Incidence and Management of Dermatologic Adverse Reactions With Intravenous Amivantamab Plus Lazertinib: Analysis of the Fully Enrolled Population

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 Trial: Investigating Enhanced Dermatologic Management With IV Amivantamab + Lazertinib[4,5,a,b]

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)[c]

- **Weeks 1-12:** Oral doxycycline or minocycline
- **Weeks 13-52:** Topical clindamycin lotion on scalp
- Chlorhexidine on nails
- Ceramide-based moisturizer on body and face

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

VTE prophylaxis was mandatory for the first 4 months

Primary Endpoint:

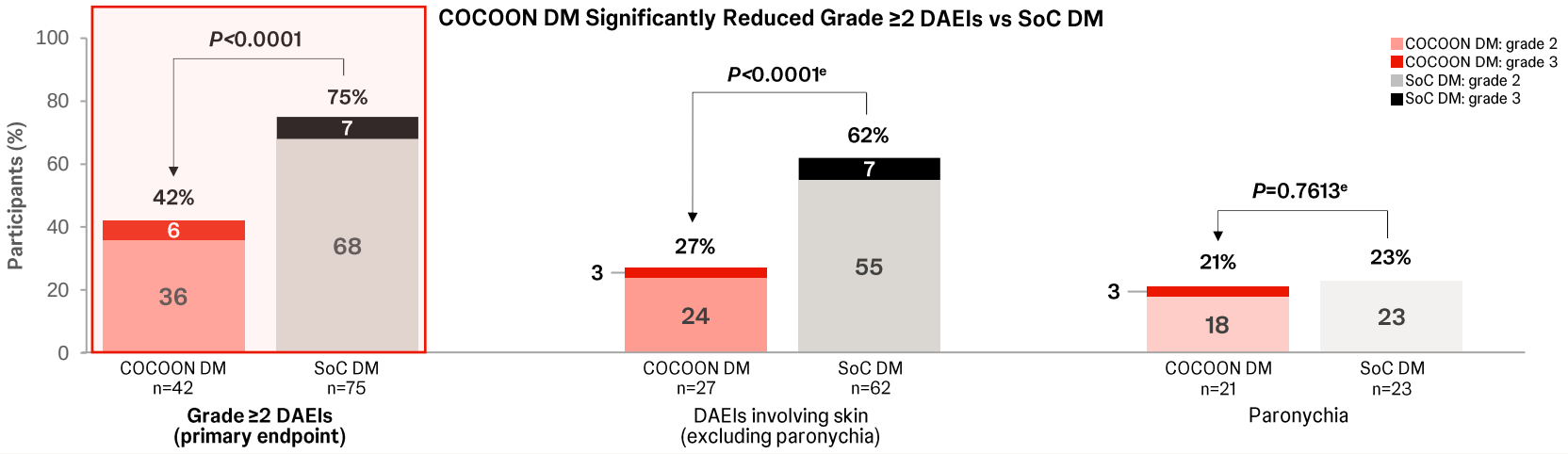
- Incidence of grade ≥2 dermatologic AEs in the first 12 weeks after initiation of amivantamab + lazertinib treatment

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

COCOON DM Enhanced Dermatologic Regimen Resulted in ~44% Reduction in Incidence of Grade ≥2 DAEIs in the First 12 Weeks[4,5]

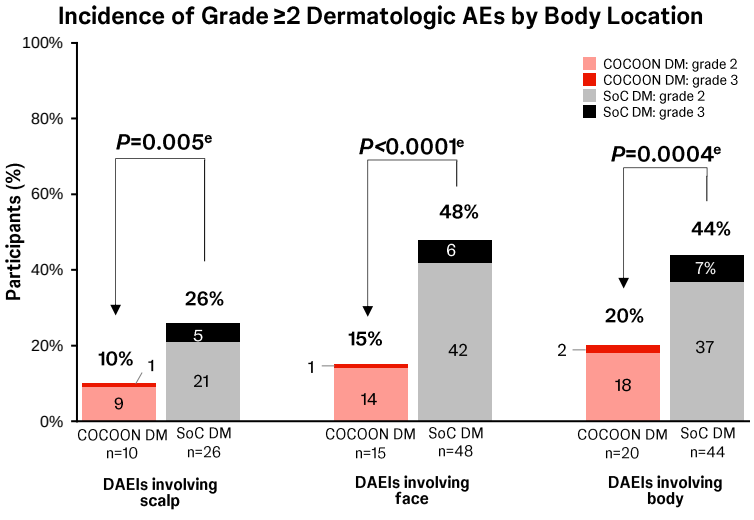
COCOON DM Significantly Reduced Grade ≥2 DAEIs vs SoC DM



The Prophylactic Regimen Significantly Reduced the Incidence of Grade ≥2 DAEIs on the Scalp, Face, and Other Body Locations; Discontinuations and Modifications of COCOON DM Components Were Rare[4,5]

In the first 12 weeks, a significant reduction of grade ≥2 DAEI (excluding paronychia) incidence was consistent across anatomic locations

Incidence of Grade ≥2 Dermatologic AEs by Body Location



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Except for significantly fewer grade ≥2 DAEIs with COCOON DM, the safety profile was comparable between arms:

	COCOON DM (n=99)	SoC DM (n=100)
Conjunctivitis	7%	10%
URTI	7%	7%
Increased ALT (Grade ≥3)	8%	5%
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- Dose interruptions due to DAEIs was less frequent with COCOON DM versus SoC DM in the first 12 weeks (10% vs 23%) and throughout the study duration (22% vs 33%)

Click to learn more about COCOON PROs → Modified COCOON Prophylactic Approach →

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AE, adverse event ALT, alanine aminotransferase; AST, aspartate aminotransferase; 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; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome; QD, once daily; SoC, standard of care; URTI, upper respiratory tract infection; VTE, venous thromboembolism.

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Incidence → First Onset →

Incidence (n=421)[1-3]

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

Median treatment duration:
27.0 months (range, 0.2–47.2)[1]

Most common dermatologic AEs, %	All	Grade 3 or 4
Paronychia	69	12
Rash	64	17
Dermatitis acneiform	30	9
Pruritus	25	<1
Dry skin	17	<1

Rash led to the following dose modifications of amivantamab in participants[2]:

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

Median time to[3,a]:

Onset of rash	Duration of rash
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]Median duration of treatment 18.5 months (range, 0.2-31.4).
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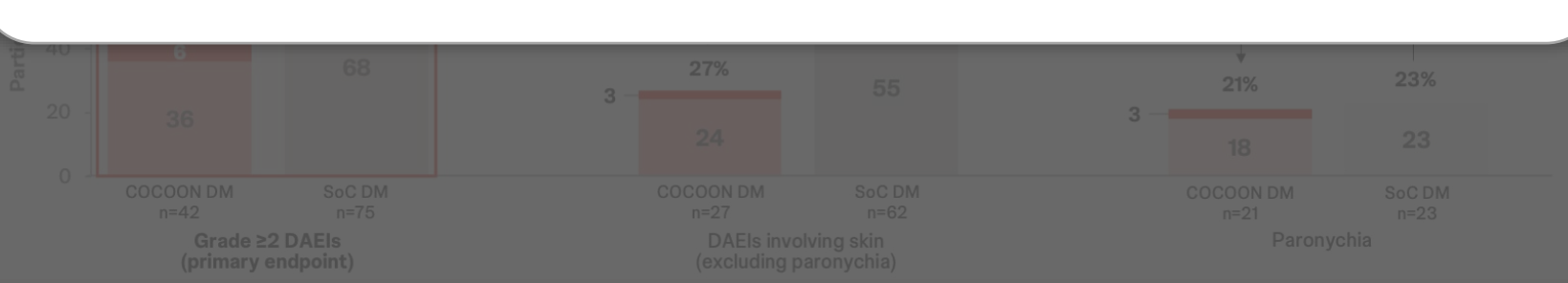

The Prophylactic Regimen Significantly Reduced the Incidence of Grade ≥2 DAEIs on the Scalp, Face, and Other Body Locations; Discontinuations and Modifications of COCOON DM Components Were Rare[4,5]

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Incidence of Grade ≥2 Dermatologic AEs by Body Location

The safety profile of amivantamab + lazertinib was consistent with previous studies, and no new safety signals were observed

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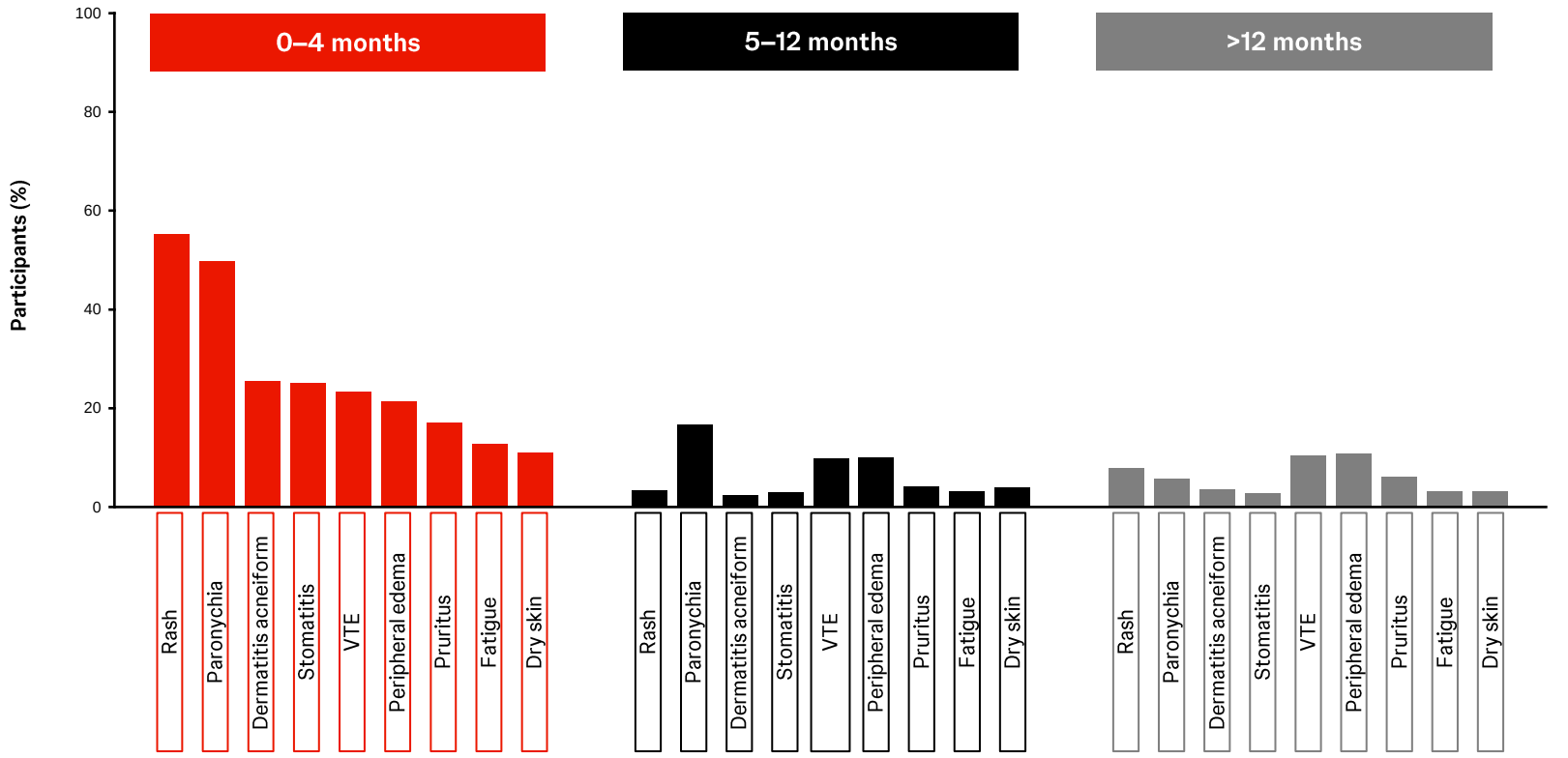
Incidence

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



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Modified COCOON Prophylactic Approach

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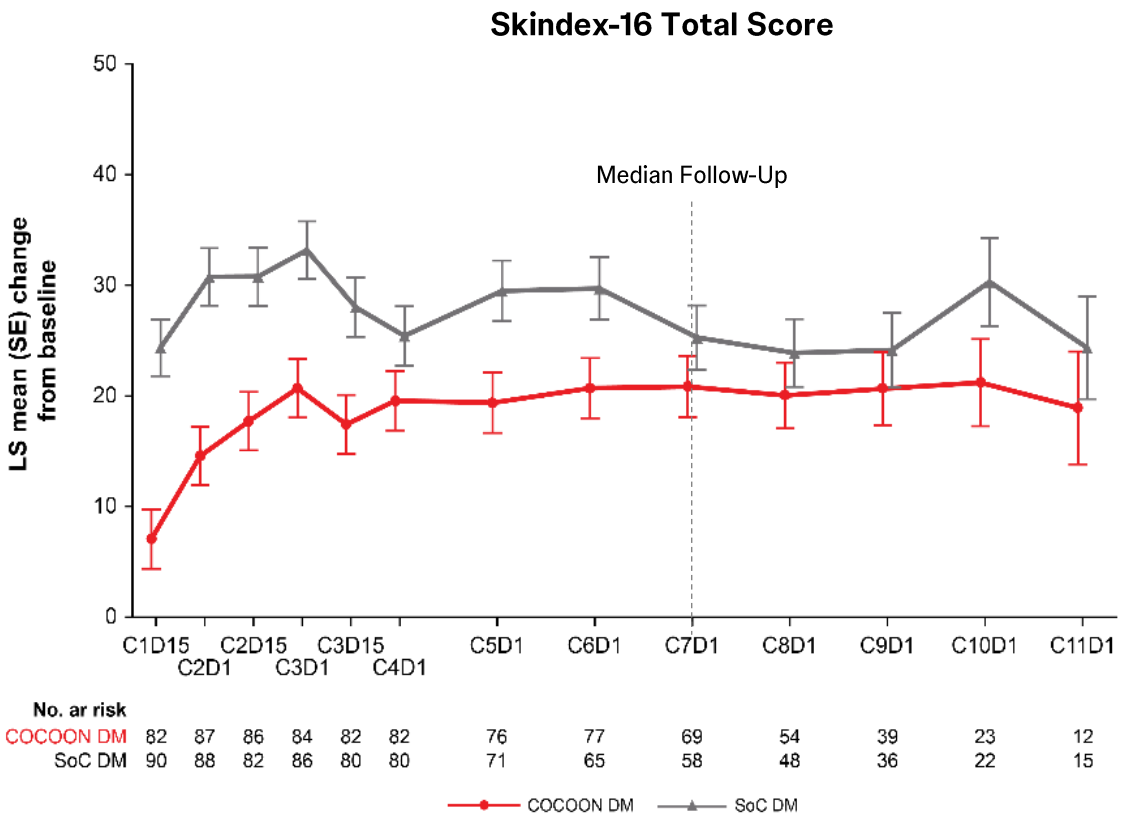
Patient-reported Outcomes Favored COCOON DM Versus SoC DM[1]



Early separation in the least squares mean change from baseline[a] in the Skindex-16 total score favored COCOON DM versus SoC DM.

Separation was maintained up to the median follow-up, even after prophylactic antibiotics were stopped (per protocol) in the COCOON DM arm.

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.

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

[a]Baseline in the graph corresponds to Cycle 1, Day 1, with values of 0 for COCOON DM and SoC DM.
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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Amivantamab Subcutaneous Expansion Cohort With Modified Enhanced Dermatologic Management and Early Intervention[1]

Background anticancer treatment (28-day cycles):
- Lazertinib 240 mg PO QD
- Amivantamab SC[a] C1: 1600 mg/2240 mg[b] QW, C2+: 3520 mg/4640 mg[b] Q4W

Prophylaxis → Early intervention: initiated if the participant presents with ≥1 of the following, at the first occurrence (grade ≥1)

Amivantamab SC + lazertinib + **modified enhanced dermatologic management** (oral tetracyclines [for 24 weeks], noncomedogenic skin moisturizer, oral zinc gluconate) →

Amivantamab SC + lazertinib + **early intervention**
DAEI involving scalp: oral propranolol 10 mg TID + clobetasol 0.05% shampoo
DAEI involving face/body: ruxolitinib 1.5% cream
Paronychia: timolol 0.5% solution + chlorhexidine 4% solution (+ ruxolitinib 1.5% cream if no improvement after 4 weeks)

[a]Weight-based dosing: <80 kg/≥80 kg. [b]Cycle 1: Days 1, 8, 15, 22; Cycles 2+: Day 1 Q4W.
C, cycle, DAEI, dermatologic adverse event of interest; PO, orally; QD, once daily; QW, weekly; Q4W; every 4 weeks; SC, subcutaneous; TID, three time per day.
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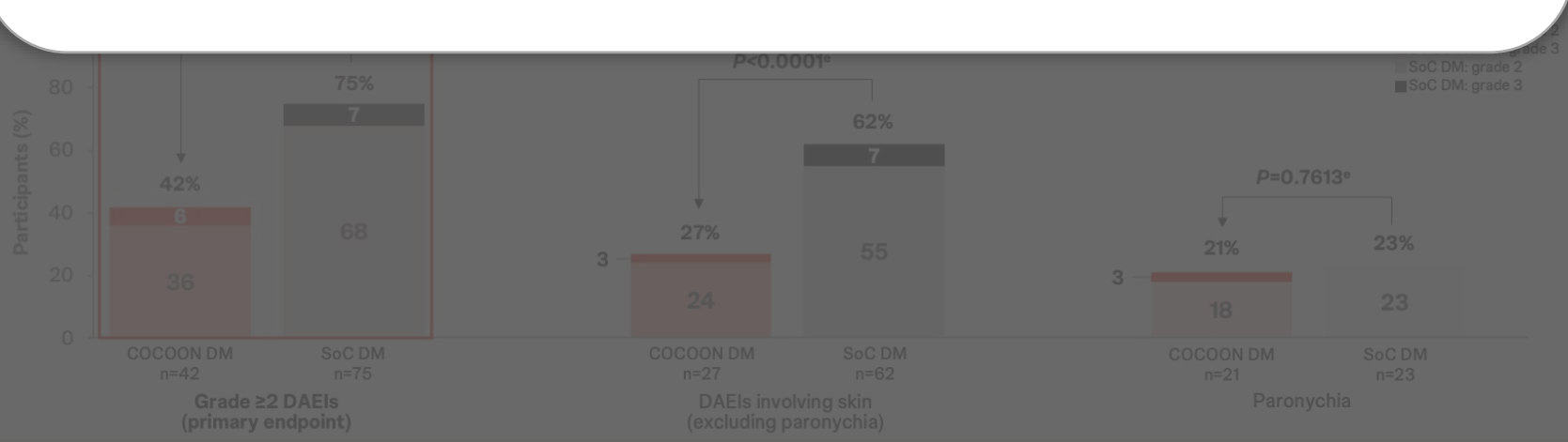

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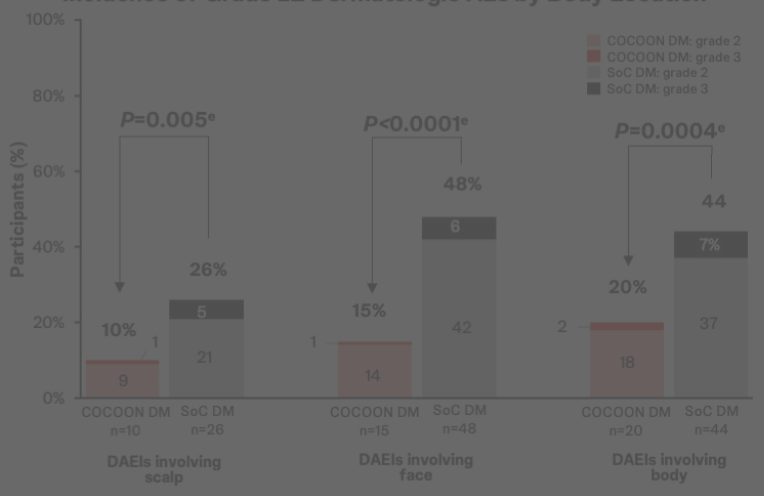

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