Cutaneous Toxicities With Amivantamab for Non-Small Cell Lung Cancer: A Practical Guide and Best Practices

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BACKGROUND: Amivantamab is an epidermal growth factor receptor (EGFR) and MET bispecific antibody approved for certain patients with advanced non-small cell lung cancer with *EGFR* variant. Cutaneous toxicities are known on-target effects of EGFR inhibition.

OBJECTIVES: This article describes the occurrence and management of cutaneous toxicities in patients whose disease progressed on platinum chemotherapy treated with amivantamab.

METHODS: Post hoc analysis evaluated incidence, severity, and time to first onset of rash and paronychia. Five nurses and advanced practice providers were interviewed.

FINDINGS: Of 380 patients, 296 (78%) experienced treatment-related rash and/or paronychia. Paronychia (43%), rash (36%), and dermatitis acneiform (35%) were most frequent, with scalp rash reported by 17%. Treatment modifications because of rash and paronychia were infrequent. Nurses and advanced practice providers collaborate with physicians to manage cutaneous toxicities by administering comedications, modifying amivantamab dose, and educating patients.

KEYWORDS
amivantamab; carcinoma; non-small cell lung cancer; rash; paronychia

AMIVANTAMAB IS A BISPECIFIC EPIDERMAL GROWTH FACTOR receptor (EGFR)–directed and mesenchymal-epithelial transition factor (MET) receptor–directed antibody approved for the treatment of patients with non-small cell lung cancer with *EGFR* exon 20 insertion variant (Ex20ins NSCLC) in combination with carboplatin–pemetrexed as a first-line treatment and as a monotherapy for patients with Ex20ins NSCLC whose disease progressed after platinum chemotherapy. Amivantamab is also approved in combination with the EGFR tyrosine kinase inhibitor lazertinib as a first-line therapy for patients with *EGFR* exon 19 deletions (Ex19del) or exon 21 L858R substitutions, and in combination with carboplatin–pemetrexed in patients with *EGFR* Ex19del or L858R whose disease progressed after osimertinib (Park et al., 2021; Johnson & Johnson, 2024; Zhou et al., 2023). The U.S. Food and Drug Administration granted initial accelerated approval based on the results of the phase 1 CHRYSALIS trial, which found an overall response rate of 40% (as assessed by blinded independent central review) and a median response duration of 11.1 months, with a safety profile consistent with what is expected with EGFR and MET inhibition (Park et al., 2021). In March 2024, the U.S. Food and Drug Administration fully approved amivantamab and added an indication for first-line treatment in combination with chemotherapy based on the results of the phase 3 PAPILLON trial, which found a significantly longer median progression-free survival for amivantamab plus chemotherapy (11.4 months) versus chemotherapy alone (6.7 months) ($p < 0.001$) (Zhou et al., 2023). In August 2024, the U.S. Food and Drug Administration also added an indication for patients with *EGFR* Ex19del or L858R as first-line treatment in combination with lazertinib, based on results from the phase 3 MARIPOSA trial (Cho et al., 2024). In MARIPOSA, median progression-free survival was significantly longer with first-line amivantamab plus lazertinib versus osimertinib (23.7 versus 16.6 months) ($p < 0.001$) (Cho et al., 2024). Amivantamab was also approved in late 2024 with chemotherapy for *EGFR* Ex19del or L858R after progression on osimertinib, based on the results of the phase 3 MARIPOSA-2 trial, in which progression-free survival was significantly prolonged for amivantamab plus chemotherapy versus chemotherapy alone (6.3 versus 4.2 months) ($p < 0.001$) (Passaro et al., 2024).