Incidence and Management of Dermatologic Adverse Reactions With Intravenous Amivantamab in Combination With Lazertinib: Interim Analysis

Rationale: Dermatologic AEs Observed With Amivantamab + Lazertinib in MARIPOSA[1-3]

Click to learn more about dermatologic AEs observed in MARIPOSA

Incidence → First Onset →

Phase 2 COCOON Interim Analysis* Trial: Investigating Enhanced Dermatologic Management With IV Amivantamab + Lazertinib[4,5]

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)

1:1 randomization (N=201)

COCOON DM:
Amivantamab + lazertinib + enhanced dermatologic management
(n=99)

SoC DM:
Amivantamab + lazertinib + standard dermatologic management
(n=102)

VTE prophylaxis was mandatory for the first 4 months

Primary Endpoint:

- Incidence of grade ≥2 dermatologic AEs in the first 12 weeks after initiation of amivantamab + lazertinib treatment

Secondary Endpoints:

- Number of grade ≥2 dermatologic AEs per participant
- Incidence and severity of paronychia
- Incidence and severity of scalp rash
- Frequency of dose reductions, interruptions, and discontinuations due to AEs
- Patient-reported outcomes by Skindex-16 and PGI-S through ~10 weeks of follow-up

*Interim analysis planned for when ~70% of participants completed Week 12 assessments[a]

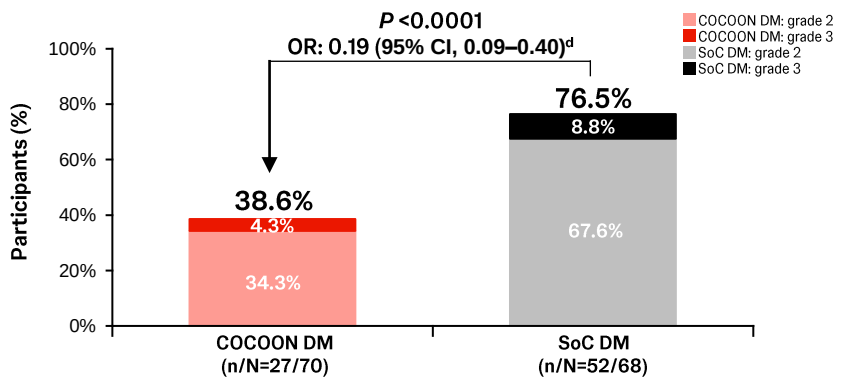
COCOON DM Enhanced Dermatologic Regimen Resulted in ~50% Reduction in Incidence of Grade ≥2 DAEIs in the First 12 Weeks[5]

COCOON DM: Agents are widely available[b]

Antibiotic prophylaxis	**Weeks 1–12** Oral minocycline or doxycycline 100 mg twice daily	**Weeks 13+** 1% Topical clindamycin lotion on the scalp daily
Nail cleaning agent	**Weeks 1+** 4% Chlorhexidine on the fingernails and toenails daily for 12 mos	
Long-acting skin hydration	**Weeks 1+** Ceramide-based moisturizer at least daily for 12 mos[c]	

Both study arms received general skin prophylaxis instructions including minimizing sunlight exposure, wearing UV protective clothing, using SPF ≥30 sunscreen, and avoiding alcohol-based skin agents.

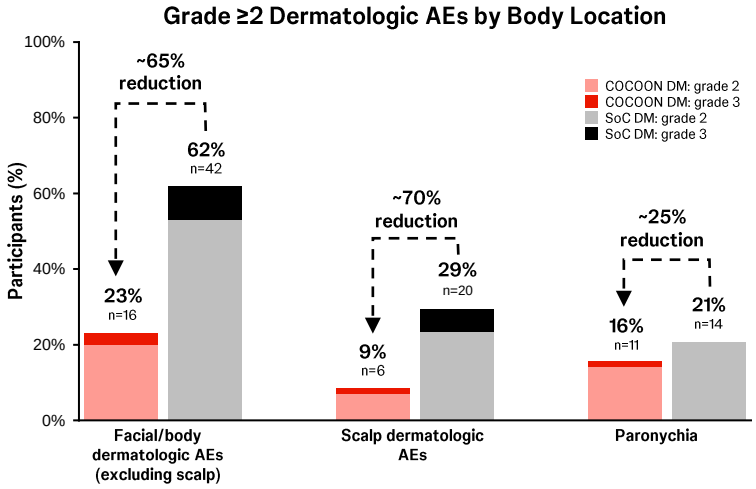
COCOON DM Reduced Grade ≥2 Dermatologic AEs by 50% vs SoC DM



Reductions in Moderate to Severe Facial/Body, Scalp, and Paronychia Dermatologic AEs, and ~50% Reduction in Discontinuations Due to Any AEs Observed With COCOON DM Compared With SoC DM[5]

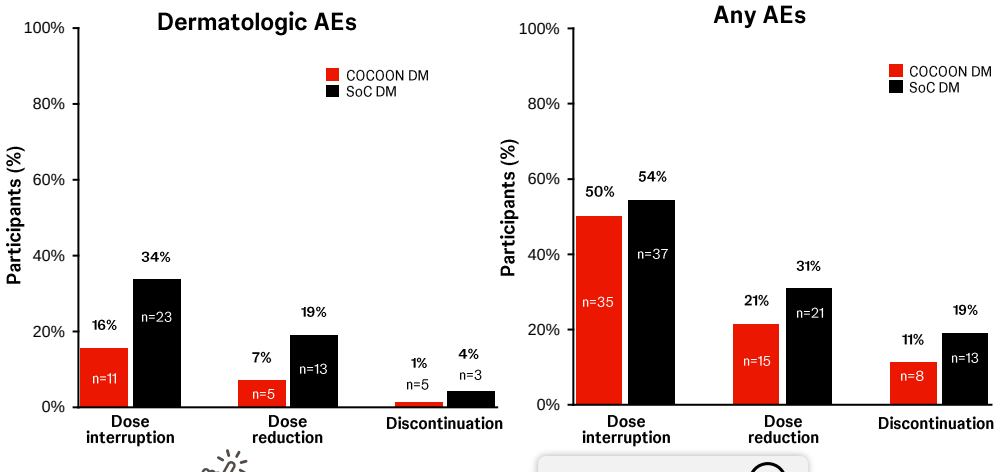
In the first 12 weeks, reductions in grade ≥2 dermatologic AEs were observed on different body locations with COCOON DM compared to SoC DM, including a 70% reduction in scalp dermatologic AEs

Grade ≥2 Dermatologic AEs by Body Location



VTE was observed in **6%** of participants with **COCOON DM** vs **7%** with **SoC DM**

Participants using the COCOON DM regimen had lower rates of amivantamab or lazertinib discontinuations due to any AEs (11% vs 19% for SoC)



Click to learn more about COCOON PROs →

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AE, adverse event; BID, twice daily; CI, confidence interval; DAEI, dermatologic adverse event of interest; DM, dermatologic management; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; IV, intravenous; NSCLC, non-small cell lung cancer; mos, months; OR, odds ratio; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome; QD, once daily; SoC, standard of care; VTE, venous thromboembolism.

[a]All analyses were performed using the safety analysis set. [b]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. [c]La Roche Posay Lipikar AP+M moisturizer was used in COCOON. [d]OR was generated by a logistic model, adjusted by race and age (continuous).

1. RYBREVANT® (amivantamab-vmjw) [prescribing information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC, et al. *N Engl J Med.* 2024;391(16):1486–1498. 3. Yang JCH, et al. Presented at: European Lung Cancer Congress (ELCC); March 26–29, 2025; Paris, France. 4. Feldman J, et al. Presented at: American Society of Clinical Oncology (ASCO); May 30–June 3, 2025; Chicago, IL, USA. 5. Girard N, et al. Presented at: European Lung Cancer Congress (ELCC); March 26–29, 2025; Paris, France.

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Rationale: Dermatologic AEs Observed With Amivantamab + Lazertinib in MARIPOSA[1-3]

Click to learn more about dermatologic AEs observed in MARIPOSA

Incidence → First Onset →

Incidence (n=421)[1,2]

Participant population: Adult participants with locally advanced or metastatic NSCLC and documented *EGFR* exon 19 deletion or exon 21 L858R mutations

Median treatment duration:
18.5 months (range, 0.2–31.4)

Most common dermatologic AEs, %	All	Grade 3 or 4
Rash[a]	86	26
Nail toxicity/paronychia[a]	71	11
Dry skin[a]	25	1
Pruritus	24	0.5

Rash led to the following dose modifications of amivantamab in participants:

- Interruptions in **37%**
- Reductions in **23%**
- Discontinuations in **5%**

Median time to:

Onset of rash	Duration of rash[2]
14 days (range, 1–556)	31 days (range, 1–663)

Note: Additional warnings and precautions associated with amivantamab and lazertinib include IRR, ILD/pneumonitis, VTE events, ocular toxicity, and embryo-fetal toxicity

AE, adverse event; EGFR, epidermal growth factor receptor; ILD, interstitial lung disease; IRR, infusion-related reaction; NSCLC, non-small cell lung cancer; VTE, venous thromboembolism.
[a]Grouped term. For rash, this includes the following preferred terms: rash, dermatitis acneiform, folliculitis, rash maculopapular, skin lesion, acne, erythema, rash pustular, dermatitis, rash pruritic, rash papular, rash erythematous, rash macular, dermatitis infected, erythema multiforme, papule, drug eruption, rash follicular, rash vesicular, skin exfoliation, and epidermolysis.
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Nail cleaning agent
Weeks 1+
4% Chlorhexidine on the fingernails and toenails daily for 12 mos

Long-acting skin hydration
Weeks 1+
Ceramide-based moisturizer at least daily for 12 mos[c]

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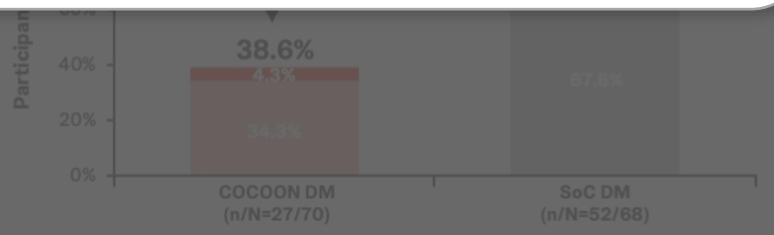

Reductions in Moderate to Severe Scalp Rash, Paronychia, and Facial/body Dermatologic AEs, and ~50% Reduction in Discontinuations Due to Any AEs Observed With COCOON DM Compared With SoC DM[5]

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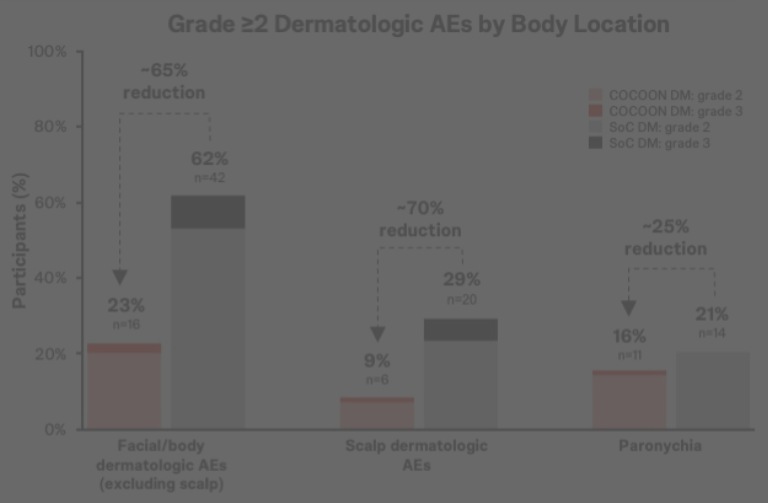

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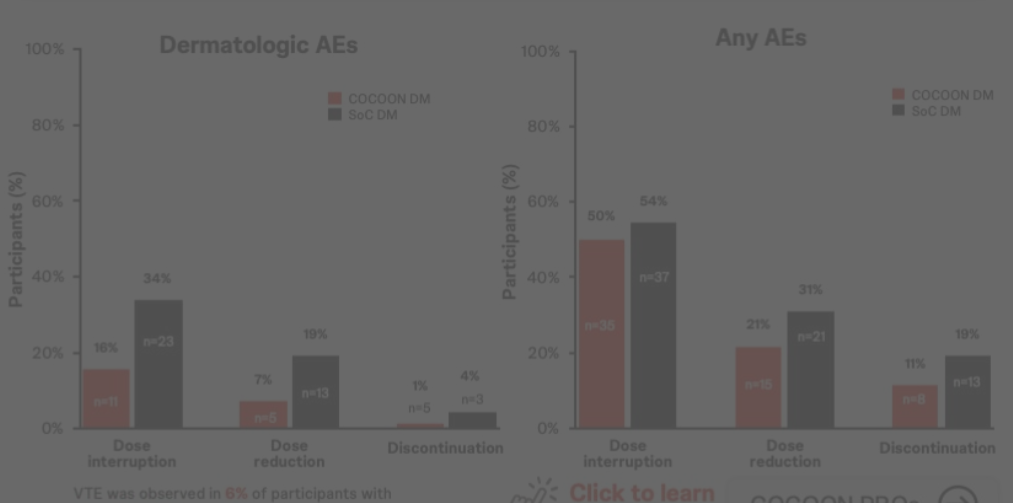

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Click to learn more about COCOON PROs →

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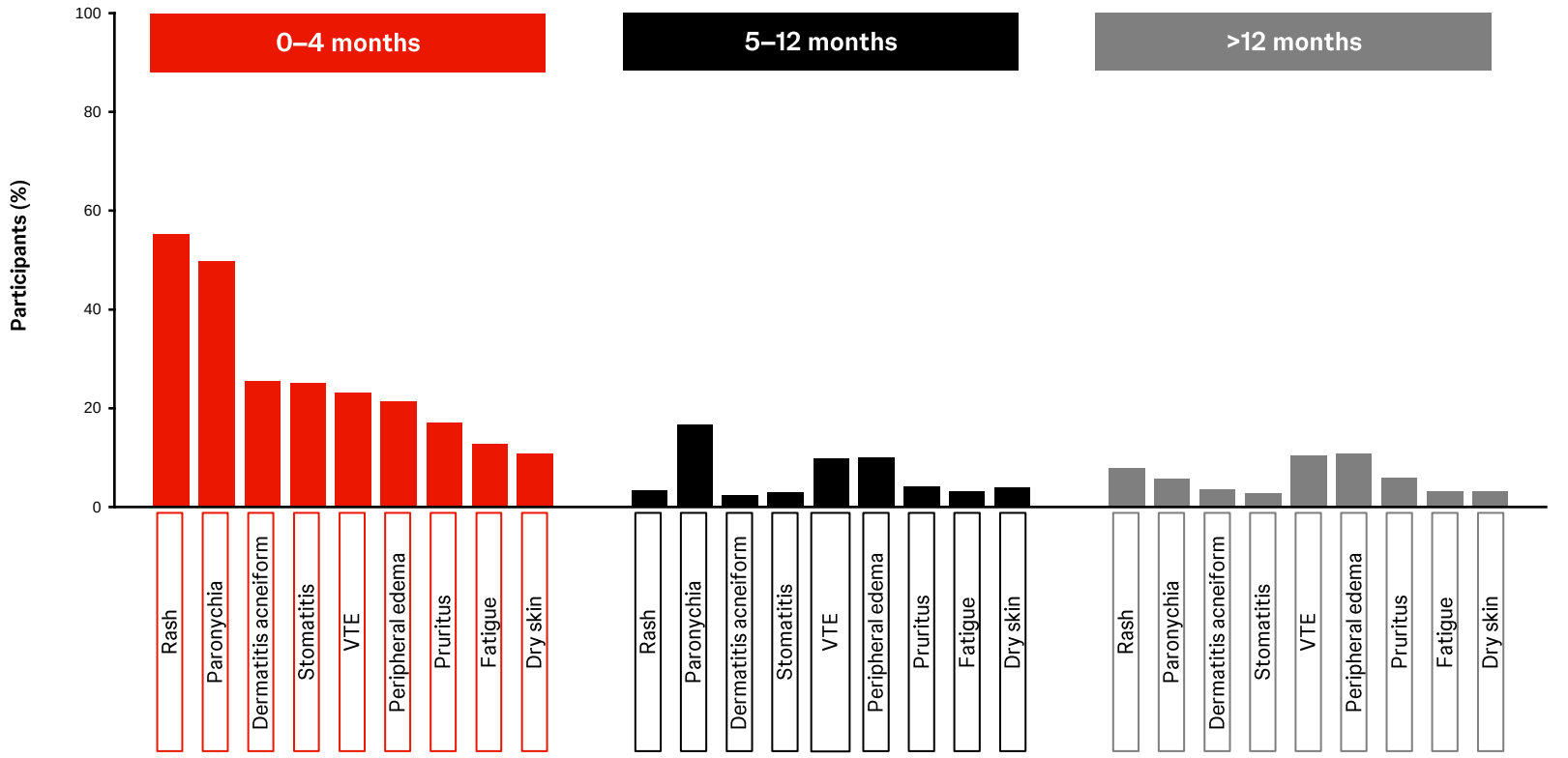
Incidence

First Onset

First Onset of Key AEs for Amivantamab + Lazertinib[1]

Most AEs occurred early (within 0–4 months), with longer-term follow-up showing no new safety signals



AE, adverse event; VTE, venous thromboembolism.

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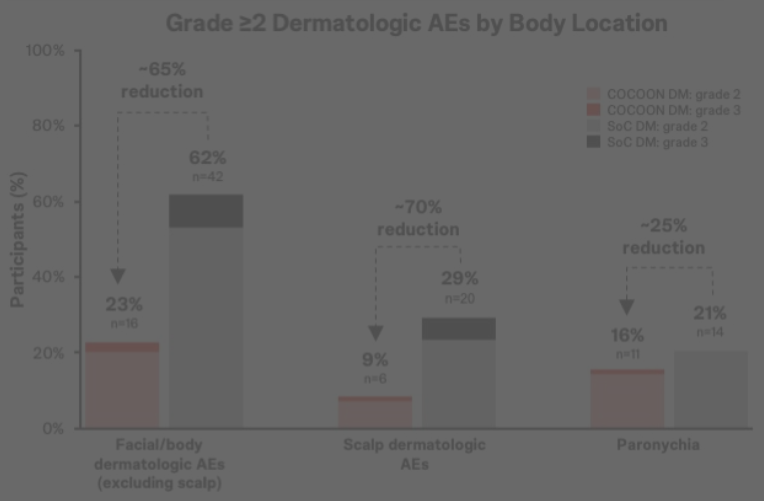

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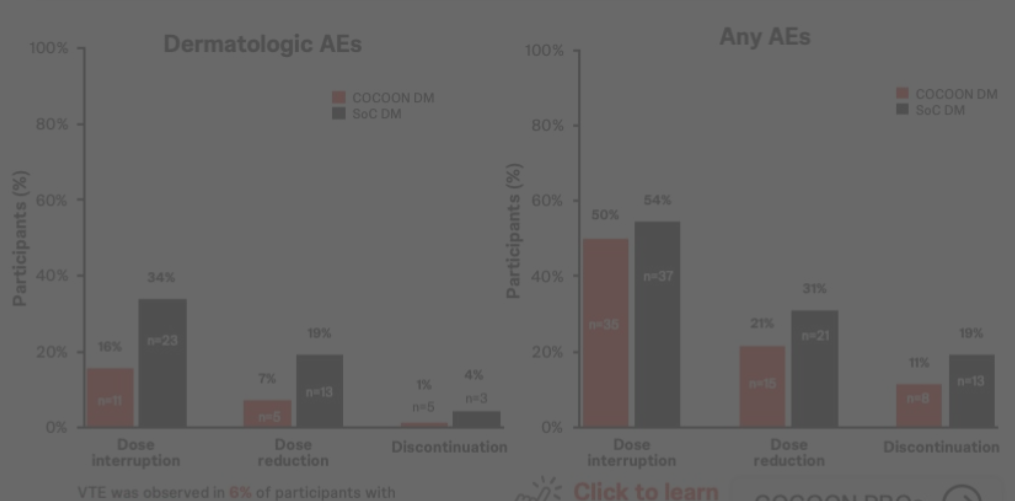

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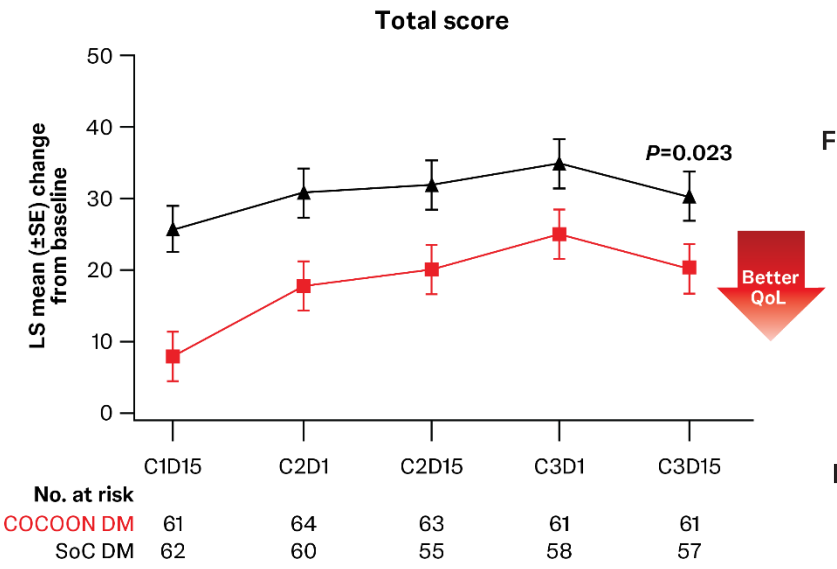
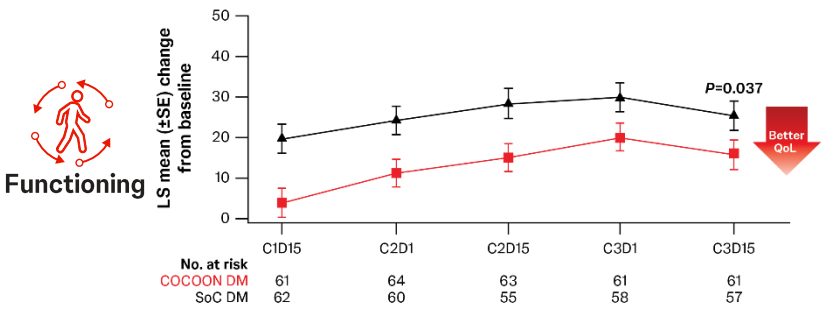
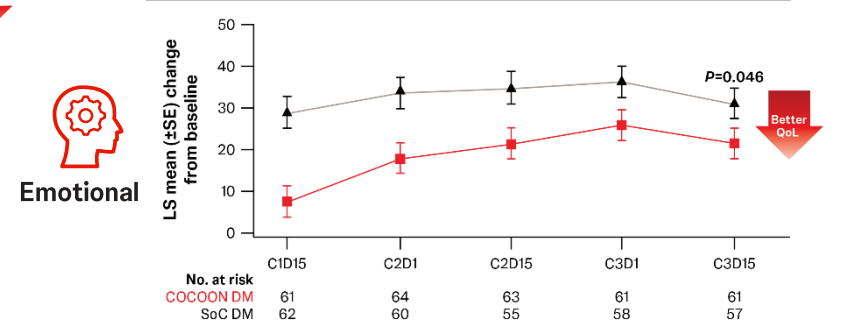
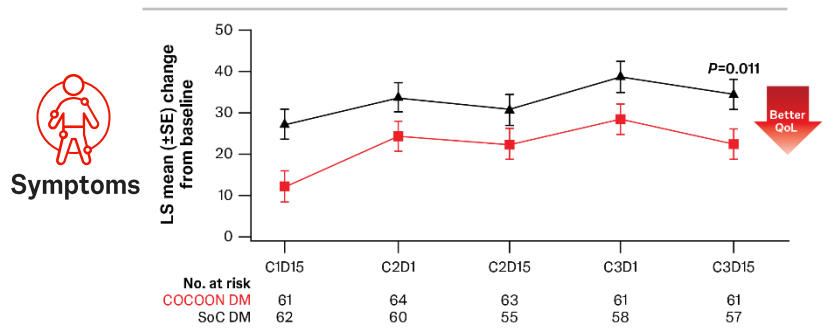
COCOON Patient-Reported Outcomes[1]

Skindex-16 – Consistent separation in total and all post-baseline scores with COCOON DM vs SoC DM





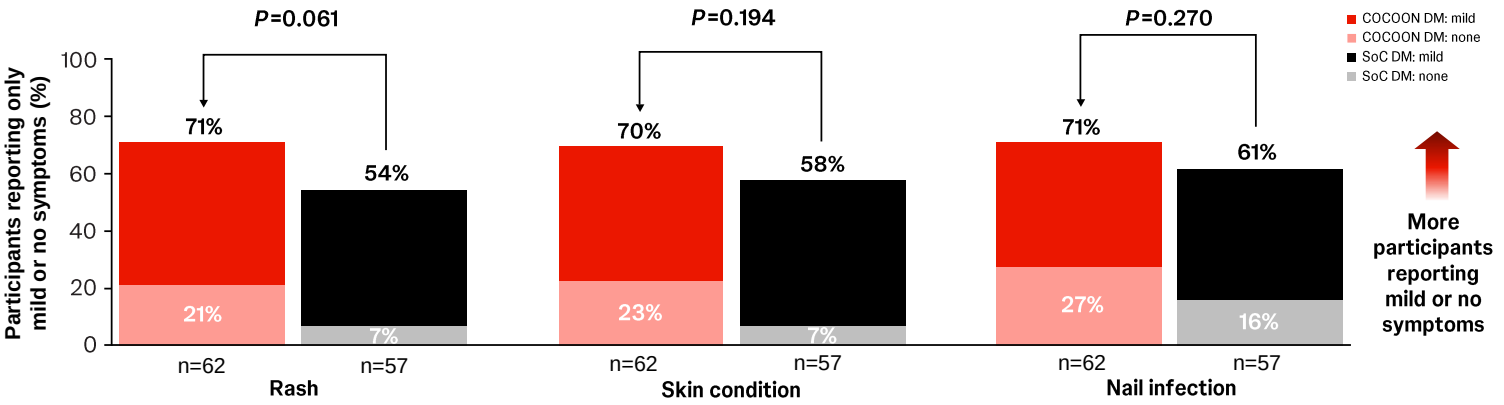




Lower average Skindex-16 total score was observed with COCOON DM vs SoC DM (*P*=0.02) at ~10 weeks after treatment initiation[a]

These endpoints were not adjusted for multiple comparisons. Therefore, the P values displayed are nominal, and statistical significance has not been established.

PGI-S results demonstrate a benefit for COCOON DM vs SoC DM, with more participants reporting mild or no symptoms on PGI-S rash, skin condition, and nail infection with COCOON DM[a]



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Among participants with locally advanced or metastatic c*EGFR*-mutant NSCLC, the prophylactic COCOON DM regimen reduced the severity of dermatologic AEs and the impact of those AEs on QoL compared to SoC DM

The Skindex-16 questionnaire provides an average score (0 [no impact] to 100 [impact experienced all the time]). A lower Skindex-16 score corresponds with better QoL. A 10-point change in total score is considered clinically meaningful. PGI-S is a participant-reported 4-point rating scale (none, mild, moderate, or severe symptoms).

[a]At C3D15, the last time point prior to Week 12. The interim analysis was planned for when participants completed Week 12 assessments.
AE, adverse event; C, cycle; D, day; DM, dermatologic management; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome; QoL, quality of life; SE, standard error; SoC, standard of care.

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