

Nursing Management of Patients Receiving EGFR-Targeted Therapy for NSCLC: A Pocket Guide

- EGFR-targeted therapies are now used across the disease spectrum

Select Preferred Agents for *EGFR*-Mutated NSCLC^{1-5,14}

Agent/MoA	FDA Indication(s)	Dosing
Osimertinib 3rd-gen irreversible EGFR TKI	- Adjuvant therapy after tumor resection for NSCLC with <i>EGFR</i> exon 19 deletions or exon 21 L858R mutations - Treatment of locally advanced, unresectable (stage III) NSCLC that has not progressed during or following concurrent or sequential platinum-based chemoradiation therapy and has <i>EGFR</i> exon 19 deletions or exon 21 L858R mutations - First-line treatment of metastatic NSCLC with <i>EGFR</i> exon 19 deletions or exon 21 L858R mutations, - First-line treatment (in combination with pemetrexed and platinum-based chemotherapy) of locally advanced or metastatic NSCLC with <i>EGFR</i> exon 19 deletions or exon 21 L858R mutations - Treatment of metastatic <i>EGFR</i> T790M mutation-positive NSCLC that has progressed on or after EGFR TKI therapy	80 mg PO QD, with or without food
Amivantamab Bispecific EGFR and MET receptor-directed antibody	- First-line treatment (in combination with lazertinib) for locally advanced or metastatic NSCLC with <i>EGFR</i> exon 19 deletions or exon 21 L858R mutations - Treatment (in combination with carboplatin and pemetrexed) for locally advanced or metastatic NSCLC with <i>EGFR</i> exon 19 deletions or exon 21 L858R mutations that has progressed on or after treatment with an EGFR TKI - First-line treatment (in combination with carboplatin and pemetrexed) for locally advanced or metastatic NSCLC with <i>EGFR</i> exon 20 insertion mutations - Treatment for locally advanced or metastatic NSCLC with <i>EGFR</i> exon 20 insertion mutations that has progressed on or after platinum-based chemotherapy	- IV dosing based on body weight - In combination with carboplatin and pemetrexed: <80 kg, 1400 mg Wk 1-4, 1750 mg Wk 7 onward; ≥80 kg, 1750 mg Wk 1-4, 2100 mg Wk 7 onward - In combination with lazertinib or as single agent: <80 kg, 1050 mg Wk 1-5 and Wk 7 onward; ≥80 kg, 1400 mg Wk 1-5 and Wk 7 onward
Afinitinib 2nd-gen irreversible EGFR TKI	- First-line treatment for metastatic NSCLC with nonresistant <i>EGFR</i> mutations - Treatment of metastatic, squamous NSCLC progressing after platinum-based chemotherapy	40 mg PO QD, at least 1 hr before or 2 hr after a meal
Datopotamab deruxtecan TROP2-directed ADC	Treatment for locally advanced or metastatic <i>EGFR</i>-mutated NSCLC after prior EGFR-directed tx and platinum-based chemotherapy	6 mg/kg (to max of 540 mg) IV Q3W
Sunvozertinib 3rd-gen irreversible EGFR TKI	Treatment for locally advanced or metastatic NSCLC with <i>EGFR</i> exon 20 insertion mutations with progression on or after platinum-based chemotherapy	200 mg PO QD with food

Additional Agents for *EGFR*-Mutated NSCLC¹⁻⁵

Agent/MoA	FDA Indication(s)	Dosing
Erlotinib 1st-gen reversible EGFR TKI	Treatment of metastatic NSCLC with <i>EGFR</i> exon 19 deletions or exon 21 (L858R) substitution mutations receiving first-line, maintenance, or second or greater line treatment after progression following ≥1 prior chemotherapy regimen	150 mg PO QD on empty stomach
Dacomitinib 2nd-gen irreversible EGFR TKI	First-line treatment of patients with metastatic NSCLC with <i>EGFR</i> exon 19 deletion or exon 21 L858R substitution mutations	45 mg PO QD with or without food
Gefitinib 1st-gen reversible EGFR TKI	First-line treatment of patients with metastatic NSCLC with <i>EGFR</i> exon 19 deletions or exon 21 (L858R) substitution mutations	250 mg PO QD with or without food

Essential AE Monitoring and Management With EGFR-Targeted Therapeutics

➤ Dermatologic AEs

- In general, rash is the most common toxicity of EGFR TKIs and amivantamab^{1-3,6}

Select EGFR Inhibitor	Any Grade Rash	Grade 3/4 Rash
Afatinib	90%	16%
Osimertinib	58%	1%
Amivantamab	84%	4%
Amivantamab + lazertinib	86%	26%
Sunvozertinib	60%	8%

- Managing dermatologic AEs with amivantamab + lazertinib combination
 - Per PI: when starting treatment, alcohol-free emollient cream recommended; prophylaxis should be considered²
 - Topical corticosteroids and topical and/or oral antibiotics recommended if reactions develop; if grade 3 reaction, add oral steroids and consider dermatologic consultation
 - Withhold or reduce dose or permanently discontinue based on severity
 - COCOON study: randomized trial showed that grade ≥ 2 dermatologic AEs were reduced from 77% with standard prophylaxis vs 39% with enhanced prophylaxis⁷

Enhanced Dermatologic Management

- ✔ **Oral doxycycline or minocycline** (100 mg BID for 12 wk)
- ✔ **Chlorhexidine** 4% topical solution (nails)
- ✔ **Clindamycin** 1% topical lotion (scalp)
- ✔ Noncomedogenic skin **moisturizer** QD

- Management of additional dermatologic AEs⁸

AE	Management Considerations
Paronychia (inflammation around nail beds)	▪ Prevention: keep nails trimmed and clean, wear loose-fitting shoes, biotin ▪ Treat with topical steroids, systemic antibiotics ▪ Nail avulsion, silver nitrate ▪ Very dilute bleach soaks: ~1/4 cup bleach to 3 gallons water
Scalp rash	▪ Consider moisturizing shampoos with selenium, brands sold for dandruff ▪ Topical solutions either in shampoo form or liquid solution that are applied and left in: fluocinolone shampoo or solution

➤ Diarrhea

- More common with oral TKIs^{1-3,6}

Select EGFR Inhibitor	Any Grade	Grade 3/4
Afatinib	96%	15%
Osimertinib	58%	2.2%
Amivantamab	16%	3.1%
Amivantamab + lazertinib	31%	2.6%
Sunvozertinib	73%	2.2%

- Usually manageable with diphenoxylate; can require dose reduction

➤ ILD/Pneumonitis^{1-3,9}

- Uncommon (1%-4%) class effect of EGFR-targeted agents but can be severe/fatal

- Monitor for new or worsening pulmonary symptoms indicative of ILD/pneumonitis; evaluate for acute onset of shortness of breath with PE protocol CT chest

Agent	Management
Osimertinib	▪ If no recent definitive platinum-based chemoradiation therapy – Withhold, promptly investigate for ILD if worsening or respiratory symptoms which may be indicative of ILD (eg, dyspnea, cough, fever) – Permanently discontinue if ILD/pneumonitis confirmed ▪ If recent definitive platinum-based chemoradiation therapy – If grade 1 ILD/pneumonitis, continue therapy or interrupt and restart as appropriate – Permanently discontinue if grade ≥ 2 ILD/pneumonitis
Amivantamab	▪ Immediately withhold if suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed
Afatinib	▪ Withhold if suspected ILD and discontinue if confirmed ILD



WORD OF CAUTION: Osimertinib given in short time frame after immunotherapy causes significantly increased rate and severity of pneumonitis

➤ VTE Risk With Amivantamab + Lazertinib²

- MARIPOSA trial, amivantamab + lazertinib vs osimertinib: any grade, 36% vs 8%; grade 3/4, 11% vs 3%
- Prophylactic anticoagulation substantially reduces VTEs; now recommended for the initial 4 mo of treatment
- Monitor for signs and symptoms of VTE and treat as medically appropriate
- Withhold amivantamab + lazertinib based on severity; after anticoagulant is started, resume at the same dose at HCP discretion; permanently discontinue amivantamab and continue lazertinib if recurrent VTE despite therapeutic anticoagulation

➤ Infusion-Related Reactions With Amivantamab

- Any grade/grade 3/4: single agent, 64%/3%; with lazertinib, 63%/6%; with carboplatin/pemetrexed, 50%/3%²

IRR Toxicity Grade ¹⁰	Treatment or Intervention	Premedication and Treatments at Subsequent Dosing
General	▪ Patients informed of symptoms of IRR and instructed to alert site staff as soon as symptoms experienced	
Grade 1 (mild reaction)	▪ If occurring with initial disease, consider infusion interruption	▪ Antihistamine, antipyretic, steroid
Grade 2 (mild to moderate reaction)	▪ Interrupt infusion and monitor until symptoms recover ▪ First interruption: restart at 50% the rate ▪ Second interruption: restart at 50% the rate at time of second interruption or consider discontinuation at that visit ▪ If no evidence of recurring IRR symptoms after 30 min, rate can be increased to prior rate ▪ Further rate escalation can resume after an additional 30 min if no evidence of recurring signs and symptoms	▪ Antihistamine, antipyretic, steroid ▪ Consider meperidine for chills and rigor
Grade 3 (severe reaction)	▪ Stop infusion	▪ Based on the severity of symptoms, consider amivantamab discontinuation ▪ Discontinue amivantamab for recurrent grade 3 IRR
Grade 4 (life-threatening reaction)	▪ Stop infusion	▪ Discontinue amivantamab

- SKIPPirr study of IRR prophylaxis in patients with advanced or metastatic NSCLC with *EGFR* exon 19 deletion or exon 21 L858R mutation and progression after prior osimertinib and platinum-based chemotherapy who were treated with amivantamab^{11,12}
 - Dexamethasone 8 mg PO BID on Days -2 and -1 and 1 dose 1 hr prior to infusion (5 total doses) resulted in 3-fold reduction in IRRs vs standard management (22.5% vs 67.4%)

➤ **Novel Agent: Datopotamab Deruxtecan^{4,13}**

- Stomatitis/oral mucositis
 - In clinical trials, occurred in 63% (any grade; grade 3/4, 8%)
 - Management recommendations:
 - Daily use of prophylactic steroid containing mouthwash (4x daily, swish 1-2 min); if not available, substitute with nonalcoholic and/or bicarbonate-containing mouthwash
 - Good oral hygiene and education
 - Cryotherapy (ice chips/water held in mouth throughout infusion)
 - Grade 1: continue agent with optimized supportive medication; grade 2/3: withhold agent until grade ≤1, restart at same dose (grade 2) or reduced dose (grade 3); grade 4: permanently discontinue
- Ocular toxicities
 - Ocular surface events: any grade, 36%; grade 3/4, 2%-3%
 - Management recommendations:
 - Consider not wearing contact lenses
 - Use lubricating eye drops 4x daily
 - Baseline eye exam with optometrist or ophthalmologist for baseline exam and annually
- ILD/pneumonitis
 - Can be severe, life-threatening, or fatal
 - In clinical trials, occurred in 7% (any grade; grade 3/4, 1%)
 - Monitor patients for new or worsening respiratory symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever)
 - If ILD/pneumonitis suspected, withhold and initiate corticosteroids; permanently discontinue if confirmed grade ≥2 or higher ILD/pneumonitis

ADC, antibody–drug conjugate; AE, adverse event; ILD, interstitial lung disease; IRR, infusion-related reaction; MoA, mechanism of action; NSCLC, non-small-cell lung cancer; PE, pulmonary embolism; TKI, tyrosine kinase inhibitor; VTE, venous thromboembolism.

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