

Positive Quality Intervention: Osimertinib (Tagrisso®) In EGFR Positive Non-Small Cell Lung Cancer

Description: Osimertinib is an indicated and preferred first line treatment option for patients with Epidermal Growth Factor Receptor (EGFR) gene mutation positive Non-Small Cell Lung Cancer (NSCLC) with Exon 19 deletion or exon 21 L858R and with EGFR T790M mutation positive disease with progression on/after EGFR tyrosine kinase inhibitor- based therapy.¹ This PQI aims to provide guidance for initiating therapy with osimertinib.

Background: Osimertinib is a third-generation tyrosine kinase inhibitor that irreversibly binds to mutated EGFR, specifically to T790M, exon 21 L858R, and exon 19 deletion.¹ Patients with EGFR mutation are seen to have a stronger response when treated with EGFR mutation directed therapy than the standard doublet chemotherapy.³ When available, multiplexed genetic sequencing panels are preferred over multiple single gene tests.⁴ EGFR mutations are more common in patients with East Asian ethnicity, no history of smoking, adenocarcinoma histology, and of female gender. However, any individual diagnosed with NSCLC may have an EGFR mutation regardless of race, gender, or smoking status and testing is imperative.⁵ EGFR mutations are found in ~10-23% in patients with adenocarcinomas of the lung.^{6,7}

The FLAURA study found that osimertinib had a longer PFS when compared to erlotinib and gefitinib, 18.9 months vs 10.2 months, respectively. The rate of \geq grade 3 adverse events were lower in the osimertinib arm, 35% vs 45%.² Most common adverse events (any grade): *diarrhea* (41% to 58%), *rash* (34% to 58%), *dry skin* (23% to 36%), *nail toxicity* (22% to 35%), and *stomatitis* (15% to 29%).¹

The BLOOM study evaluated the use of osimertinib in patients with EGFR mutation-positive advanced NSCLC who had progressed on prior EGFR-TKI therapy and had leptomeningeal disease. The BLOOM study included both T790M positive and T790M unselected patients. Patients were given osimertinib at an off-label increased dose of 160mg once daily with a median duration of response of 8.3 months.⁹

The ADAURA study evaluated the use of osimertinib in patients with EGFR mutation-positive stage 1B, II, or IIIA NSCLC with complete resection. Data was released early due to overwhelming efficiency. An 80% reduction in risk of recurrence/death across as stages of disease studied at the 3 year mark of this study.¹⁰

PQI Process:

Upon receipt of an osimertinib prescription:¹

- Review EGFR mutational testing, including T790M, exon 21 L858R, and exon 19 deletion
- Verify the dose/frequency is correct
 - Dosing: 80 mg orally once daily with or without food
 - 160 mg orally once daily for leptomeningeal disease (off-label)⁹
 - If patient cannot swallow the osimertinib tablet whole, the tablet can be dissolved in water
 - Stir tablet in 60 mL of water - tablet will not completely dissolve but stir until dispersed into small pieces, rinse the container used to dissolve the tablet with 120mL - 240mL of water and drink immediately
- Review patient medication list for possible drug-drug interactions
 - Strong CYP3A4 inducer: increase osimertinib starting dose to 160 mg once daily
 - Strong CYP3A4 inhibitors: No dos reduction, but monitor for adverse drug reactions

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PQI Process Continued:

- Evaluate patient for the need for baseline cardiac monitoring
 - Monitor LVEF in patients with cardiac risk factors
 - Monitor QTc and electrolytes in patients with history of QTc prolongation or on other QTc prolonging medications
 - QTc >500 msec on at least 2 separate ECGs: hold osimertinib, resume at 40 mg/d when QTc <481 msec or patient returns to baseline QTc
 - QTc with life threatening arrhythmias: permanently discontinue
- Ensure supportive care is addressed (See *Supplemental Information* section)

Patient Centered Activities:

- Patient Education
 - Provide [Oncology Chemotherapy Education \(OCE\)](#) sheet and [Oncology Chemotherapy Education Supplemental](#) Sheet
 - Instruct patient to report any adverse events, such as rash, nail changes, diarrhea, dry or itchy skin, nausea/vomiting, mouth sores, or inflammation
 - Ensure patient has access to supportive medications
 - Anti-nausea: ex. metoclopramide, prochlorperazine, or 5-HT3 receptor antagonist
 - Anti-diarrheal: ex. loperamide
 - Instruct patient to avoid sun exposure when possible. If unavoidable, utilize sunscreen
- Medication Access Assistance
 - Co-Pay Foundation assistance
 - AstraZeneca Access 360 Patient Savings Program
 - AZ&ME AstraZeneca Prescription Savings Program

References:

1. Tagrisso (osimertinib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals.
2. Soria JC, Ohe Y, Vansteenkiste J, et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. *N Engl J Med*. 2018;378(2):113-125.
3. Sequist LV, Yang JC, Yamamoto N, et al. Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. *J Clin Oncol*. 2013;31(27):3327-34.
4. Kalemkerian GP, Narula N, Kennedy EB, et al. Molecular Testing Guideline for the Selection of Patients with Lung Cancer for Treatment with Targeted Tyrosine Kinase Inhibitors: American Society of Clinical Oncology Endorsement of the College of American Pathologists/International Association for the Study of Lung Cancer/Association for Molecular Pathology Clinical Practice Guideline Update. *J Clin Oncol*. 2018;36(9):911-919.
5. Sag SO, Gorukmez O, Ture M, et al. Spectrum of EGFR gene mutations and ALK rearrangements in lung cancer patients in Turkey. *Springerplus*. 2016;5:482.
6. Lazarus DR, Ost DE. How and when to use genetic markers for nonsmall cell lung cancer. *Curr Opin Pulm Med*. 2013;19:331-339.
7. Cheng L, Alexander RE, MacLennan GT, et al. Molecular pathology of lung cancer: key to personalized medicine. *Mod Pathol*. 2012;25:347-369.
8. Goss G, Tsai CM, Shepherd FA, et al. CNS response to osimertinib in patients with T790M-positive advanced NSCLC: pooled data from two phase II trials. *Ann Oncol*. 2018;29(3):687-693. doi: 10.1093/annonc/mdx820.
9. Yang JC-H, Cho BC, Kim D-W et al. Osimertinib for patients (pts) with leptomeningeal metastases (LM) from EGFR-mutant non-small cell lung cancer (NSCLC): updated results from the BLOOM study. *J Clin Oncol* 2017; 35(Suppl): abstr 2020.
10. Wu YL, Tsuboi M, He J, et al. Osimertinib in resected EGFR-mutated non-small-cell lung cancer. *N Engl J Med*. 2020;383(18):1711-1723.
11. Hirsh V, Blais N, Burkes R, Verma S, Croitoru K. Management of diarrhea induced by epidermal growth factor receptor tyrosine kinase inhibitors. *Curr Oncol*. 2014;21(6):329-36.
11. Chu CY, Choi J, Eaby-sandy B, Langer CJ, Lacouture ME. Osimertinib: A Novel Dermatologic Adverse Event Profile in Patients with Lung Cancer. *Oncologist*. 2018;23(8):891-899.

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Supplemental Information

Diarrhea management¹¹ - The onset of diarrhea is typically within the first four weeks

<u>Grade 1 Diarrhea (Mild)</u>	<u>Grade 2 Diarrhea (Moderate)</u>	<u>Grade 3 Diarrhea (Severe)</u>
Increase of <4 stools per day over baseline	Increase of 4-6 stools per day over baseline	Increase of ≥7 stools per day over baseline
Start loperamide*	Continue loperamide*	Continue loperamide*
Continue osimertinib	Hold osimertinib if diarrhea does not improve after 48 hours When diarrhea has improved to grade 1, restart at original dose	Hold osimertinib, when diarrhea has improved to grade 1, restart at reduced dose **Permanently discontinue if diarrhea does not return to grade 1 within 14 days

*Loperamide dosing: 4 mg followed by 2 mg after each loose stool (up to 20 mg daily)

Rash management¹²

<u>Grade 1 Rash (mild)</u>	<u>Grade 2 Rash (Moderate)</u>	<u>Grade 3 Rash (Severe)</u>
Covering <10% of BSA	Covering 10-30% of BSA	Covering >30% of BSA
Topical corticosteroid: triamcinolone 0.1% or hydrocortisone 2.5% daily or twice daily	Topical corticosteroid: triamcinolone 0.1% or hydrocortisone 2.5% twice daily	Topical corticosteroid: clobetasol 0.05% cream twice daily
± topical antibiotic: clindamycin 1% gel or lotion (alcohol free preparation)	AND oral antibiotic: 4-week course of an oral tetracycline antibiotic	AND oral antibiotic: 4-week course of an oral tetracycline antibiotic
Continue osimertinib	Continue osimertinib, if rash is intolerable osimertinib can be held	Hold osimertinib, resume at 50% of original dose when patient has improved to ≤ grade 2

- Rash or acne with osimertinib was found to occur at a lower rate when compared with standard EGFR-TKI therapy (osimertinib any grade: 58%, grade ≥3 1%; standard EGFR-TKI any grade: 78%, grade ≥3: 7%)
- Due to the low frequency of acneiform rash, prophylactic management is not recommended, patient should contact their provider if toxicities appear. The onset of rash is typically within the first two weeks
- Pruritus¹²
 - Grade 1-2:
 - Continue osimertinib unless symptoms are intolerable
 - Consider: topical antipruritic and oral antihistamine
 - Grade 3:
 - Hold osimertinib, resume or reduce dose when patient has improved to ≤ grade 2
 - Consider: topical oral antihistamine, GABA agonist, aprepitant, or doxepin

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