Written By: Danny Nguyen, MD
Nishan Tchekmedyian, MD
André K.D. Liem, MD
City of Hope National Medical Center

Positive Quality Intervention: Mobocertinib (Exkivity™) Side Effect Management

Description: Mobocertinib (Exkivity™) is an oral EGFR tyrosine kinase inhibitor (TKI) designed to specifically target *EGFR* ex20ins mutations.[1] This PQI will discuss effective strategies for side effect management.

Background: Mobocertinib is indicated in locally advanced or metastatic non-small cell lung cancer (NSCLC). Mobocertinib demonstrated meaningful clinical benefit in 114 platinum-pretreated patients (PPP) with *EGFR* ex20ins+ NSCLC in a phase 1/2 study (NCT02716116), with confirmed objective responses by independent assessment reported in 28% of patients and median duration of response of 17.5 months.[2]

PQI Process: By far, the most common side effect associated with mobocertinib is diarrhea (92%), followed by rash (78%), stomatitis (46%), vomiting (40%) and nausea (37%). Mobocertinib also includes a boxed warning for QTc prolongation and Torsades de Pointes. Below are tips that may improve patient quality of life on mobocertinib thereby maximizing the benefit patients may receive from mobocertinib:

- Monitoring:[4]
  - Monitor QTc and electrolytes at baseline and periodically during treatment
  - Monitor for new or worsening pulmonary symptoms indicative of Interstitial Lung Disease (ILD)/pneumonitis and immediately withhold in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed
  - Monitor cardiac function, including left ventricular ejection fraction, at baseline and during treatment. Withhold, then resume at reduced dose or permanently discontinue based on severity
  - Monitor electrolytes and advise patients to start an antidiarrheal agent at first episode of diarrhea and to increase fluid and electrolyte intake. Withhold, reduce, or permanently discontinue based on severity
- Drug-Drug Interactions: [4]
  - Mobocertinib is a CYP3A substrate
    - Avoid concomitant use of mobocertinib with strong or moderate CYP3A inhibitor. If concomitant use is unavoidable, reduce the dose and monitor the QTc interval more frequently with ECGs
    - Avoid concomitant use with strong/moderate CYP3A inducers, may reduce anti-tumor activity
    - Avoid concomitant use of hormonal contraceptives, but ensure effective contraception is used
    - Avoid concomitant use of other medications known to prolong the QTc interval. If concomitant use is unavoidable, monitor the QTc interval more frequently with ECGs

Diarrhea Severity	**Intervention**
Grade 0 or Cycle 1, Day 1	Consider prophylaxis when prescribing mobocertinib: a) Loperamide 2 mg PO daily to BID (titrate to 1-2 BM per day)
Grade 1	Loperamide 4 mg, followed by 2 mg after each loose stool (max: 16 mg/day)
Grade 2	Interventions listed in Grade 1 and: a) Diphenoxylate/atropine 5 mg QID until control achieved (max: 20 mg/day) b) Consider cholestyramine 4 g orally BID (30 minute prior to meals) c) Consider budesonide 9 mg daily for 4 weeks d) Assess the need for IV hydration (saline) frequently
Grade 3	Interventions listed in Grade 1 and 2 and: a) Consider holding mobocertinib until resolution of diarrhea to Grade ≤ 1 b) Opium tincture (morphine 10 mg/mL) 6 mg of undiluted opium tincture QID c) Octreotide 100 to 150 mcg sq TID d) Strongly consider IV hydration unless contraindicated

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Rash Severity	Intervention
Grade 0 or Cycle 1, Day 1	Consider prophylaxis with: a) Doxycycline 100 mg PO BID or Minocycline 100 mg PO BID b) Daily moisturizing lotion, bland emollient
Grade 1	Interventions listed in Grade 0 and: a) Face: hydrocortisone 1.0% to 2.5% BID to affected area Body: triamcinolone 0.1% BID to affected area b) Derma-Smoothe* 0.01% (or similar) apply topical TID to affected area copiously
Grade 2	Interventions listed in Grade 0 and 1 and: a) Add clindamycin 1.0% cream BID to affected area
Grade 3	Interventions listed in Grade 0 and: a) Hold mobocertinib until resolution of rash to Grade ≤ 1 b) Increase clindamycin 1.0% to 2.0% cream BID to affected area c) Start on oral prednisone 5 to 10 mg PO daily. Increase by 5 to 10 mg PO weekly depending on improvement. Alternatively, can start on a Medrol DosePak
Grade 4	Interventions listed in Grade 3
Stomatitis Severity	**Intervention**
Grade 0 or on Cycle 1, Day 1	Consider prophylaxis with: a) Dexamethasone 0.5 mg/5mL oral solution: 10 mL swish and spit QID 1 hour NPO b) Biotène mouthwash Doxycycline 100 mg PO BID or minocycline 100 mg PO BID
Grade 1	Interventions listed in Grade 0
Grade 2	Interventions listed in Grade 0 and: Magic mouthwash[1]
Grade 3	Interventions listed in Grade 2 and: a) Hold mobocertinib until resolution of mucositis to Grade ≤ 1 Start on oral prednisone 5 to 10 mg PO daily. Increase by 5 to 10 mg PO weekly depending on improvement. Alternatively, can start on a Medrol DosePak

*Special consideration for folliculitis/Rash involving the scalp

Patient Centered Activities:[3]

- Provide Oral Chemotherapy Education (OCE) Sheet
- Provide complimentary Treatment Support Kit
- Counsel patient on how to take mobocertinib and the common side effects
- Some patients may find that certain foods or may worsen symptoms and should be avoided
- Patients should be encouraged to maintain hydration, especially if they are experiencing diarrhea
- Taking mobocertinib at different times in the day may improve symptoms; instituting a brief dose hold on mobocertinib may be required to improve symptoms, but should be minimized (impact on effectiveness)[3]
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Riely GJ, Neal JW, Camidge DR, et al. Activity and safety of mobocertinib (TAK-788) in previously treated non–small cell lung cancer with *EGFR* exon 20 insertion mutations from a phase 1/2 trial. *Cancer Discov*. 2021;11(7):1688-1699.
2. Zhou C, Ramalingam SS, Kim TM, et al. Mobocertinib in platinum-pretreated patients with *EGFR* exon 20 insertion-positive metastatic non-small cell lung cancer: phase 1/2 open-label study. *JAMA Oncol*. 2021. In press.
3. Nguyen D, Ramalingam SS, Spira AI, et al. (2021, Oct). Characterization of GI Toxicities and Their Impact on Efficacy in Patients With *EGFR* Exon 20 Insertion+ (ex20ins+) Non–Small Cell Lung Cancer (NSCLC) Treated With Mobocertinib (TAK-788) Who Previously Received Platinum Chemotherapy. European Society for Medical Oncology (Virtual).
4. EXKIVITY (mobocertinib) [prescribing information].