

## 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.<sup>1</sup> 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.<sup>2</sup>

**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:<sup>4</sup>
  - 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:<sup>4</sup>
  - 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
    - 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 (CTCAE Grade)	Intervention
Grade 0 or on Cycle 1, Day 1	Consider prophylaxis when prescribing mobocertinib: <ul style="list-style-type: none"> <li>a) Loperamide 2 mg PO daily to BID (titrate to 1-2 BM per day)</li> </ul>
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: <ul style="list-style-type: none"> <li>a) Diphenoxylate/atropine 5 mg QID until control achieved (max: 20 mg/day)</li> <li>b) Consider cholestyramine 4 g orally BID (30 minute prior to meals)</li> <li>c) Consider budesonide 9 mg daily for 4 weeks</li> <li>d) Assess the need for IV hydration (saline) frequently</li> </ul>
Grade 3	Interventions listed in Grade 1 and 2 and: <ul style="list-style-type: none"> <li>a) Consider holding mobocertinib until resolution of diarrhea to Grade ≤ 1</li> <li>b) Opium tincture (morphine 10 mg/mL) 6 mg of undiluted opium tincture QID</li> <li>c) Octreotide 100 to 150 mcg sq TID</li> <li>d) Strongly consider IV hydration unless contraindicated</li> </ul>

**Important notice:** NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. *Updated 11.8.21*



Rash Severity (CTCAE Grade)	Intervention
Grade 0 or on 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

\*Special consideration for folliculitis/rash involving the scalp

Stomatitis Severity (CTCAE Grade)	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 afterwards b) Biotène mouthwash c) 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: a) Magic mouthwash <sup>1</sup>
Grade 3	Interventions listed in Grade 2 and: a) Hold mobocertinib until resolution of mucositis to Grade ≤ 1 b) 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

### Patient Centered Activities:<sup>3</sup>

- Provide [Oral Chemotherapy Education](#) (OCE) Sheet
- Provide [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 as they may impact overall effectiveness of mobocertinib<sup>3</sup>

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## 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]. Lexington, MA: Takeda Pharmaceuticals America.

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