Preventing Moderate to Severe Dermatologic Adverse Events in First-line *EGFR*-mutant Advanced NSCLC Treated with Amivantamab Plus Lazertinib

Early Success of the COCOON Trial

For use by Medical Science Liaisons (MSLs) and Value & Evidence Scientific engagement (V&ESE).

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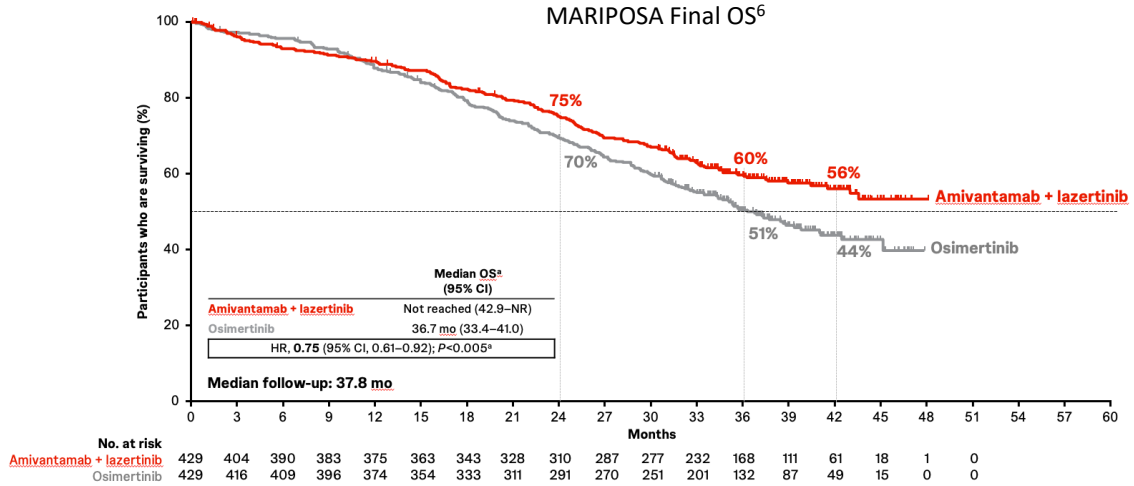
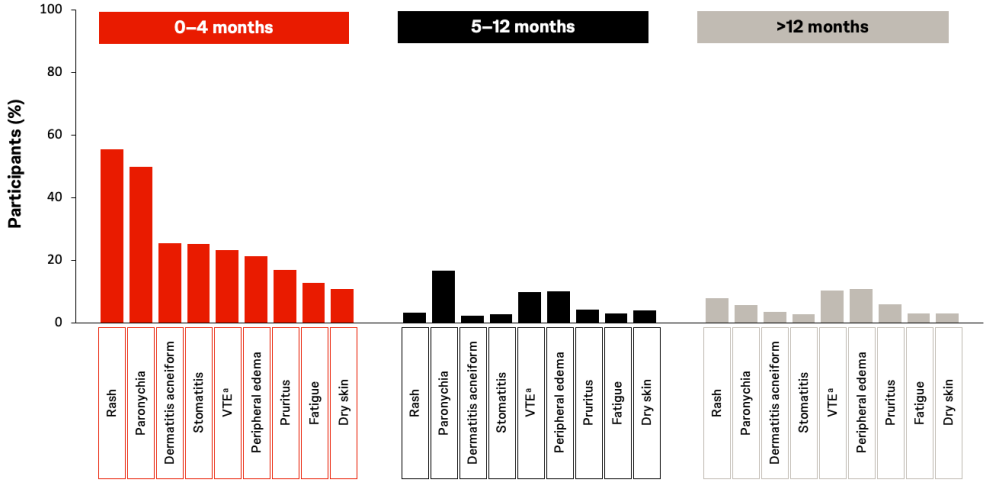
Background

- EGFR-targeted therapies have been associated with dermatologic AEs, which are often treated reactively in clinical practice[1-3]
- First-line amivantamab + lazertinib is FDA- and EMA-approved for *EGFR*-mutated advanced NSCLC based on the results of the phase 3 MARIPOSA study (NCT04487080)[4,5]
  - The first onset of dermatologic AEs often occurs in the first 4 months of treatment[6]
  - Early management of dermatologic AEs is expected to allow patients to remain on treatment longer with amivantamab + lazertinib
- COCOON (NCT06120140) prospectively evaluated a simple prophylactic regimen to prevent moderate to severe *EGFR*-related dermatologic AEs

MARIPOSA Final OS[6]



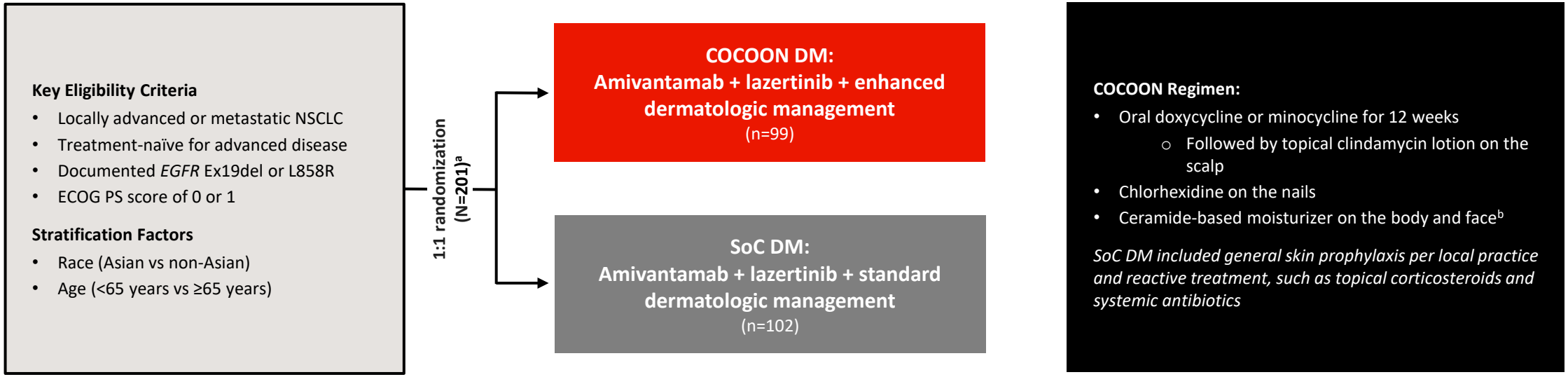
First Onset of Key AEs[6]



[a]In total, 390 deaths had occurred in the amivantamab + lazertinib (173 deaths) and osimertinib (217 deaths) arms. *P*-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified Cox regression model.

1. Peng Y, et al. *Biosci Trends*. 2019;12(6):537-552. 2. Basse C, et al. *Lung Cancer*. 2022;173:116-123. 3. Petrelli F, et al. *Br J Dermatol*. 2016;175(6):1166-1174. 4. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024. 5. European Commission approves Lazcluze (lazertinib) in combination with Rybrevant (amivantamab) for the first-line treatment of patients with EGFR-mutated advanced non-small cell lung cancer. News release. Johnson & Johnson. January 21, 2025. Accessed January 27, 2025. https://www.jnj.com/media-center/press-releases/european-commission-approves-lazcluze-lazertinib-in-combination-with-rybrevant-amivantamab-for-the-first-line-treatment-of-patients-with-egfr-mutated-advanced-non-small-cell-lung-cancer. 6. Yang JC-H, et al. Presented at: European Lung Cancer Congress (ELCC); March 26-29, 2025; Paris, France.

Phase 2 COCOON study design



VTE prophylaxis was mandatory for the first 4 mo

Primary Endpoint:

Incidence of grade ≥2 dermatologic AEs[c] in the first 12 weeks after initiation of amivantamab + lazertinib treatment[d]

Key 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

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

COCOON (ClinicalTrials.gov Identifier: NCT06120140).

[a]Planned enrollment of 200 participants was estimated to provide a power of 82% to detect a 35% difference in DAEIs. [b]La Roche Posay Lipikar AP+M moisturizer was used in COCOON. [c]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. [d]Severity per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v5.0. [e]All analyses were performed using the safety analysis set.

Baseline demographics and clinical characteristics

- At a median follow-up of 4.2 months,[a] 138 participants received ≥1 dose of amivantamab + lazertinib (safety analysis set)[b] and had ≥12 weeks of follow-up[c]
- The median duration of amivantamab + lazertinib treatment was **4.2 months** with **COCOON DM**[d] vs **4.1 months** with **SoC DM**

Characteristic, n (%)	COCOON DM (n=70)	SoC DM (n=68)[e]
Median age, years (range)	62.5 (36–78)	62.5 (37–83)
Female	42 (60)	37 (54)
Race[f]		
Asian	52 (74)	49 (72)
White	17 (24)	19 (28)
ECOG PS 1	44 (63)	36 (53)
History of smoking	24 (34)	21 (31)
History of brain metastases	23 (33)	27 (40)
EGFR mutation type		
Ex19del	35 (50)	37 (54)
L858R	35 (50)	31 (46)

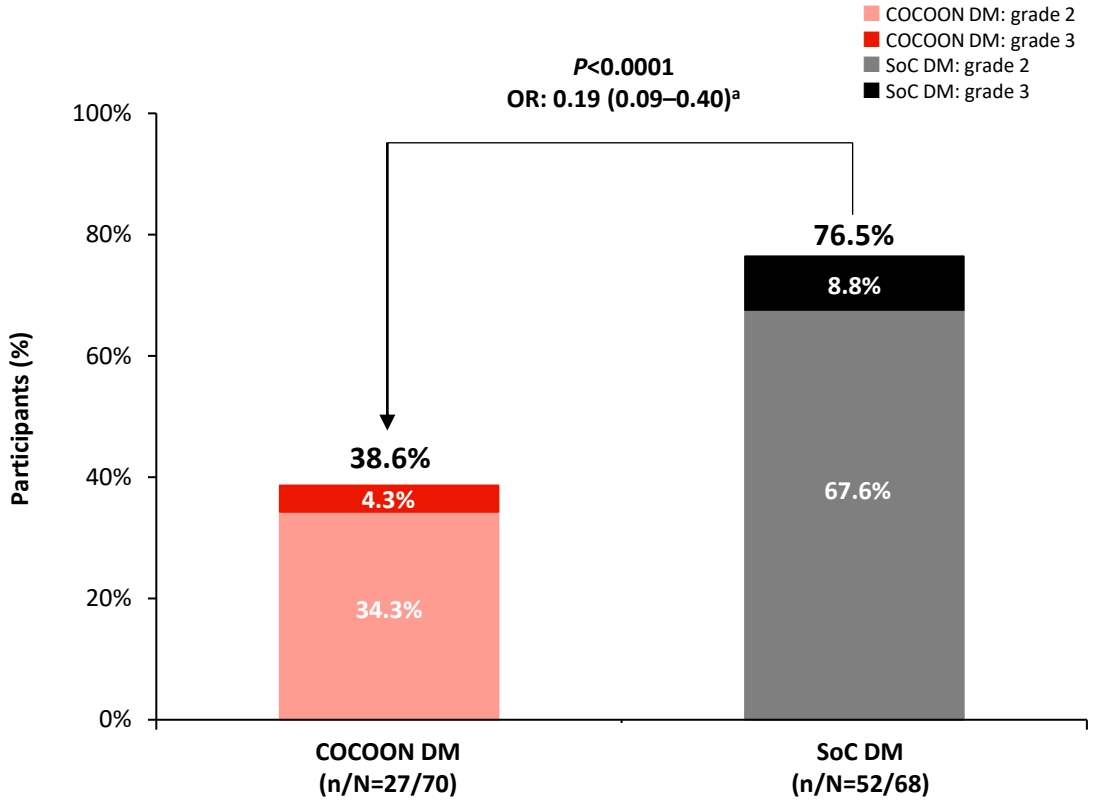
Baseline characteristics were well balanced across arms

Note: percentages may not sum to 100 due to rounding.
[a]Due to limited follow-up at the interim analysis, efficacy results will be reported at a future congress. [b]All analyses were performed using the safety analysis set. [c]138 participants had the opportunity to receive treatment for 12 weeks; however, some discontinued prior to Week 12. [d]In the COCOON DM arm, 48 participants received doxycycline for a median duration of 2.7 months, and 24 participants received minocycline for a median duration of 2.8 months. [e]2 Participants randomized to SoC DM did not meet inclusion criteria at C1D1 and discontinued the study prior to receiving amivantamab + lazertinib. [f]Participant in the COCOON DM arm was American Indian or Alaska Native.
DM, dermatologic management; ECOG PS, Eastern Cooperative Oncology Group performance status; Ex19del, exon 19 deletion; L858R, exon 21 L858R substitution; SoC, standard of care.

COCOON: Primary endpoint reached at first analysis

In the first 12 weeks:

- 2-fold reduction in grade ≥2 dermatologic AEs with **COCOON DM** vs **SoC DM** (**38.6%** vs **76.5%**)
- 2-fold reduction in grade 3 dermatologic AEs with **COCOON DM** vs **SoC DM** (**4.3%** vs **8.8%**)
- 3-fold reduction in the number of participants who reported 2 or more different grade ≥2 dermatologic AEs with **COCOON DM** vs **SoC DM** (**6%** vs **18%**)



COCOON DM reduced grade ≥2 dermatologic AEs by 50% vs SoC DM

[a]OR was generated by a logistic model, adjusted by race and age (continuous).
CI, confidence interval; DM, dermatologic management; IA, interim analysis; OR, odds ratio; SoC, standard of care.

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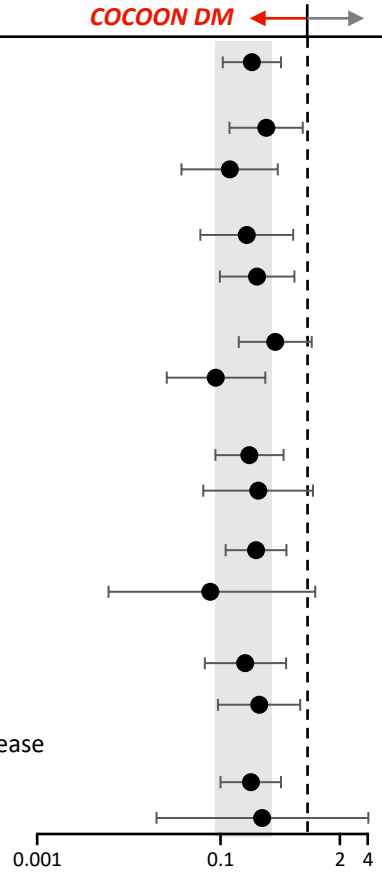
Consistent reductions in grade ≥2 dermatologic AEs were observed across all subgroups



Subgroup	OR (95% CI)[b]	Events/N	
		COCOON DM	SoC DM
All participants[a]	0.19 (0.09–0.40)	27/70	52/68
Age category			
<65 years	0.28 (0.11–0.71)	17/41	28/39
≥65 years	0.11 (0.03–0.375)	10/29	24/29
ECOG PS score			
0	0.17 (0.05–0.55)	11/26	26/32
1	0.22 (0.085–0.57)	16/44	26/36
Sex			
Female	0.35 (0.14–0.89)	19/42	26/37
Male	0.08 (0.02–0.27)	8/28	26/31
Race			
Asian	0.18 (0.08–0.43)	20/52	38/49
Non-Asian	0.23 (0.06–0.915)	7/18	14/19
Weight category			
<80 kg	0.215 (0.10–0.46)	25/63	46/61
≥80 kg	0.07 (0.005–0.97)	2/7	6/7
EGFR mutation type			
Ex19del	0.16 (0.06–0.46)	13/35	29/37
L858R	0.23 (0.08–0.66)	14/35	23/31
History of dermatologic disease			
No	0.19 (0.09–0.41)	24/63	49/64
Yes	0.25 (0.02–3.77)	3/7	3/4

Note: Gray box indicates 95% CI of OR for all participants. [a]Safety analysis set. [b]Unadjusted OR.
CI, confidence interval; DM, dermatologic management; ECOG PS, Eastern Cooperative Oncology Group performance status; Ex19del, exon 19 deletion; OR, odds ratio; SoC, standard of care.

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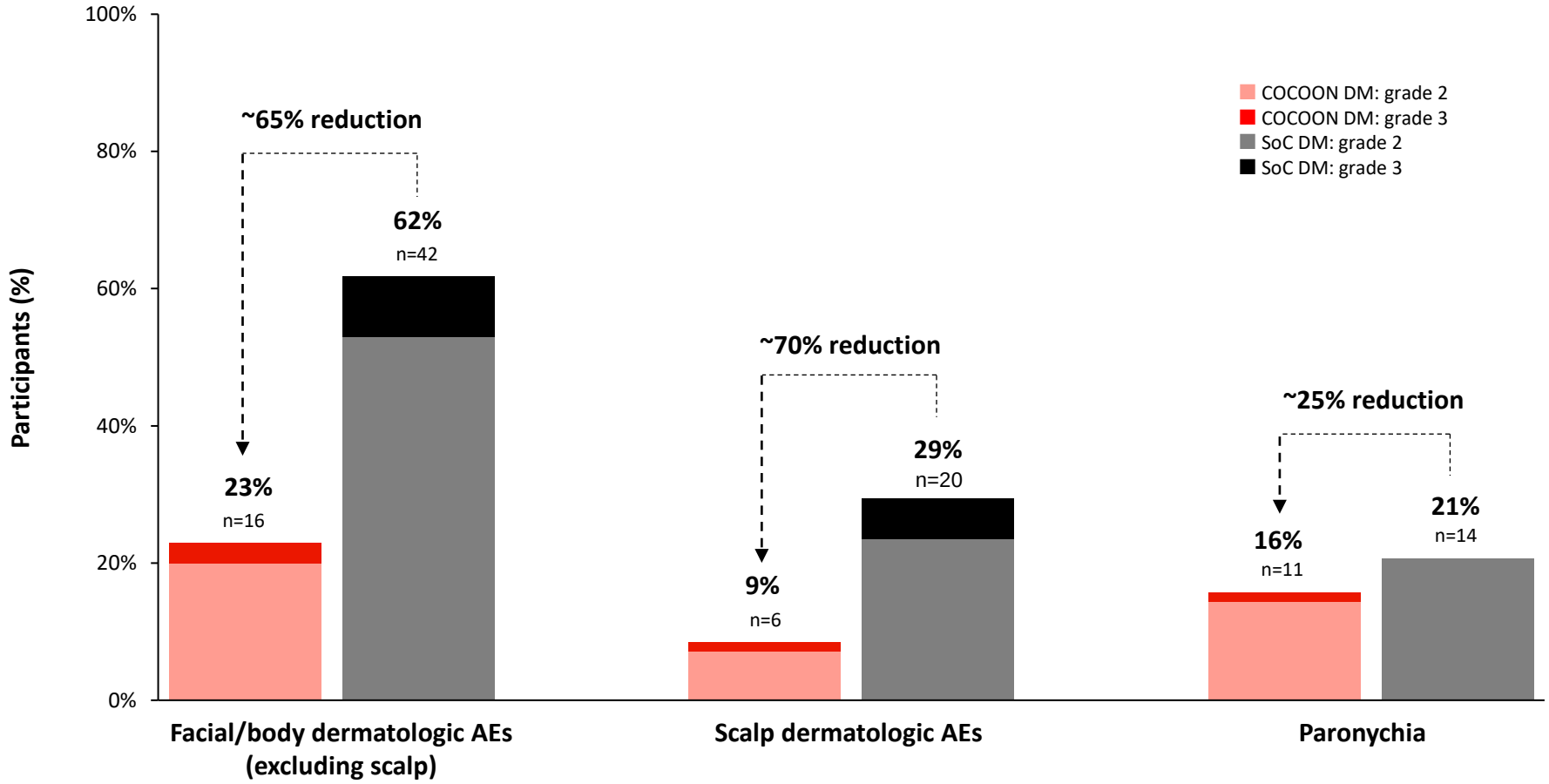
Grade ≥2 dermatologic AEs by body location



In the first 12 weeks, substantial 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

DM, dermatologic management; SoC, standard of care.

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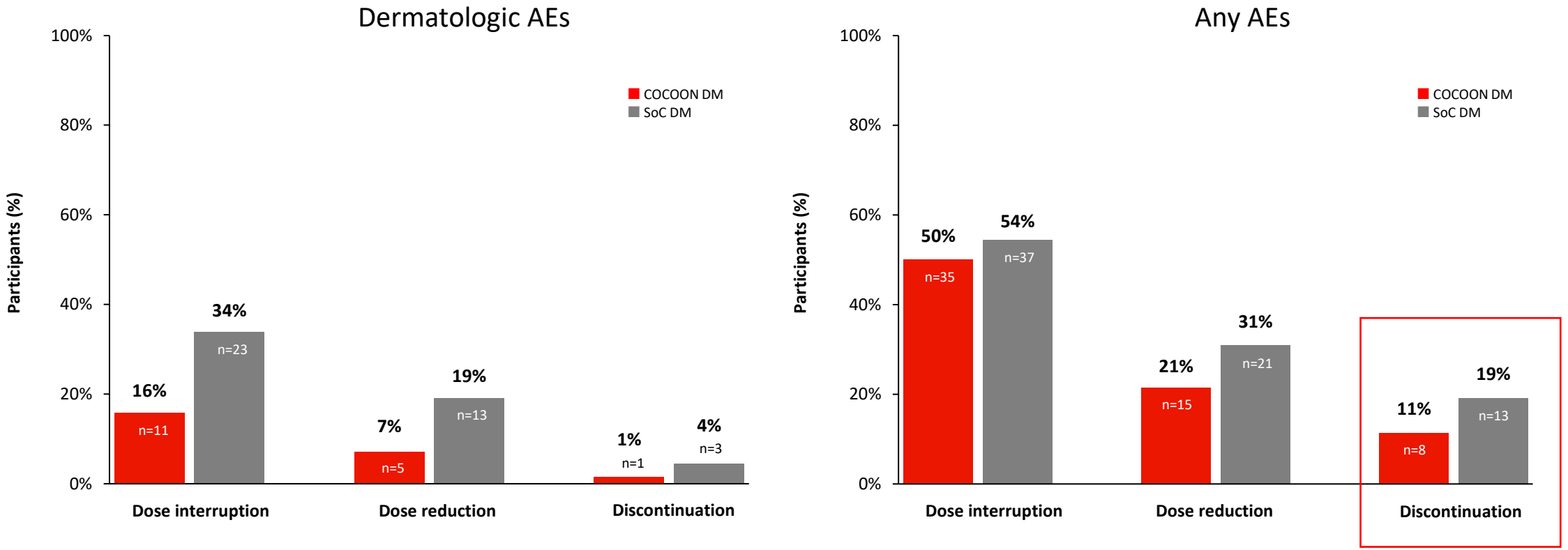
Dose modifications of amivantamab/lazertinib due to AEs



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

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

DM, dermatologic management; SoC, standard of care.

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Summary

- At the first pre-planned interim analysis, the primary endpoint was met: The prophylactic COCOON DM regimen significantly reduced the incidence of grade ≥2 dermatologic AEs[a] vs SoC DM in the first 12 weeks
  - Incidence of grade ≥2 dermatologic AEs was reduced by 50% with COCOON DM vs SoC DM (*P*<0.0001)
  - Grade 3 dermatologic AEs were reduced by >50% with COCOON DM vs SoC DM
  - >3-fold reduction in moderate to severe scalp dermatologic AEs with COCOON DM compared with SoC DM
- ~50% reduction in discontinuations due to AEs with COCOON DM vs SoC DM

The prophylactic COCOON DM regimen, with widely available agents, significantly reduced the incidence and severity of dermatologic AEs with 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.
1L, first-line; AE, adverse event; DM, dermatologic management; IV, intravenous; SoC, standard of care.

Preventing AEs with amivantamab + lazertinib

Begin Amivantamab + Lazertinib

	IRR Prophylactic Regimen (SKIPPirr)[1]	VTE Prophylactic Regimen (PALOMA-2, PALOMA-3)[2,3]	
	2 Days to 1 hour before start Oral 8-mg dexamethasone BID 2 days and 1 day prior and 8-mg 1 hour before first infusion[a]	**First 4 months** Oral anticoagulants as per NCCN or local guidelines	
	Dermatologic Prophylactic Regimen (COCOON)[b]		
Antibiotic prophylaxis	**Weeks 1–12** 100-mg BID doxycycline or minocycline	**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 months		
Long-acting skin hydration	**Weeks 1+** Ceramide-based moisturizer at least daily for 12 months[c]		

[a]Includes standard premedication (antihistamines, antipyretics, and glucocorticoids). [b]Prophylactic antibiotics: oral doxycycline or minocycline 100 mg BID; topical clindamycin lotion 1% on scalp daily before bedtime. Paronychia prophylaxis: chlorhexidine 4% on the fingernails and toenails daily. Skin moisturization: La Roche Posay Lipikar AP+M moisturizer on the body and face at least daily. [c]La Roche Posay Lipikar AP+M moisturizer was used in COCOON.

AE, adverse event; BID, twice daily; IRR, infusion-related reaction; VTE, venous thromboembolism.

1. Spira AI, et al. *J Thorac Oncol.* 2025 Jan 24:S1556-0864(25)00051-6. 2. Scott SC, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA.
3. Leighl NB, et al. *J Clin Oncol.* 2024 Oct 20;42(30):3593-3605.

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