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Cone Health

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

Description: Osimertinib is an indicated as adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, in the first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, in combination with pemetrexed and platinum-based chemotherapy, the first-line treatment of adult patients with locally advanced or metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, and the treatment of adult patients with metastatic EGFR T790M mutation positive NSCLC whose disease has progressed on or after EGFR TKI therapy. 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 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 ≥ 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 (ASCO 2023). 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, add an additional 120 mL-240 mL 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 dose reduction, but monitor for adverse drug reactions
- Evaluate patient for the need for baseline cardiac monitoring
  - Monitor LVEF in patients with cardiac risk factors
  - Monitor QTc and electrolytes in those with history of QTc prolongation or on 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

Patient-Centered Activities:

- Patient Education
  - Provide Oral Chemotherapy Education (OCE) Sheet and Oral 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: metoclopramide, prochlorperazine, or 5-HT3 receptor antagonist
    - Anti-diarrheal: loperamide
  - Instruct patient to avoid sun exposure when possible and if unavoidable, utilize sunscreen
- Patient Assistance: NCODA Financial Assistance Tool

References:

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Supplemental Information:

Diarrhea management[11] - The onset of diarrhea is typically within the first four weeks

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

Rash management[12]

Grade 1 Rash (mild)	**Grade 2 Rash (Moderate)**	**Grade 3 Rash (Severe)**
Covering <10% of BSA	Covering 10-30% of BSA	Covering >30% of BSA
Topical corticosteroid: triamcinolone 0.1% or hydrocortisone 2.5% daily/BID	Topical corticosteroid: triamcinolone 0.1% or hydrocortisone 2.5% twice daily	Topical corticosteroid: clobetasol 0.05% cream BID
± topical antibiotic: clindamycin 1% gel or lotion (alcohol free)	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 improved to ≤ Grade 2

- Rash/acne 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 (onset of rash is typically within the first two weeks)

- Prutitus[12]
    - 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