Dermatologic prophylaxis and impact on patient-reported outcomes in first-line *EGFR*-mutant advanced NSCLC treated with amivantamab plus lazertinib: Results from the phase 2 COCOON trial

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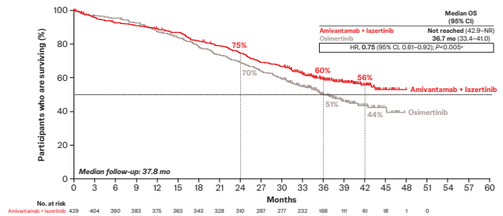
Background

- First-line amivantamab + lazertinib is approved by the FDA, EMA, and other global regulatory agencies for epidermal growth factor receptor (*EGFR*)–mutant advanced non-small cell lung cancer (NSCLC) based on the results of the phase 3 MARIPOSA study (ClinicalTrials.gov Identifier: NCT04487080)[1,2]
  - In MARIPOSA, first-line (1L) amivantamab + lazertinib significantly improved overall survival versus osimertinib (hazard ratio, 0.75; 95% CI, 0.61–0.92; *P*<0.005; **Figure 1**)[3]

FIGURE 1: MARIPOSA final OS[3]

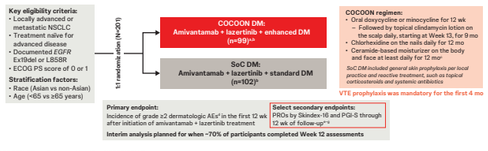


Note: Last participant was enrolled in May 2022. Clinical cutoff date was December 4, 2024. In total, 390 deaths had occurred in the amivantamab + lazertinib (173 deaths) and osimertinib (217 deaths) arms.
[a]*P* value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or non-Asian), and history of brain metastasis (present or absent).
HR was calculated from a stratified Cox regression model.
CI, confidence interval; Ex19del, exon 19 deletion; HR, hazard ratio; NR, not reached; OS, overall survival.

- The phase 2 COCOON trial (NCT06120140) prospectively evaluated an uncomplicated prophylactic regimen (COCOON dermatologic management [DM]) to prevent moderate to severe EGFR-related dermatologic adverse events (AEs) associated with amivantamab + lazertinib, which are often treated reactively in clinical practice
- COCOON DM achieved early success at a prespecified interim analysis (median follow-up: 4.2 months), showing a significant reduction in grade ≥2 dermatologic AEs versus standard-of-care (SoC) DM (38.6% vs 76.5%; *P*<0.0001)[4]
  - Fewer treatment discontinuations due to AEs were observed in COCOON DM versus SoC DM (11.4% vs 19.1%), allowing participants to remain on treatment[4]
- Here, we present patient-reported outcomes (PROs) from the first 12 weeks of COCOON to demonstrate that reducing dermatologic AEs impacts the quality of life (QoL) of patients with *EGFR*-mutant advanced NSCLC receiving amivantamab + lazertinib

Methods

FIGURE 2: Phase 2 COCOON study design



COCOON (ClinicalTrials.gov Identifier: NCT06120140).
[a]The COCOON DM arm received a digital health tool with training on dermatologic AEs and reminders to increase adherence to the DM regimen. [b]Amivantamab and lazertinib were given at the approved doses in 28-day cycles. [c]La Roche-Posay Lipikar AP+M moisturizer was used in COCOON. [d]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. [e]Dermatologic symptoms and impact on participants' health-related QoL were measured with PRO instruments every 2 weeks. [f]Three 28-day amivantamab + lazertinib treatment cycles. †All *P* values are nominal.
AE, adverse event; DM, dermatologic management; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; NSCLC, non-small cell lung cancer; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome; QoL, quality of life; SoC, standard of care; VTE, venous thromboembolism.

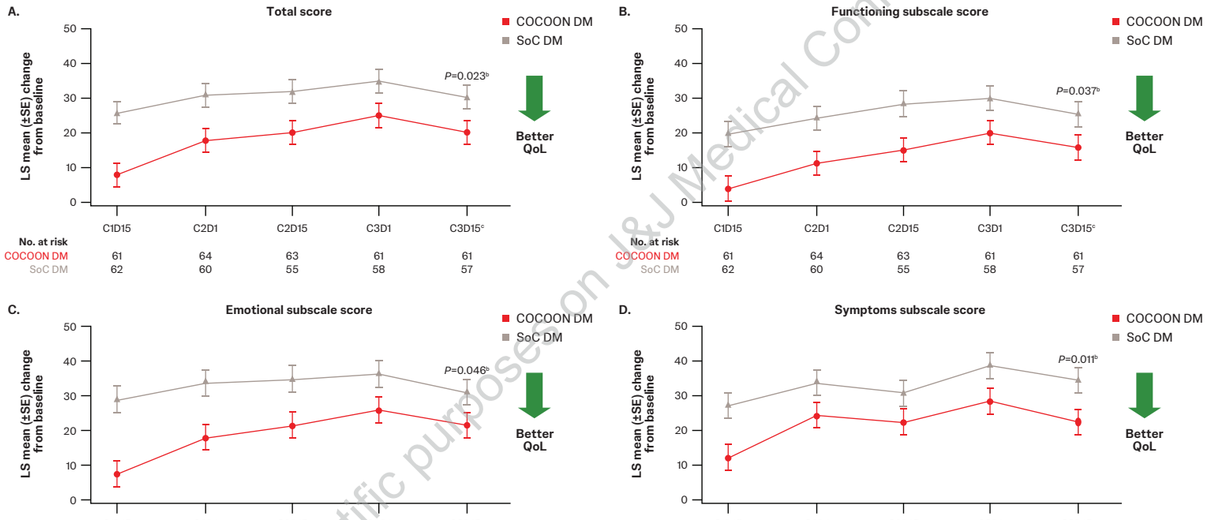
- To provide a robust analysis of the association between dermatologic symptoms and participants' health-related QoL, PRO instruments were utilized, with responses collected every 2 weeks (**Figure 2**)
- The Skindex-16 questionnaire was validated to assess the impact of skin conditions on QoL using 3 subscales (functioning, emotional, and symptoms) and an average score (0 [no impact] to 100 [impact experienced all the time])
- Patient Global Impression of Severity (PGI-S) is a participant-reported 4-point rating scale (none, mild, moderate, or severe symptoms) that assesses the severity of rash, skin condition, and nail infection over time
- The interim analysis was planned for when participants completed Week 12 assessments, and PROs described here are from the first 12 weeks of treatment, which is when most first-onset dermatologic AEs take place[3]

Results

Skindex-16

- At Cycle (C) 3 Day (D) 15, a lower average Skindex-16 total score was observed with COCOON DM versus SoC DM (*P*=0.023; **Figure 3A**)
- Substantial and consistent separation favoring COCOON DM was observed in all postbaseline subscales, indicating lower severity of dermatologic AEs and reduced impact of those AEs on QoL (**Figure 3B–D**)

FIGURE 3: Skindex-16[a] (A) total score and (B) functioning, (C) emotional, and (D) symptoms subscale scores

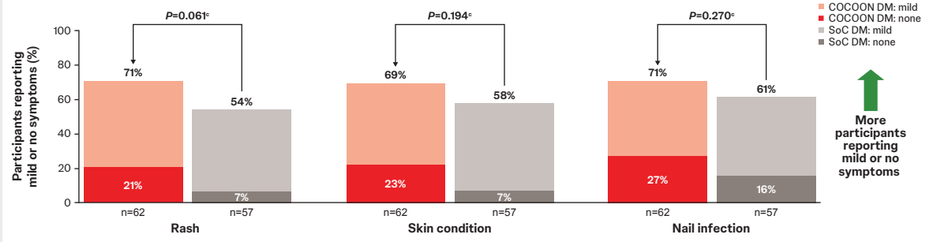


Note: LS means are derived from a mixed-effects model with baseline as a covariate; race (Asian or non-Asian), age (<65 vs ≥65 years), visit, treatment, and visit-by-treatment interaction as fixed effects; and individual subject as a random effect.
[a]The Skindex-16 questionnaire provides an average 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. [b]All *P* values are nominal. [c]C3D15 was the last time point prior to Week 12. The interim analysis was planned for when participants completed Week 12 assessments.
C, Cycle; D, Day; DM, dermatologic management; LS, least squares; QoL, quality of life; SE, standard error; SoC, standard of care.

PGI-S

- At C3D15, most participants in the COCOON DM arm did not report any moderate or severe symptoms on the PGI-S
  - This benefit was observed consistently at all earlier time points
  - A substantial benefit was observed for COCOON DM versus SoC DM, with more participants reporting mild or no symptoms on the PGI-S for rash, skin condition, and nail infection with COCOON DM (**Figure 4**)
  - With COCOON DM, 3-fold more participants reported no symptoms of rash or skin condition, and 1.7-fold more reported no symptoms of nail infection versus participants in the SoC DM arm

FIGURE 4: Proportion of participants with mild or no dermatologic symptoms[a,b]



[a]PGI-S is a participant-reported 4-point rating scale (none, mild, moderate, or severe symptoms). [b]C3D15 was the last time point prior to Week 12. The interim analysis was planned for when participants completed Week 12 assessments. [c]All *P* values are nominal.
C, Cycle; D, Day; DM, dermatologic management; PGI-S, Patient Global Impression of Severity; SoC, standard of care.

Key takeaways

- Among participants with *EGFR*-mutant advanced NSCLC, 1L amivantamab + lazertinib significantly improved OS[3]
- COCOON DM, an uncomplicated regimen with widely available agents, achieved a significant reduction in the impact of this anticancer treatment on QoL compared to SoC DM

Conclusions

- At this analysis, which evaluated the first 12 weeks of treatment, participants in the COCOON DM arm experienced lower severity of dermatologic symptoms and a reduced impact on QoL than participants in the SoC DM arm
- Substantial and consistent separation favoring COCOON DM was observed in all postbaseline Skindex-16 subscales
- Most participants in the COCOON DM arm reported mild or no dermatologic symptoms
  - This benefit was consistently observed across the first ~10 weeks of treatment

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