Incidence and Management of Dermatologic Adverse Reactions with Intravenous Amivantamab in Combination with Lazertinib

MARIPOSA[1]
Amivantamab + Lazertinib

Patient Population: Adult patients with locally advanced or metastatic NSCLC and documented ***EGFR* exon 19 deletion or exon 21 L858R mutations**

Incidence of Dermatologic AEs[1]
(n=421)

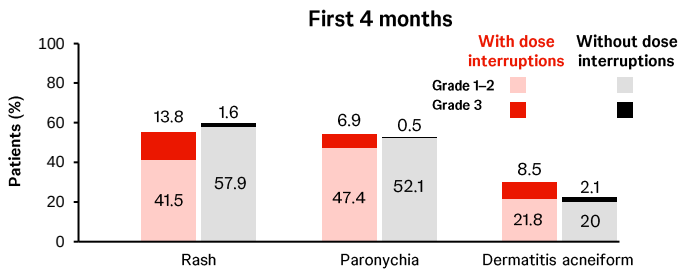
Most Common Dermatologic AEs, %	All	Grade 3 or 4	Dose interruptions of amivantamab, %	Dose reductions of amivantamab, %	Discontinuations of amivantamab, %
Rash*	86	26	37	23	5
Nail Toxicity/Paronychia*	71	11	NR	NR	NR
Dry Skin*	25	1	NR	NR	NR
Pruritus	24	0.5	NR	NR	NR

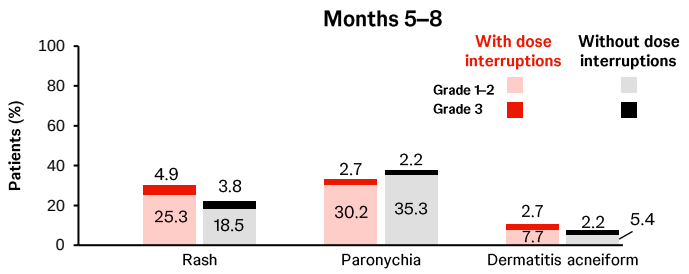
Median Time to Onset of Rash: 14 days (range, 1–556); Median Treatment Duration: 18.5 months (range, 0.2–31.4)

Note: Specific incidence values that are not publicly available for AEs are labeled NR. *Additional warnings and precautions associated with amivantamab and lazertinib include IRR, ILD/pneumonitis, VTE events, ocular toxicity, and embryo-fetal toxicity*

Prevalence and Severity of Key Dermatologic AEs Over Time in the MARIPOSA Study[3]

This analysis is not included in the Prescribing Information for amivantamab and lazertinib. This was a post hoc exploratory analysis.





Median duration of rash* with amivantamab + lazertinib in MARIPOSA: 31 days (range, 1–663)[2]

Proactive Management of Rash

Limit sun exposure during and for 2 months after treatment[1]

Wear protective clothing and use broad-spectrum UVA/B sunscreen[1]

When initiating treatment with amivantamab, administer alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream to reduce the risk of dermatologic adverse reactions[1]

Consider prophylactic measures (e.g., use of oral antibiotics) to reduce the risk of dermatologic adverse reactions[1]

The information below is based on published literature for EGFR-related dermatologic AE management.
These are not recommendations for individual patient care. Interventions should be based on patient presentation and the clinical judgement of the treating physician.

In a meta-analysis,† the use of prophylactic antibiotics§ with or without topical skin therapies resulted in:[4]

- **46%** Reduction in all grades of skin rash
- **64%** Reduction in the risk of developing Grade 2–4 skin rash eruptions
- **39%** Reduction in the risk of paronychia

Multinational Association of Supportive Care in Cancer (MASCC) Guidelines recommend proactive measures (Weeks 1–6) and ongoing monitoring to reduce the risk of severe reactions:[5]

- Hydrocortisone 1% cream + moisturizer and sunscreen, twice daily topically
- Doxycycline 100 mg, twice daily orally OR
- Minocycline 100 mg, once daily orally

Phase 2 COCOON Trial: Investigating Enhanced Dermatologic Management with IV Amivantamab + Lazertinib[6,7]

This is an investigational study, results pending.

Key Inclusion Criteria (N≈180)

- Treatment-naïve patients with *EGFR*-mutated (exon 19 deletion or L858R mutations) NSCLC
- Locally advanced or metastatic NSCLC

Stratification:
Race (Asian vs non-Asian)
Age (<65 years vs ≥65 years)

	Weeks 1–12	Weeks 13–52
Prophylactic antibiotics	Oral doxycycline or minocycline 100mg BID	Topical clindamycin lotion 1% on the scalp QD before bed
Paronychia prophylaxis	Chlorhexidine 4% on the fingernails and toenails QD	
Skin moisturization	Ceramide-based moisturizer on the body and face at least QD	

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*Grouped term. For rash, this includes the following preferred terms: rash, dermatitis acneiform, folliculitis, rash maculopapular, skin lesion, acne, erythema, rash pustular, dermatitis, rash pruritic, rash papular, rash erythematous, rash macular, dermatitis infected, erythema multiforme, papule, drug eruption, rash follicular, rash vesicular, skin exfoliation, and epidermolysis. †A meta-analysis of 13 studies assessed the efficacy of antibiotic prophylaxis in the prevention of skin toxicities in patients with solid tumors treated with EGFR inhibitors. The pooled OR values with 95% CI were calculated by both the fixed- and random-effects models. §ie, doxycycline, minocycline, and tetracycline.
AE, adverse event; BID, twice daily; C, cycle; EGFR, epidermal growth factor receptor; IV, intravenous; NSCLC, non-small cell lung cancer; OR, odds ratio; QD, once daily; UVA/B, ultraviolet A/B.

1. RYBREVANT® (amivantamab-vmjw) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC ,et al. *N Engl J Med.* 2024. doi:10.1056/NEJMoa2403614. (Supplementary appendix). 3. Campelo MdRG, et al. Presented at the European Lung Cancer (ELCC) Congress 2024; March 20-23, 2024; Prague, Czech Republic. 4. Petrelli F, et al. *Br J Dermatol.* 2016;175(6):1166–1174. 5. Lacouture ME, et al. *Support Care Cancer.* 2011;19(8):1079–1095. 6. Clinicaltrials.gov. Accessed September 20, 2024. https://clinicaltrials.gov/study/NCT06120140. 7. Cho BC, et al. Presented at the World Conference on Lung Cancer (WCLC); September 7-10, 2024; San Diego, CA, USA.

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This protocol summarizes interventions investigators in the MARIPOSA study were instructed to perform to monitor and manage dermatologic adverse reactions. These are not recommendations for individual patient care. Interventions should be based on patient presentation and the clinical judgment of the treating physician.

Protocol-Based Reactive Management of Rash in MARIPOSA[1]

✓ **Consult with a dermatologist**	If Grade 3, atypical in appearance or distribution, or does not improve within 2 weeks (for Grade 2 rash)
✓ **Initiate topical corticosteroid BID**	eg, betamethasone valerate 0.05% (face) or triamcinolone acetonide 0.1% (body)
✓ **Initiate systemic antibiotic or increase dosing if already administered**	eg, doxycycline 100 mg BID, minocycline 100 mg BID, or cephalexin 500 mg BID
✓ **If associated skin infection is suspected**	Obtain bacterial and fungal cultures, then adjust antibiotic or antifungal therapy based on culture and susceptibility determination

Protocol-Based Management for Rash, Paronychia, Pruritus, and Scalp Rash in MARIPOSA[1]

Rash management

1 or 2	3 or 4	Severe bullous, blistering, or exfoliating skin conditions, including TEN
• Initiate reactive management as above	• Initiate reactive management as above • Start moderate strength topical corticosteroids (e.g., hydrocortisone 2.5% cream or fluticasone propionate 0.5% cream), systemic antibiotics, and systemic prednisone (0.5 mg/kg) for 7 days • Consider low doses of acitretin or isotretinoin (20–30 mg/day) • Reassess weekly† • Consider dermatology consultation and manage rash per recommendation	• **Consult a dermatologist and manage rash per recommendation**

Paronychia management

1	2 or 3
• Use antimicrobial soaks once or BID for 5 minutes, rinse, pat dry, and apply either emollient or topical treatments below • Apply topical antiseptic (povidone-iodine 10% solution) BID • Apply a topical steroid ointment (e.g., betamethasone valerate 0.1% or clobetasol) or topical calcineurin inhibitor BID (e.g., tacrolimus 0.1%) • Per the study protocols, if using topical steroid, once resolved, switch to topical calcineurin inhibitor daily or decrease to twice per week to maintain	**In addition to management for Grade 1:** • Apply topical antibiotic/antifungal agent BID (e.g., mupirocin, fusidic acid, clotrimazole, or miconazole) • Initiate oral antibiotic for at least 14 days (e.g., doxycycline 100 mg BID, minocycline 100 mg BID, or cephalexin 500 mg BID) • Consult a dermatologist or podiatrist

Pruritus management

Based only on the MARIPOSA protocol

1	2
• Apply topical low to moderate strength steroid cream (e.g., hydrocortisone 2.5%, desonide 0.05%, or betamethasone valerate 0.05%), topical calcineurin inhibitor, or topical antipruritic containing numbing agent and menthol	• Apply topical moderate to high strength steroid cream (e.g., betamethasone valerate 0.1%, triamcinolone acetate 0.1%) or topical antipruritic containing numbing agent (pramoxine) and menthol • Initiate an oral antipruritic one dose BID (e.g., certirizine, fexofenadine, rupatadine, bilastine) • If still pruritic after 2–5 days, may increase to double dose BID

3

- Initiate an oral antipruritic (e.g., certirizine, fexofenadine, rupatadine, bilastine)
- Initiate oral pregabalin or gabapentin
- Initiate an oral corticosteroid (e.g., prednisone 0.5–1.0 mg/kg QD or equivalent for 5 days)

Scalp rash

Any grade

- Use a topical steroid shampoo (e.g., clobetasol 0.05%) or an anti-dandruff shampoo with anti-inflammatory, antibacterial, and antifungal properties (e.g., ketoconazole, selenium sulfide, zinc pyrithione) twice weekly, massaging into scalp, and leaving on for 2–5 minutes before rinsing
- Topical acetic acid 0.25% solution irrigation (per the MARIPOSA study protocol)
- Application of a steroid lotion may be effective (e.g., betamethasone valerate 0.1% lotion, mometasone furoate 0.1% lotion, or betamethasone dipropionate 0.05% lotion)
- Initiation of a systemic antibiotic may also be used to treat acute scalp infection (e.g., doxycycline 100 mg BID, minocycline 100 mg BID)
- While wearing hats to avoid sun damage to the scalp is suggested in a prophylactic setting, avoiding any headwear for a participant with established scalp rash is strongly recommended to prevent further spread of the rash

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*Grading per NCI – CTCAE (Version 5.0). †MARIPOSA protocol suggests reassessing weekly for Grade 3 and after 2 weeks for Grade 4.
BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events; NCI, National Cancer Institute; QD, once daily; TEN, toxic epidermal necrolysis.

1. Cho BC, et al. *N Engl J Med.* 2024. doi:10.1056/NEJMoa2403614. (Supplementary protocol).