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Improving prevention of moderate to severe dermatologic adverse events in EGFR-mutant advanced NSCLC treated with first-line (1L) subcutaneous (SC) amivantamab + lazertinib: First results from a new COCOON cohort

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Background

Dermatologic AEs are associated with EGFR-targeted therapies such as amivantamab (ami) + lazertinib (laz). EGFR inhibitor-associated secondary zinc deficiency is linked to increased risk of severe skin AEs. In the phase 2 COCOON study (NCT06120140), enhanced dermatologic management (DM; tetracycline for 12 wks, ceramide-based moisturizer, topical clindamycin, chlorhexidine) led to significantly reduced grade ≥ 2 dermatologic AEs of interest (DAEIs) by Wk 12 vs standard of care DM (42% vs 75%; $P < 0.0001$) in pts receiving 1L intravenous (IV) ami + laz; scalp DAEIs were also meaningfully reduced (10% vs 26%; $P = 0.005$). With COCOON DM, dose interruptions, reductions and discontinuations due to AEs were 55%, 27% and 12% (Cho *JTO* 2025). SC ami has shown shorter administration time (< 5 min) and higher pt convenience vs IV (Leighl *JCO* 2024). Here are first results from a new COCOON cohort using an optimized DM regimen with zinc supplementation in pts receiving SC ami + laz.

Methods

70 pts receiving SC ami on standard Q4W dosing + oral laz were enrolled. Pts also received optimized COCOON DM (oral tetracycline for 24 wks; ceramide-based moisturizer + oral zinc gluconate throughout the study; chlorhexidine for nails and clindamycin for scalp were omitted). Primary endpoint was incidence of grade ≥ 2 DAEIs by Wk 12.

Results

As of 24-Apr-26, 70 pts (median age, 63 y; 66% female) received ≥ 1 dose of SC ami + laz plus optimized COCOON DM (median follow-up, 3.8 mo). Among 65 pts with ≥ 12 wks of follow-up, overall incidence of grade ≥ 2 DAEIs by Wk 12 was 34%; 1 pt had grade 3 DAEIs; no grade 4–5 DAEIs were reported. Incidence of grade ≥ 2 DAEIs by Wk 12 was 5% for scalp and 18% for paronychia. Few pts had dose reductions (11%) or discontinuations (3%) due to AEs; 29% had interruptions. Updated results will be presented at the meeting.

Conclusions

These results suggest that SC ami + laz with an optimized COCOON DM regimen led to numerical reductions in grade ≥ 2 DAEIs vs IV ami + laz with standard COCOON DM. Few AE-related dose modifications/discontinuations were observed, supporting the benefit of proactive DM in pts receiving SC ami + laz.

Clinical trial identification

NCT06120140.

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Legal entity responsible for the study

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Disclosure

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