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. 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.

**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:**
  - 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:**
  - 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

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

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**Rash Severity (CTCAE Grade)** | **Intervention**
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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
   - b) 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

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**Stomatitis Severity (CTCAE Grade)** | **Intervention**
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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

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:**
- 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

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References:
4. EXKIVITY (mobocertinib) [prescribing information]. Lexington, MA: Takeda Pharmaceuticals America.

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