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

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WHAT DO THESE RESULTS MEAN FOR INDIVIDUALS WITH NON-SMALL CELL LUNG CANCER (NSCLC)?

Individuals with advanced epidermal growth factor receptor (*EGFR*)–mutant NSCLC using the COCOON Dermatologic Management (DM) set of preventive treatments versus standard-of-care (SoC DM) had 50% fewer moderate to severe skin, scalp, and nail reactions with reduced severity during their treatment with amivantamab plus lazertinib, which enabled them to stay on their cancer treatment longer

WHAT WAS THE PURPOSE OF THIS STUDY?

- Researchers wanted to see if a set of preventive treatments (COCOON DM) could reduce moderate to severe skin, scalp, and nail reactions in participants with advanced *EGFR*-mutant NSCLC who received amivantamab plus lazertinib for their cancer

WHO WAS IN THE STUDY AND HOW WAS IT CARRIED OUT?

- COCOON (NCT06120140), a phase 2 clinical trial, was conducted by randomly assigning participants into 1 of 2 groups: 1 group received an enhanced dermatologic care regimen designed to prevent skin, scalp, and nail reactions (COCOON DM), while the other received standard dermatologic care (SoC DM). Both groups received amivantamab plus lazertinib as treatment for their cancer
- The main goal of the study was to see if COCOON DM could reduce moderate to severe skin, scalp, and nail reactions related to amivantamab plus lazertinib in the first 12 weeks of treatment

Figure 1: COCOON study design

Participants with *EGFR* exon 19 deletions or exon 21 L858R mutations who had not previously received treatment for advanced NSCLC

Numbers of participants in this interim analysis:

70 participants
COCOON DM + amivantamab + lazertinib

68 participants
SoC DM + amivantamab + lazertinib

Venous thromboembolism prophylaxis was mandatory for the first 4 months of treatment

SoC DM included general preventive measures recommended by the doctor and general treatment of skin, scalp, and nail reactions, such as with corticosteroid creams or oral antibiotics; SoC DM was also available for COCOON DM participants

Primary objective:

- To evaluate whether COCOON DM can reduce incidence of severe skin, scalp, and nail reactions when compared with SoC DM

Other key secondary objectives:

- Occurrence of nail infections and scalp rashes and their severity
- How often treatment doses were reduced, paused, or stopped because of side effects

Both study arms received general skin or nail prevention instructions, including minimizing sunlight exposure, wearing UV protective clothing, using SPF ≥30 sunscreen, and avoiding applying anything alcohol based on their skin

EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; SoC, standard-of-care; SPF, sun protection factor.

WHAT WERE THE RESULTS?

Figure 2: Preventing side effects with prophylactic regimens

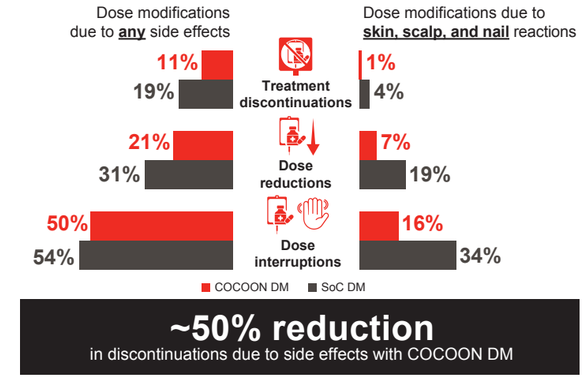
Begin amivantamab + lazertinib

Infusion-related reaction prophylactic regimen	Venous thromboembolism prophylactic regimen
2 days to 1 hour before start Oral 8-mg dexamethasone twice a day 2 days and 1 day prior and 8-mg 1 hour before first infusion	**First 4 months** Oral anticoagulants based on guidelines

COCOON prophylactic skin, scalp, and nail regimen

	Weeks 1–12	Week 13+
Antibiotic prophylaxis	Take 100 mg of an antibiotic (doxycycline or minocycline) by mouth 2 times daily	Apply an antibiotic lotion (1% clindamycin) once daily on the scalp before bedtime
Nail cleaning agent	Week 1+ Use an antiseptic solution (chlorhexidine 4%) for washing fingernails and toenails once daily for 12 months	
Long-acting skin hydration	Week 1+ Use a ceramide-based moisturizing cream at least once daily on the body and face for 12 months	

Figure 4: Treatment dose modifications

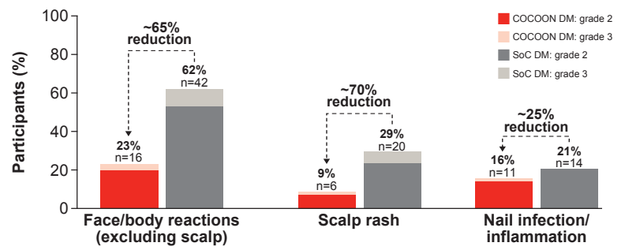


SoC, standard-of-care.

Figure 3: Skin, scalp, and nail reactions that occurred in the first 12 weeks

~50% reduction in the occurrence of moderate to severe skin, scalp, and nail reactions by Week 12

	COCOON DM (27/70)	SoC DM (52/68)
Moderate to severe skin, scalp, and nail reactions (grade ≥2)	39%	76%
Severe skin, scalp, and nail reactions (grade 3)	4%	9%



SoC, standard-of-care.

Glossary of terms

***EGFR* mutation**	EGFR is a protein that relays chemical signals that tell the cell to grow, divide, or survive. Mutations in the *EGFR* gene are common in NSCLC and can affect how the cancer responds to treatment	**Infusion-related reactions**	Side effects that occur during or after receiving a medication infusion	**Venous thromboembolism**	A blood clot that forms in a vein	**SPF**	Sun protection factor, a measure of how well a sunscreen will protect skin from harmful sun rays (UV-B)
Exon 21 L858R substitution mutation	An alteration to the DNA sequence of *EGFR* that changes the function of the protein. In the case of L858R, a small part of DNA is replaced with a different one within the *EGFR* gene	**UV protective clothing**	Clothing designed to protect the skin from harmful UV radiation	**Exon 19 deletion mutation**	An alteration to the DNA sequence of *EGFR* that changes the function of the protein. In the case of exon 19 deletions, DNA was deleted in the part of the *EGFR* gene called exon 19		

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*AI was used in the preparation of these summaries.