

Improving prevention of moderate to severe dermatologic adverse events in *EGFR*-mutant advanced NSCLC treated with first-line subcutaneous amivantamab + lazertinib

First results from new COCOON cohorts

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Disclosures

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Background

- In MARIPOSA, IV amivantamab + lazertinib significantly improved OS versus osimertinib in 1L common *EGFR*-mutant advanced NSCLC (HR, 0.75; $P=0.005$), but was associated with dermatologic AEs, including rash and paronychia, commonly occurring early in treatment and leading to discontinuations¹
- In the phase 2 COCOON study (NCT06120140), enhanced dermatologic management^a with 1L IV amivantamab + lazertinib significantly reduced grade ≥ 2 dermatologic AEs during the first 12 weeks versus standard dermatologic care in participants with *EGFR*-mutant advanced NSCLC²
- We further evaluated a simplified dermatologic prophylaxis regimen in combination with SC amivantamab, which was previously shown to improve overall treatment experience and help patients stay on treatment longer^{3–5}

Here we report the first results from 2 new COCOON cohorts using a simplified dermatologic prophylaxis regimen in participants receiving 1L SC amivantamab^b + lazertinib

^aOral tetracycline for 12 weeks, ceramide-based moisturizer, topical clindamycin, chlorhexidine. ^bCo-formulated with recombinant human hyaluronidase PH20.

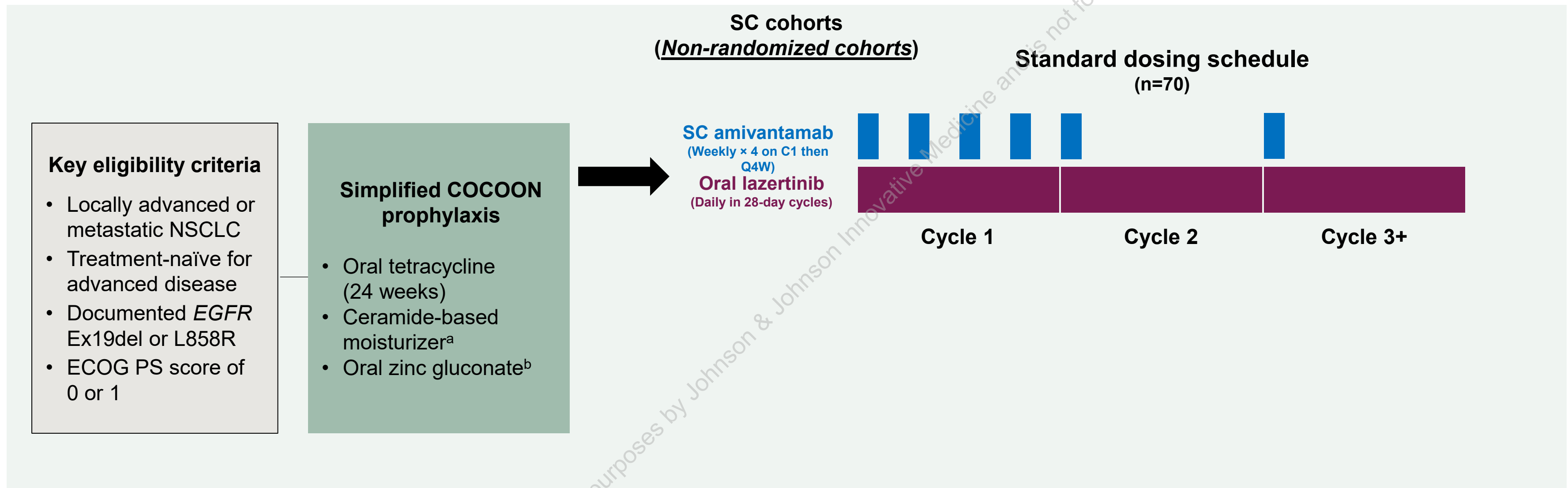
1L, first-line; HR, hazard ratio; IV, intravenous; SC, subcutaneous.

1. Yang JCH, et al. *N Engl J Med*. 2025;393(17):1681–1693. 2. Cho BC, et al. *J Thorac Oncol*. 2025;20(10):1517–1530. 3. Leighl NB, et al. *J Clin Oncol*. 2024;42:3593–3605. 4. Alexander MA, et al. *Eur J Cancer*. 2025;227:115624.

5. Halmos B. Presented at World Conference on Lung Cancer (WCLC) 2026; September 12–15, 2026; Seoul, Republic of Korea.



Methods



- Primary endpoint was incidence of grade ≥ 2 dermatologic AEs in the first 12 weeks after initiation of anticancer treatment; no prespecified formal comparisons between cohorts
- Additional site-directed interventions were evaluated for concomitant use when clinically indicated
- Preferred terms^c for dermatologic AEs included rash, dermatitis acneiform, pruritus, skin fissures, acne, folliculitis, erythema, eczema, rash maculopapular, 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

COCOON (ClinicalTrials.gov Identifier: NCT06120140). ^aLa Roche-Posay Lipikar AP+M moisturizer was used in COCOON. ^b70 mg once daily for up to 52 weeks. ^cSeverity per NCI CTCAE v5.0.

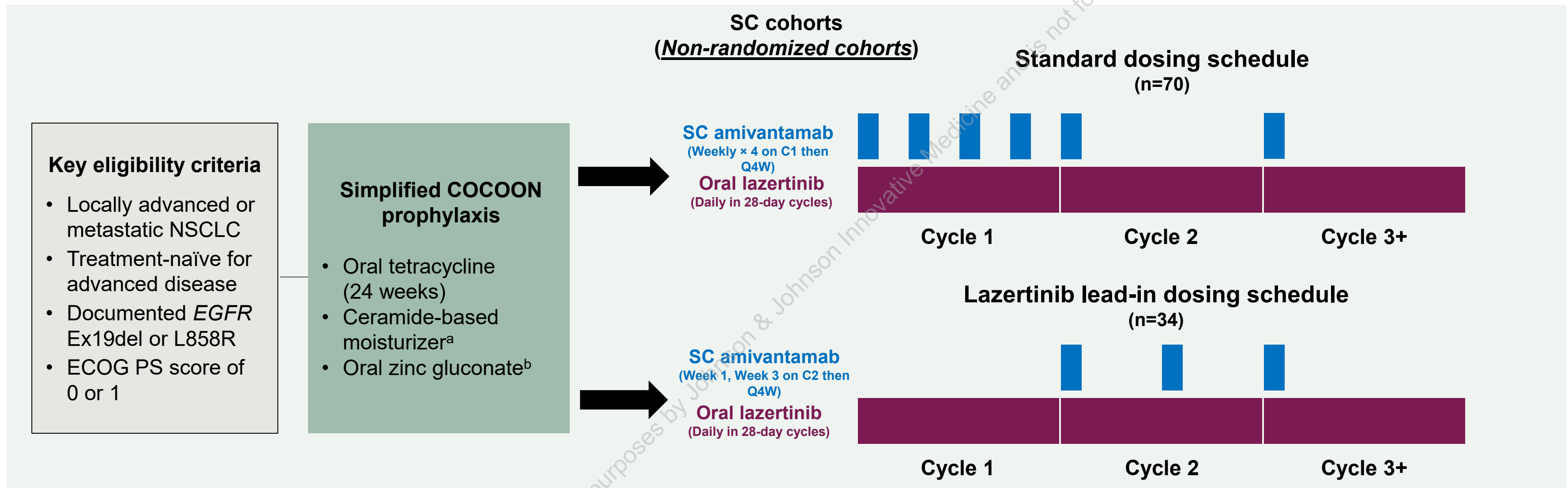
C, Cycle; D, Day; Q, every; SC, subcutaneous; W, week.

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Demographic and Baseline Disease Characteristics

Characteristic, n (%)	Main COCOON study (n=199) ¹ (IV amivantamab + lazertinib)		SC amivantamab + simplified dermatologic prophylaxis (n=104)	
	SoC DM (n=100)	COCOON DM (n=99)	Standard schedule (n=70) Median (range) follow-up, 8.1 (1.0–9.7) months	Laz lead-in (n=34) Median (range) follow-up, 5.5 (1.6–6.0) months
Median age (range), y	62.5 (28–83)	63 (34–80)	63 (35–87)	66 (36–81)
Female	57 (57)	61 (62)	46 (66)	21 (62)
Race ^a				
Asian	65 (65)	66 (67)	47 (67)	28 (82)
White	32 (32)	32 (32)	22 (31)	5 (15)
Black or African American	1 (1)	0	0	1 (3)
Multiple	2 (2)	0	1 (1)	0
ECOG PS score of 1	55 (55)	59 (60)	43 (61)	27 (79)
History of brain metastases	43 (43)	32 (32)	21 (30)	16 (47)
History of smoking	33 (33)	34 (34)	13 (19)	10 (29)
Histologic type ^b				
Adenocarcinoma	97 (97)	94 (95)	70 (100)	33 (97)
Squamous cell carcinoma	2 (2)	2 (2)	0	1 (3)
Large cell carcinoma	0	1 (1)	0	0
Mutation type				
Ex19del	54 (54)	50 (51)	41 (59)	14 (41)
L858R	46 (46)	49 (49)	29 (41)	20 (59)

Clinical cutoff: September 1, 2026. ^aOne participant in the COCOON DM cohort self-reported their race as American Indian or Alaska Native. ^bFor 2 participants in the COCOON DM cohort and 1 participant in the SoC DM cohort, histologic type was reported as “Other”. DM, dermatologic management; IV, intravenous; laz, lazertinib; SC, subcutaneous; SoC, standard of care.

1. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530.

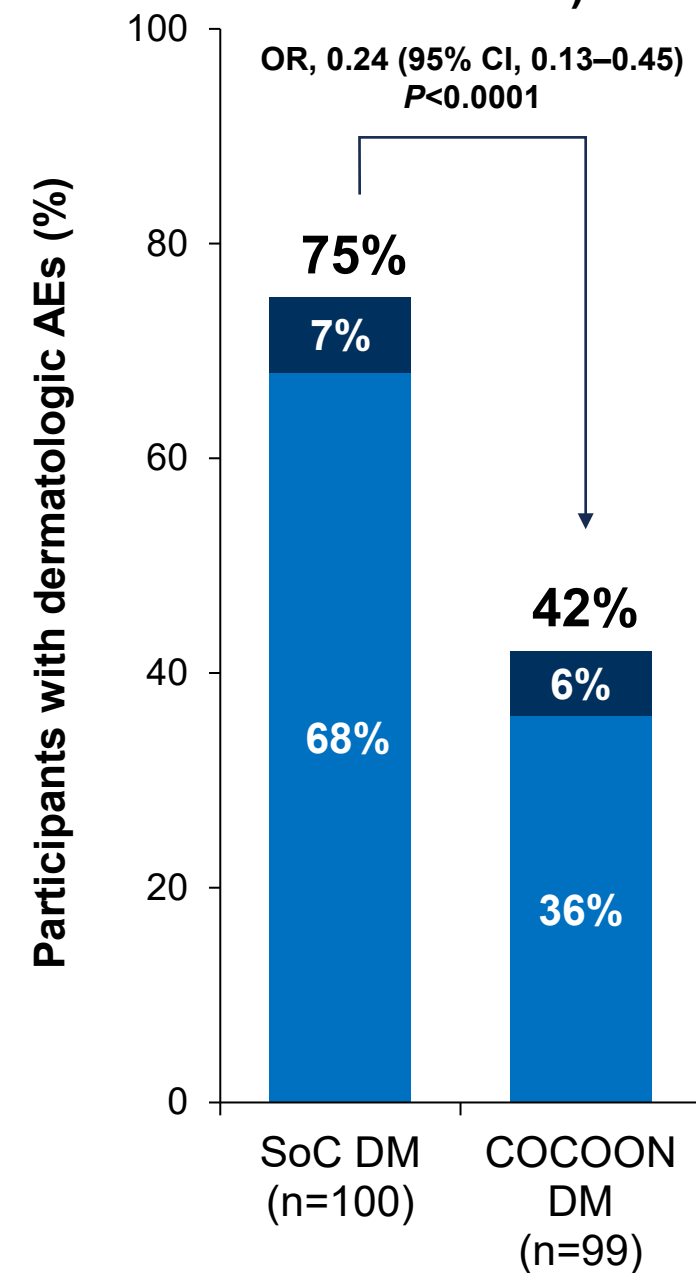
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Primary Endpoint: Grade ≥ 2 Dermatologic AEs by Week 12

Main COCOON study¹
(IV amivantamab +
lazertinib)



■ Grade 2
■ Grade >2

- Dermatologic prophylaxis has previously been shown to reduce dermatologic AEs by Week 12¹

DM, dermatologic management; IV, intravenous; OR, odds ratio; SoC, standard of care.

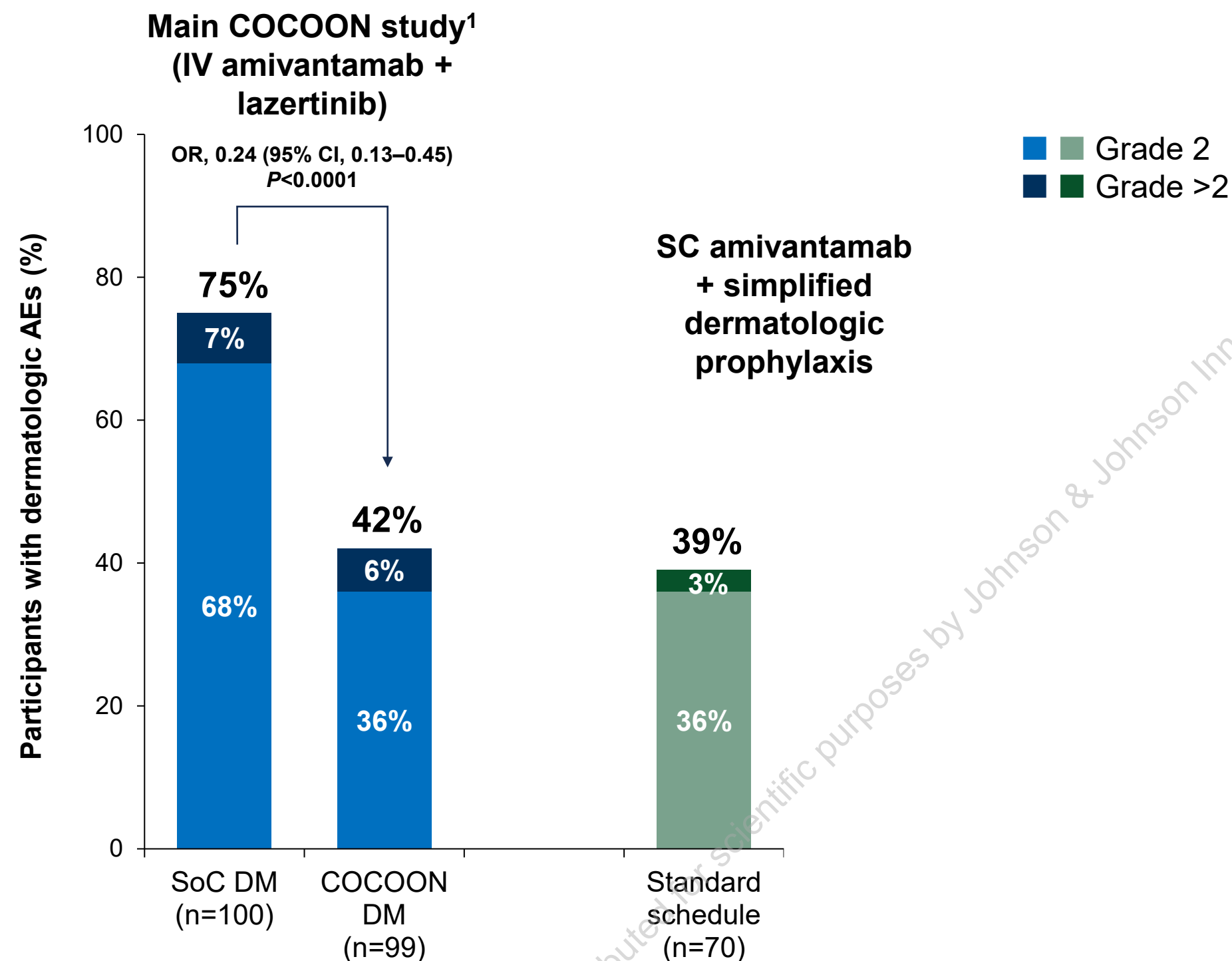
1. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530.

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Primary Endpoint: Grade ≥ 2 Dermatologic AEs by Week 12



- Dermatologic prophylaxis has previously been shown to reduce dermatologic AEs by Week 12¹
- Simplified prophylaxis is associated with a similar reduction in dermatologic AEs as the full COCOON DM regimen

DM, dermatologic management; IV, intravenous; OR, odds ratio; SC, subcutaneous; SoC, standard of care.

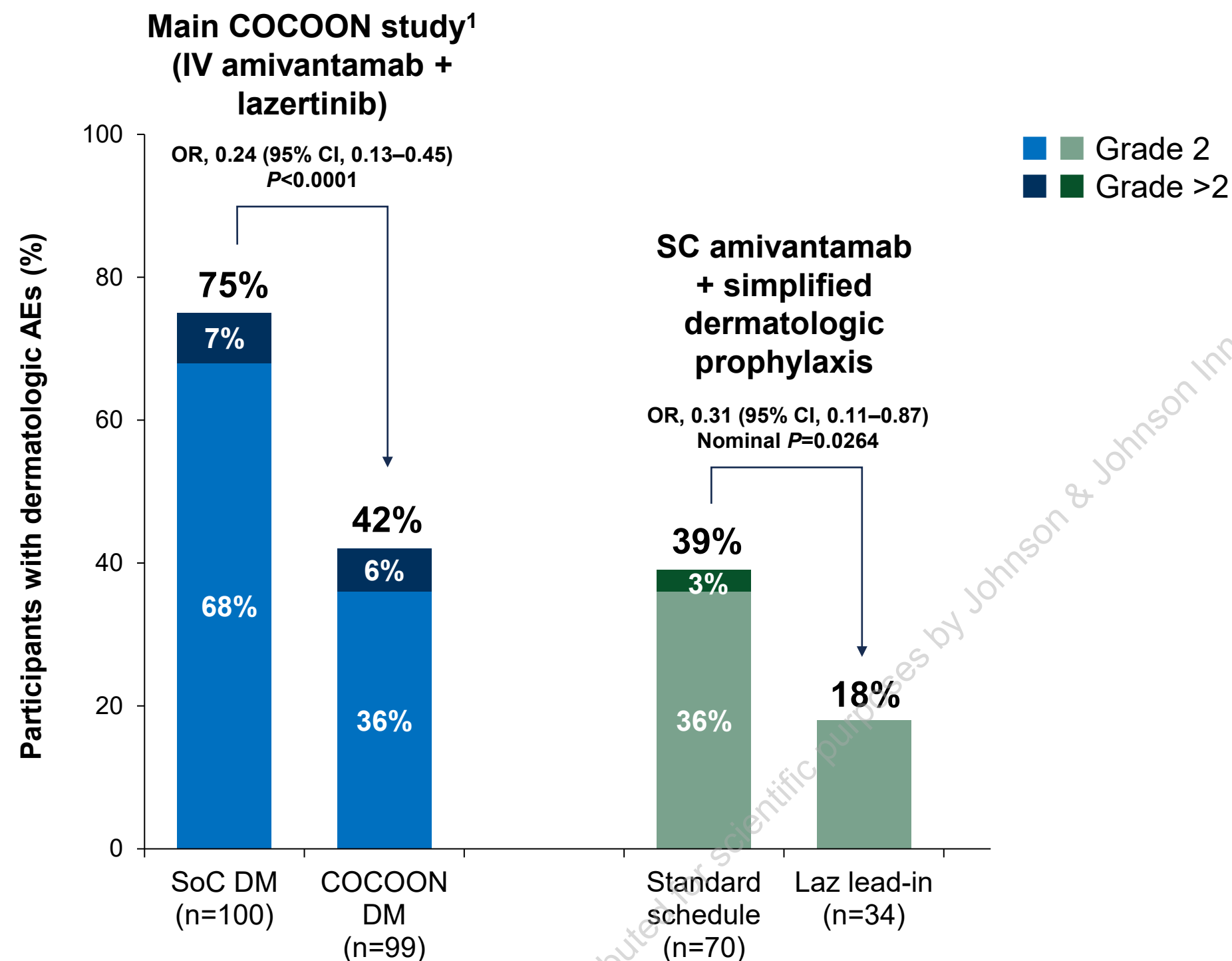
1. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530.

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Primary Endpoint: Grade ≥ 2 Dermatologic AEs by Week 12



- Dermatologic prophylaxis has previously been shown to reduce dermatologic AEs by Week 12¹
- Simplified prophylaxis is associated with a similar reduction in dermatologic AEs as the full COCOON DM regimen
- Lazertinib lead-in prior to starting amivantamab + lazertinib at Cycle 2 further reduced early dermatologic AEs^a

^aIn a preliminary analysis, investigator-assessed overall response rates were consistent between standard and lazertinib lead-in cohorts (71% vs 70%).

DM, dermatologic management; IV, intravenous; laz, lazertinib; OR, odds ratio; SC, subcutaneous; SoC, standard of care.

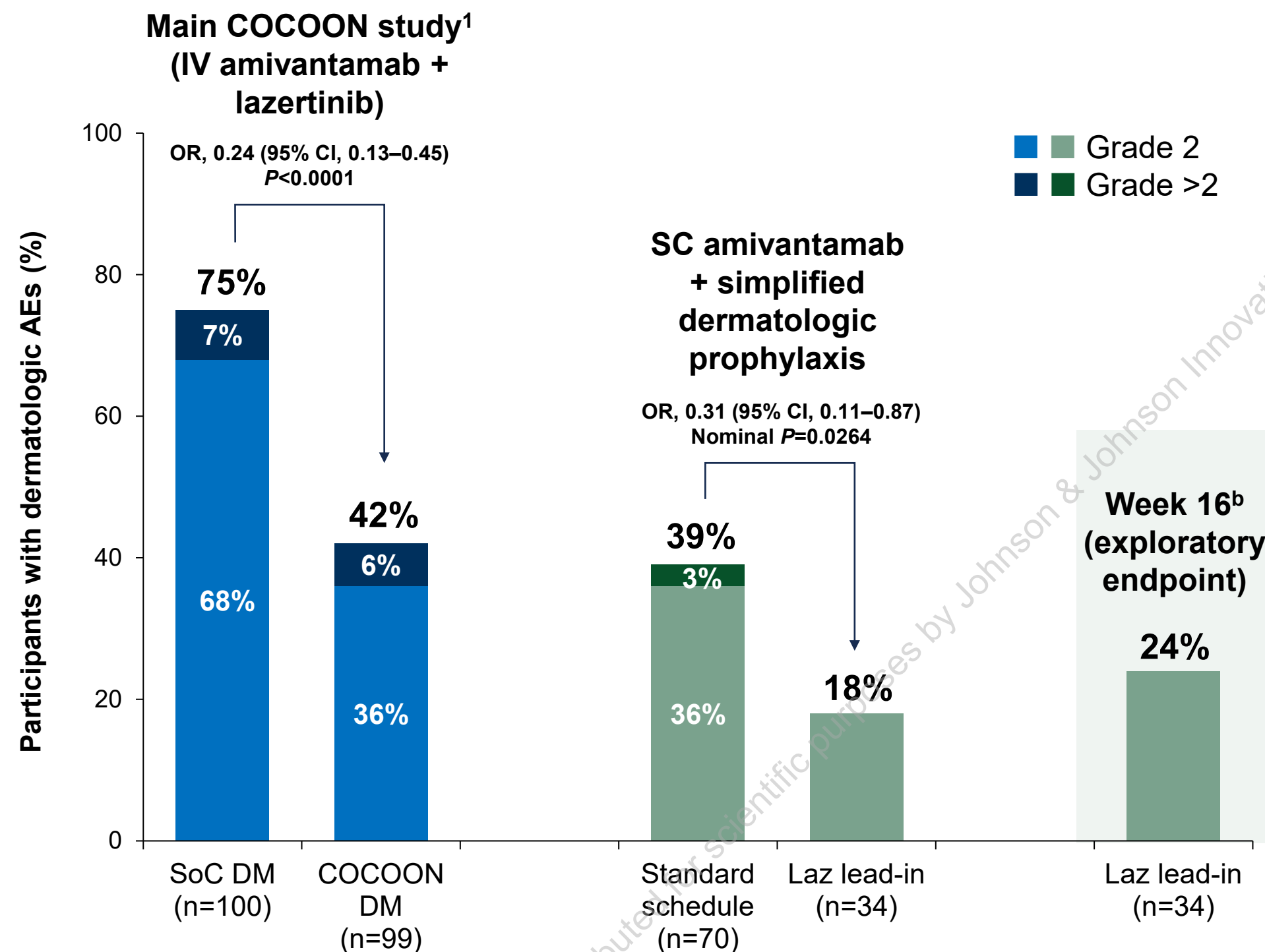
1. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530.

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Primary Endpoint: Grade ≥ 2 Dermatologic AEs by Week 12



- Dermatologic prophylaxis has previously been shown to reduce dermatologic AEs by Week 12¹
- Simplified prophylaxis is associated with a similar reduction in dermatologic AEs as the full COCOON DM regimen
- Lazertinib lead-in prior to starting amivantamab + lazertinib at Cycle 2 further reduced early dermatologic AEs^a
 - An exploratory analysis of Week 16 data showed consistent findings^b

^aIn a preliminary analysis, investigator-assessed overall response rates were consistent between standard and lazertinib lead-in cohorts (71% vs 70%).

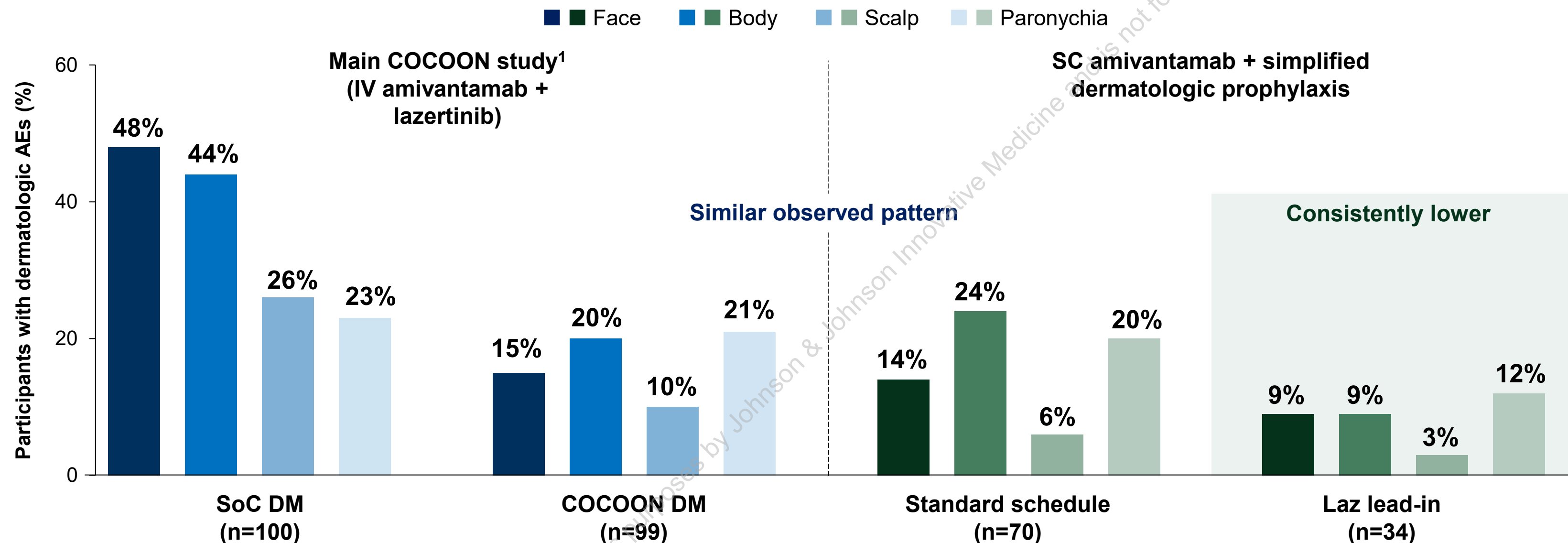
^bAt Week 16, participants had up to 12 weeks of amivantamab exposure and 16 weeks of lazertinib exposure.

DM, dermatologic management; IV, intravenous; laz, lazertinib; OR, odds ratio; SC, subcutaneous; SoC, standard of care.

1. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530.



Location of Grade ≥ 2 Dermatologic AEs by Cohort



- In the first 12 weeks, the incidence of grade ≥ 2 dermatologic AEs across body locations was similar for COCOON DM and simplified dermatologic prophylaxis
- Rates were consistently lower for the lazertinib lead-in cohort

DM, dermatologic management; laz, lazertinib; SC, subcutaneous; SoC, standard of care.

1. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530.

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Other Key AEs

	Main COCOON study (n=199) ¹ (IV amivantamab + lazertinib)		SC amivantamab + simplified dermatologic prophylaxis (n=104)	
	SoC DM (n=100)	COCOON DM (n=99)	Standard schedule (n=70)	Laz lead-in (n=34)
Any grade AEs, %				
ARR	56	61	1 ^a	0
VTE	13	13	9 ^b	15 ^c
Peripheral edema	30	35	37	32

- The incidence of ARR was reduced with SC amivantamab
- Incidence of VTE and peripheral edema is consistent with prior reports¹

^aNone grade ≥3. ^bGrade ≥3, 1%. ^cGrade ≥3, 3%.

ARR, administration-related reaction; DM, dermatologic management; laz, lazertinib; SC, subcutaneous; SoC, standard of care; VTE, venous thromboembolism.

1. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530.



Dose Modifications

Amivantamab dose modifications in the first 12 weeks, %	Main COCOON study (n=199) ¹ (IV amivantamab + lazertinib)		SC amivantamab + simplified dermatologic prophylaxis (n=104)	
	SoC DM (n=100)	COCOON DM (n=99)	Standard schedule (n=70)	Laz lead-in (n=34)
Dose modifications due to dermatologic AEs				
Dose interruptions	21	8	1	0
Dose reductions	9	2	3	3
Discontinuations	2	2	1	0
Dose modifications due to AEs				
Dose interruptions	45	42	21	26
Dose reductions	16	12	3	6
Discontinuations	12	9	6	12

- Both SC cohorts showed lower rates of dose modifications due to dermatologic AEs and any AEs in the first 12 weeks

DM, dermatologic management; laz, lazertinib; SC, subcutaneous; SoC, standard of care.

1. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530.

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Conclusions

- Simplified dermatologic prophylaxis along with 1L SC amivantamab + lazertinib achieved a similar reduction in grade ≥ 2 dermatologic AEs as the full COCOON regimen, supporting a streamlined approach that may reduce treatment burden while maintaining patient benefit
- Lazertinib lead-in for 1 cycle prior to 1L SC amivantamab + lazertinib further reduced early dermatologic AEs, suggesting that flexible treatment initiation may also lead to an improved safety profile
- Outcomes in the COCOON study will continue to be evaluated as data mature

Overall, these findings support a simplified and flexible regimen to help patients remain on treatment, potentially maximizing the long-term survival benefit of 1L amivantamab + lazertinib



Simplified COCOON Regimen for Derm Prophylaxis and Management¹



PROPHYLAXIS

Start on Day 1 of treatment to reduce the risk of developing dermatologic AEs

1 START PROPHYLAXIS ON DAY 1 OF AMIVANTAMAB + LAZERTINIB



ORAL TETRACYCLINE
Doxycycline or minocycline
100 mg by mouth twice daily

Weeks 1–12



CERAMIDE-BASED MOISTURIZER
Apply to face and body
At least once daily

Weeks 1+

CONCOMITANT / EARLY INTERVENTION

Begin site-directed treatment at first onset of grade 1 dermatologic AEs, as clinically indicated

2 IF A DERMATOLOGIC AE EMERGES



FACE / BODY
Corticosteroids²
Tailor to location and severity
Topical ruxolitinib cream or tacrolimus^a



SCALP^b
Clobetasol 0.05% shampoo²
3 times weekly
Propranolol 10 mg
By mouth once daily until resolution



PARONYCHIA^b
Timolol 0.5% solution²
Apply twice daily
Chlorhexidine 4% solution²
Apply once daily

OTHER CONSIDERATIONS

Escalate care based on severity/persistence, consider early dermatology referral, and see amivantamab label for dose modifications

Oral zinc gluconate and extended tetracycline treatment were also evaluated in COCOON, but clinical benefit has not been established.

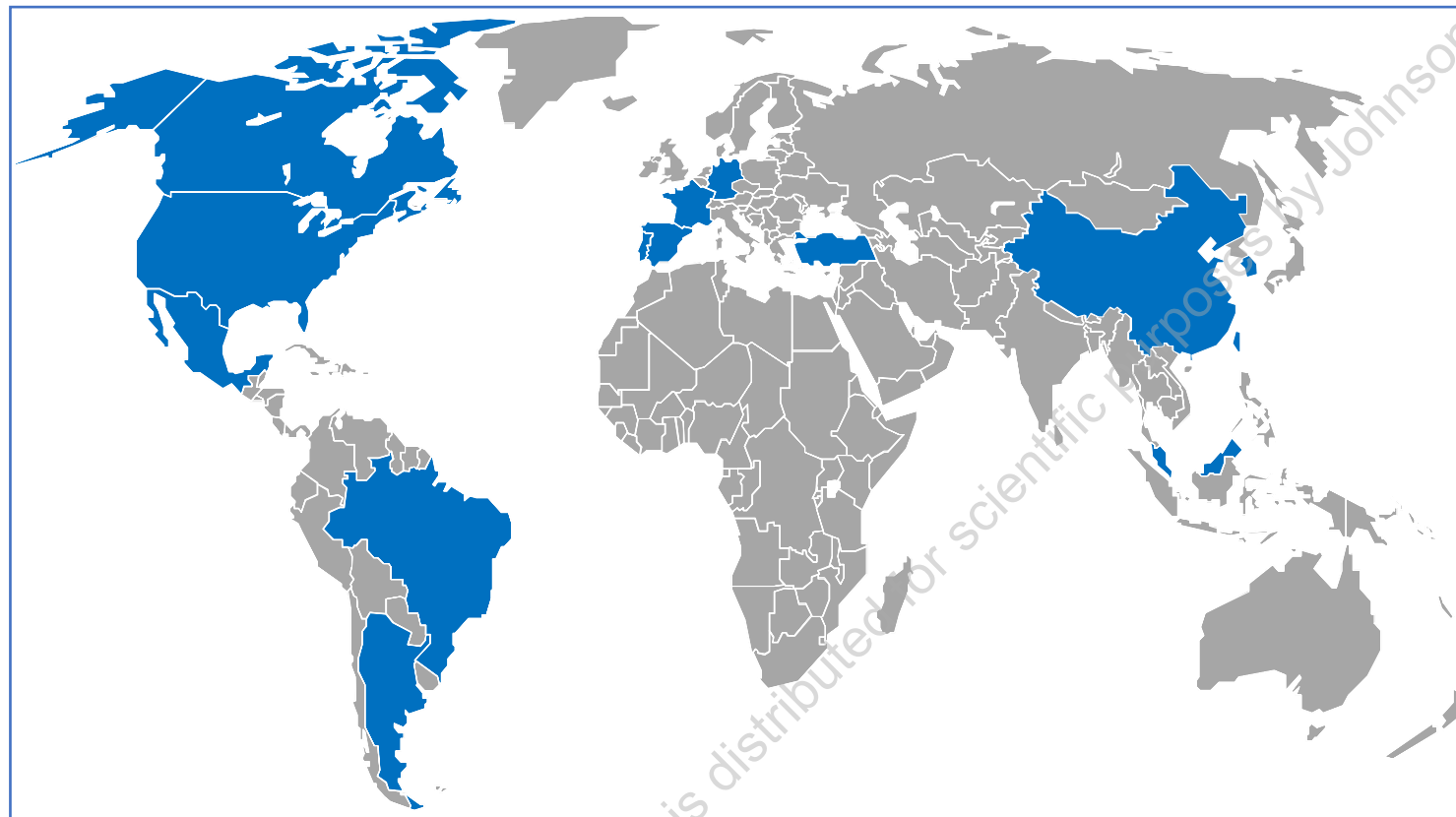
^aInvestigational treatment under evaluation in COCOON. ^bCombination regimen under investigation in COCOON.

1. Figure adapted from Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530. 2. Nikolaou V, et al. *Lung Cancer.* 2026;213:108950. 3. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]. Janssen Biotech, Inc.; 2025.

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- Staff members at the study sites and involved in data collection/analyses
- Medical writing assistance was provided by Lumanity Communications Inc. and funded by Johnson & Johnson

A total of 305 participants from 11 countries were enrolled in the COCOON study



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