG PS, Eastern Cooperative Oncology Group performance status; Ex19del, exon 19 deletion; L858R, exon 21 L858R substitution; mo, months; SoC, standard of care; VTE, venous thromboembolism; wk, weeks.

Results: Baseline Demographic and Clinical Characteristics

- A total of 199 participants were treated with amivantamab plus lazertinib[a]
  - 99 received COCOON DM
  - 100 received SoC DM
- As of the clinical cutoff,[b] median follow-up was 7.1 months, with 74% ongoing treatment
- Baseline demographic and clinical characteristics were balanced between arms (**Table 1**)

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	COCOON DM (n=99)	SoC DM (n=100)
Median (range) age, years	63.0 (34–80)	62.5 (28–83)
Female, n (%)	61 (62)	57 (57)
Race, n (%)		
Asian	66 (67)	65 (65)
White	32 (32)	32 (32)
Other[c]	1 (1)	3 (3)
Median (range) body weight, kg	63.0 (29–97)	64.2 (39–106)
ECOG PS score of 1, n (%)	59 (60)	55 (55)
History of brain metastases, n (%)	32 (32)	43 (43)

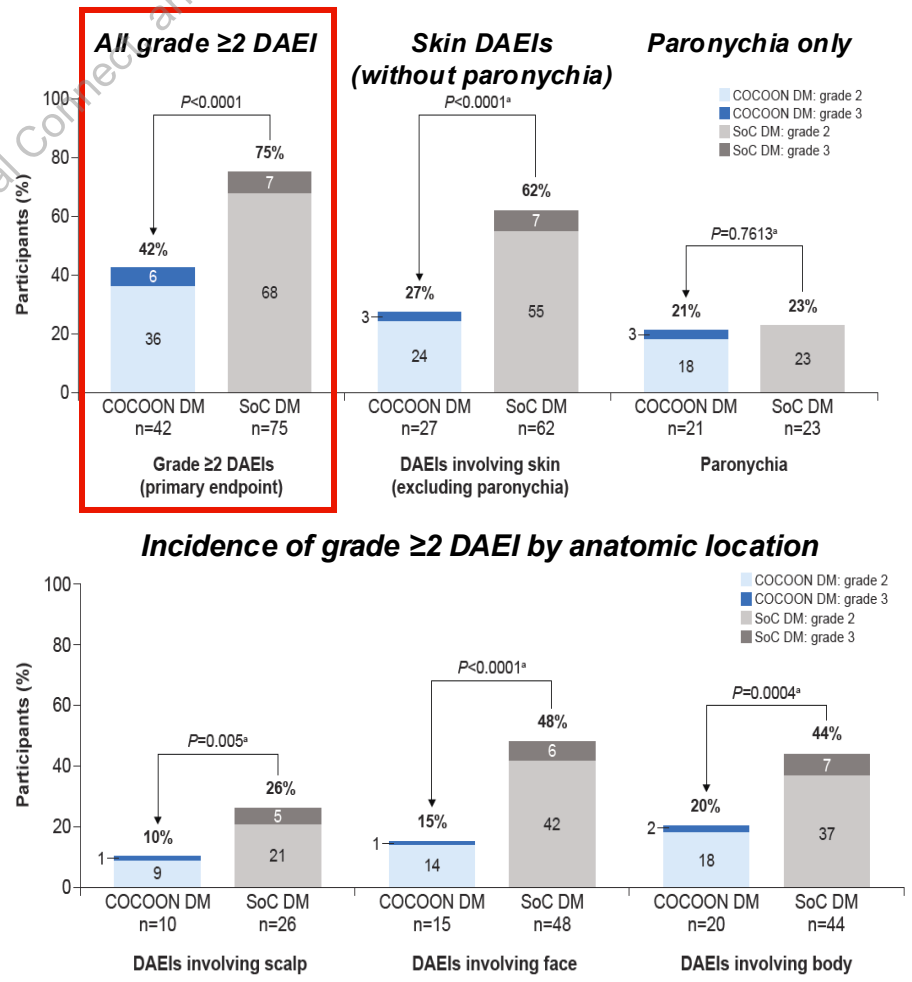
[a]Safety population. Two participants randomized to SoC DM did not meet inclusion criteria at C1D1 and discontinued the study prior to receiving amivantamab + lazertinib. [b]Clinical cutoff was November 13, 2024.
[c]Includes American Indian or Alaska Native, Black or African American, and multiple.
DM, dermatologic management; ECOG PS, Eastern Cooperative Oncology Group performance status; SoC, standard of care.

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Results: Primary Endpoint

- In the first 12 weeks (primary endpoint), grade ≥2 DAEI incidence was significantly lower with COCOON DM versus SoC DM (42% vs 75%; OR, 0.24 [95% CI, 0.13–0.45]; *P*<0.0001; **Figure 2, top**)
  - A significant reduction of grade ≥2 skin DAEI (excluding paronychia) incidence was consistent across anatomic locations (**Figure 2, bottom**)
  - Paronychia incidence was comparable between arms in the first 12 weeks of treatment

Figure 2. Incidence of Grade ≥2 DAEIs in the First 12 Weeks After Initiation of Amivantamab + Lazertinib



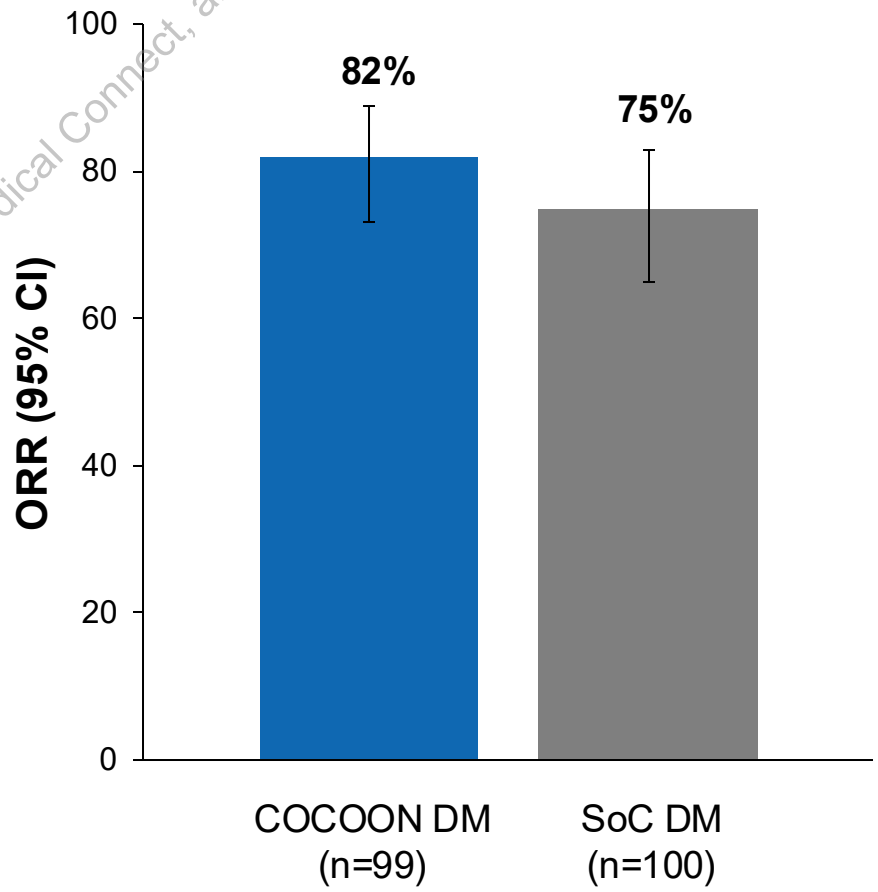
[a]Nominal *P* value.
DAEI, dermatologic adverse event of interest; DM, dermatologic management; SoC, standard of care.

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Results: Antitumor Efficacy

- The investigator-assessed ORR[a] was 82% (95% CI, 73–89) in the COCOON DM arm and 75% (95% CI, 65–83) in the SoC DM arm (**Figure 3**)

Figure 3. ORR[b]



[a]Among unconfirmed responders. [b]Median follow-up was 7.1 months.
CI, confidence interval; DM, dermatologic management; ORR, objective response rate; SoC, standard of care.

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Results: Prophylactic Dermatologic Intervention and Reactive Management

- In the SoC DM arm, 28% (28/100) of participants received some component of prophylactic dermatologic intervention (mostly sunscreen or moisturizing creams)
  - Few participants received prophylactic antibiotics or antiseptics, including systemic tetracyclines,[a] (3%), topical doxycycline (1%), and chlorhexidine (3%)
- Participants in the SoC DM arm received the following reactive management for DAEIs[b]: corticosteroids (83%), topical anti-infectives (67%), systemic antibacterials (61%; mostly tetracyclines [54%]), and emollients and antiseptics (38% each)

[a]2% received systemic doxycycline and 1% received systemic minocycline. [b]In the COCOON DM arm, reactive management included: corticosteroids (57%), topical anti-infectives (53%), systemic antibacterials (35%; mostly tetracyclines [25%]), antiseptics (28%), and emollients (14%).

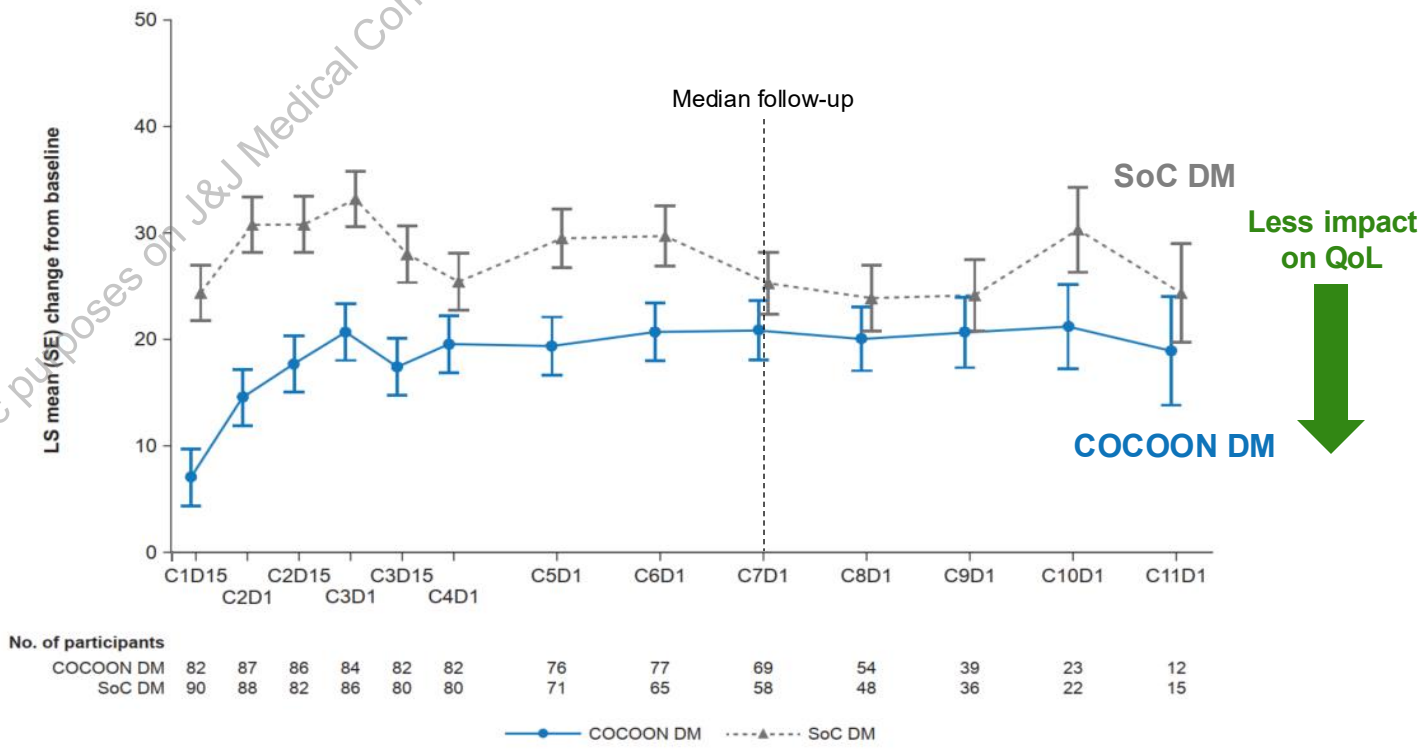
DAEI, dermatologic adverse event of interest; DM, dermatologic management; SoC, standard of care.

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Results: Patient-reported Outcomes

- Mean (SE) Skindex-16[a] total scores at baseline were comparable in COCOON DM and SoC DM arms (4.05 [1.01] vs 4.05 [1.02])
- Early separation in the least squares mean change from baseline[b] in the Skindex-16 total score favored COCOON DM versus SoC DM (**Figure 4**)
  - Separation was maintained up to the median follow-up, even after prophylactic antibiotics were stopped (per protocol) in the COCOON DM arm

Figure 4. Change from Baseline in Skindex-16 Total Score in the First 12 Months After Initiation of Amivantamab + Lazertinib



[a]Skindex-16 measures the impact of skin conditions on quality of life, including 3 subscales: functioning, emotional, and symptoms. [b]Baseline in the graph corresponds to Cycle 1, Day 1, with values of 0 for COCOON DM and SoC DM.
DM, dermatologic management; LS, least squares; QoL, quality of life; SoC, standard of care.

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Results: Safety

- The safety profile of amivantamab + lazertinib was consistent with previous studies, and no new safety signals were observed
  - Except for significantly fewer grade ≥2 DAEIs with COCOON DM, the safety profile was comparable between arms, including a similar incidence of infections and liver function alterations
    - Other than paronychia, infections were uncommon in both the COCOON DM and SoC DM arms; conjunctivitis (7% vs 10%) and upper respiratory tract infection (both 7%) were the most frequent infections
    - Incidence of grade ≥3 increased alanine aminotransferase (8% vs 5%) and aspartate aminotransferase (2% vs 1%) was similar in the COCOON DM and SoC DM arms, respectively
- VTE was reported in 13% of participants in both arms, with the majority being grade 1 or 2
  - Incidence of AEs related to per-protocol VTE prophylaxis was low (grade ≥3 bleeding was 1%[c])
- Discontinuations and dose modifications of the COCOON DM components due to related AEs were rare, with interruptions, reductions, and discontinuations occurring in 8%[a], 3%, and 1% of participants, respectively
- Interruption of amivantamab or lazertinib due to DAEIs was less frequent with COCOON DM versus SoC DM in the first 12 weeks (10% vs 23%, respectively) and throughout the study duration[b] (22% vs 33%)

[a]Interruptions of COCOON DM components due to related AEs were reported by 7 (7%) participants for doxycycline and/or minocycline and by 1 (1%) participant for clindamycin. [b]Up to the clinical cutoff date. [c]During the first 4 months of treatment.
DAEI, dermatologic adverse event of interest; DM, dermatologic management; VTE, venous thromboembolism.

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Conclusions

- COCOON DM is an uncomplicated, widely available, prophylactic regimen that significantly reduced the incidence of grade ≥2 DAEIs on the scalp, face, and other body locations
- Participants on COCOON DM reported a lower impact of anticancer treatment on dermatologic symptoms and quality of life compared with SoC DM
- Discontinuations and modifications of COCOON DM components were rare, which demonstrates the feasibility of using the regimen
- A modified prophylactic approach with longer oral antibiotic use, noncomedogenic skin moisturizer, and oral zinc in combination with early intervention is being investigated
- As first-line amivantamab plus lazertinib has demonstrated a clinically meaningful and statistically significant OS improvement versus osimertinib, and the COCOON DM regimen further enhances the benefit-risk profile for this regimen, amivantamab plus lazertinib represents a new standard of care

DAEI, dermatologic adverse event of interest; DM, dermatologic management.

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Key Takeaway

Participants receiving COCOON dermatologic management had a significantly lower incidence of grade ≥2 dermatologic adverse events and a reduced impact of skin conditions on quality of life versus standard dermatologic management

Presented by BC Cho at the World Conference on Lung Cancer (WCLC); September 6-9, 2025; Barcelona, Spain

Journal of Thoracic Oncology

IASLC INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

IASLC

ORIGINAL ARTICLE

Enhanced Versus Standard Dermatologic Management With Amivantamab-Lazertinib in *EGFR*-Mutated Advanced NSCLC: The COCOON Global Randomized Controlled Trial

Acknowledgments

- The authors would like to thank the individuals who participated in this study and their families and caregivers, the physicians and nurses who cared for the participants, the staff members who supported this clinical trial, and the staff members at the study sites and involved in data collection/analyses
- This study was funded by Janssen Research & Development, LLC, a Johnson & Johnson company
- Medical writing assistance was provided by Lumanity Communications Inc. and was funded by Johnson & Johnson