

Enhanced vs standard dermatologic management with amivantamab-lazertinib in EGFRm advanced NSCLC: the COCOON global RCT

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Key Takeaway



Participants who received COCOON DM had a significantly lower incidence of grade ≥2 dermatologic AEs and a reduced impact of skin conditions on quality of life versus SoC DM

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 who received COCOON DM reported a lower impact of anticancer treatment on dermatologic symptoms and quality of life compared with SoC DM Discontinuations and dose modifications of the 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,





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Background

- Amivantamab plus lazertinib significantly improved progression-free survival and prolonged overall survival (OS) versus osimertinib among participants with epidermal growth factor receptor (EGFR)-mutant non-small cell lung cancer (NSCLC) in the MARIPOSA trial, with a projected >1-year median OS benefit12
- Consistent with EGFR-targeted therapies, amivantamab plus lazertinib is associated with dermatologic adverse events (AEs), including rash, dermatitis acneiform, pruritus, and paronychia^{1,2}
- Dermatologic AEs are mostly grade 1 or 2 and 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 dermatologic management (DM) versus standard of care (SoC) DM on the incidence of dermatologic AEs among participants with EGFR-mutant NSCLC who were 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 SoC DM in the first
- Here, we present results from the fully enrolled (N=201) COCOON study

- COCOON enrolled adult participants with histologically or cytologically confirmed locally advanced or metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations who were treatment naïve and had an Eastern Cooperative Oncology Group performance status score of 0 or 1 (Figure 1)
- Participants were randomized 1:1 to enhanced COCOON DM or SoC DM
- Venous thromboembolism (VTE) prophylaxis was mandatory for all participants for the
- Efficacy endpoints presented here include the incidence of grade ≥2 dermatologic AEs of interest (DAEIs) in the first 12 weeks (primary endpoint) and the change from baseline in patient-reported outcomes

Figure 1: COCOON study design



Documented EGFR Ex19d
 ECOG PS score of 0 or 1

Stratification factors:

Results

Baseline demographic and clinical characteristics

- · A total of 199 participants were treated with amivantamab plus lazertinib (safety population)
- 99 received COCOON DM
- 100 received SoC DM
- As of the clinical cutoff (November 13, 2024), 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^a

Characteristic	(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 ^b	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)
Safety population. Two participants randomized to SoC DM did n	ot meet the inclusion criteria at C1D1 and	discontinued the study prior to receiving

Primary endpoint

- In the first 12 weeks (primary endpoint), the incidence of grade ≥2 DAEIs was significantly lower with COCOON DM versus SoC DM (42% vs 75%, respectively; odds ratio, 0.24 [95% confidence interval (CI), 0.13-0.45]; P<0.0001; Figure 2A)
- A significant reduction in the incidence of grade ≥2 skin DAEIs (excluding paronychia) was consistent across anatomic locations (Figure 2B)
- The incidence of paronychia was comparable between arms in the first 12 weeks of treatment

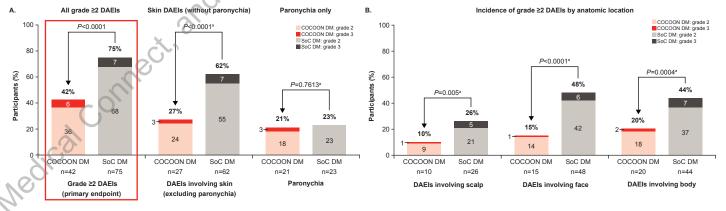
Antitumor efficacy

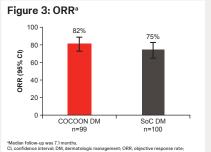
The investigator-assessed objective response rate was 82% (95% CI, 73-89) in the COCOON DM arm and 75% (95% CI, 65-83) in the SoC DM arm among unconfirmed responders (Figure 3)

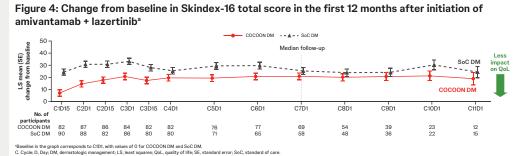
Prophylactic dermatologic intervention and reactive management

- 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 (3%), topical doxycycline (1%), and
- 2% of participants received systemic doxycycline and 1% received systemic minocycline
- Participants in the SoC DM arm received the following reactive management for DAEIs: corticosteroids (83%), topical anti-infectives (67%), systemic antibacterials (61%; mostly tetracyclines [54%]), and emollients and antiseptics (38% each)
- 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%)

Figure 2: Incidence of grade ≥2 DAEIs in the first 12 weeks after initiation of amivantamab + lazertinib







Patient-reported outcomes

- Mean (standard error) Skindex-16 total scores at baseline were comparable in the COCOON DM and SoC DM arms (4.05 [1.01] vs 4.05 [1.02], respectively)
- Skindex-16 measures the impact of skin conditions on quality of life, including 3 subscales; functioning, emotional, and symptoms
- Early separation in the least squares mean change from baseline 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

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%, respectively) and upper respiratory tract infection (both 7%) were the most frequent infections
- The 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,
- VTE was reported in 13% of participants in both arms, with the majority being grade 1 or 2.
- The incidence of AEs related to per-protocol VTE prophylaxis was low (grade ≥3 bleeding was 1% during the first 4 months of treatment)
- · Discontinuations and dose modifications of the COCOON DM components due to related AEs were rare, with interruptions, reductions, and discontinuations occurring in 8%, 3%, and 1% of participants, respectively
- 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
- 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 (22% vs 33%; up to the clinical cutoff date)

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