Positive Quality Intervention: Trifluridine/Tipiracil (Lonsurf®) for Treatment of Gastric Cancer

Description: This PQI will review patient identification and clinical considerations for trifluridine/tipiracil treatment option for gastric cancer.

Background: Trifluridine/tipiracil is approved for use in patients with gastric or gastroesophageal junction (GEJ) cancer who have failed at least two prior lines of chemotherapy including a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy. This approval is based on results from the TAGS trial, a Phase III, multinational, randomized, double-blind trial that compared trifluridine/tipiracil plus best supportive care vs. placebo plus best supportive care in metastatic GEJ/gastric cancer patients previously treated with at least 2 prior regimens. Median overall survival was 5.7 months (95% CI 4.8–6.2) in the trifluridine/tipiracil group and 3.6 months (3.1–4.1) in the placebo group. The most common adverse effects being neutropenia, anemia, thrombocytopenia, decreased appetite, nausea, vomiting, diarrhea, and infections. Sequencing of treatment in advanced gastric cancer is still not well defined, but trifluridine/tipiracil serves as a viable option for 3rd and subsequent lines of treatment and is currently NCCN category 1 recommended for 3rd line (or later) therapy. Trifluridine and Tipiracil is also indicated for the treatment of patients with metastatic colorectal cancer as a single agent or in combination with bevacizumab (see Trifluridine and Tipiracil (Lonsurf®) for Metastatic Colorectal Cancer PQI).

PQI Process: Upon receiving a prescription for trifluridine and tipiracil:

- Verify the correct dose
  - 35 mg/m² based on trifluridine component (maximum 80 mg or 160 mg/day) orally twice daily within 1 hour of a meal on days 1-5, and days 8-12, repeated every 28 days until disease progression or unacceptable toxicity
    - Round to the nearest 5 mg increment
    - Absence of food does not affect AUC but can cause CMAX to spike leading to adverse effects
    - It is not recommended to start at a lower dose to prevent dose limiting toxicities
  - Bevacizumab 5 mg/kg on days 1 and 15 (if applicable)
- Obtain complete blood counts prior to Day 1 and on Day 15 of each cycle
  - Make sure platelets are greater than or equal to 75,000/mm³ and ANC > 1500mm³ prior to the start of each cycle
- Check liver function
  - Do not initiate therapy in patients with moderate to severe hepatic impairment (Bilirubin >1.5 ULN and any AST elevation)
- Check renal function
  - CrCl 15-29: Reduce to 20 mg/m² orally two times daily
    - Consider reduction to 15 mg/m² orally two times daily if further reduction is needed
- Withhold trifluridine and tipiracil for any of the following
  - Absolute neutrophil count (ANC) less than 500/mm³ or febrile neutropenia
  - Platelets less than 50,000/mm³ or Grade 3 or 4 non-hematological adverse reactions
  - After recovery, resume after reducing the dose by 5 mg/m²/dose from the previous dose level for the following only if there is more than a week delay of the next cycle:
    - Febrile neutropenia
    - Uncomplicated Grade 4 neutropenia (recovered to ≥1,500/mm³) or thrombocytopenia

IMPORTANT NOTICE: NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, 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. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual’s sole responsibility to seek guidance from a qualified healthcare professional. Updated 5.3.24
• Timing of presentation of adverse events:
  o Cycles 1-3 are the cycles with the highest incidence of adverse events
  o Neutropenia:
    ▪ Dose holidays are preferred for neutropenia
    ▪ Retrospective data shows neutropenia at the 1-month mark showed trend towards overall survival benefit

Patient-Centered Activities:
• Provide Oncology Chemotherapy Education (OCE) sheet and counsel on potential side effects
• Counsel patient on dosing schedule and administration
  o Consider starting on a Monday to complete days 1-5 from Monday to Friday, break on the weekend (days 6-7), and resume Monday to Friday for days 8-12; no medication on days 13-28
  o Notify the patient that dose delays may be beneficial when managing adverse effects, and should not interfere with their ability to receive treatment or achieve benefit
• Provide medication and clinic appointments calendar
• Ensure patient has access to at home antiemetic and antidiarrheal medications
• Counsel patient on safe storage, handling, and disposal of cytotoxic drugs (wear gloves)
• Provide support kit - Lonsurf® Starter Kits contain patient and caregiver brochures, pillboxes, and thermometer
• Patient Assistance: NCODA Financial Assistance Tool

References:
1. Lonsurf® (trifluridine/tipiracil) [package insert].
3. NCCN Guidelines Gastric Cancer.

Supplemental Information:
Dosing According to Body Surface Area: (dosage calculator and calendar creator at http://www.lonsurfhcp.com/dosing/dosage-calculator)

<table>
<thead>
<tr>
<th>BSA (m²)</th>
<th>Total daily dose (mg)</th>
<th>Dose (mg) administered twice daily</th>
<th>Tablets per dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>15 mg</td>
</tr>
<tr>
<td>&lt;1.07</td>
<td>70</td>
<td>35</td>
<td>1</td>
</tr>
<tr>
<td>1.07 – 1.22</td>
<td>80</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>1.23 – 1.37</td>
<td>90</td>
<td>45</td>
<td>3</td>
</tr>
<tr>
<td>1.38 – 1.52</td>
<td>100</td>
<td>50</td>
<td>2</td>
</tr>
<tr>
<td>1.53 – 1.68</td>
<td>110</td>
<td>55</td>
<td>1</td>
</tr>
<tr>
<td>1.69 – 1.83</td>
<td>120</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>1.84 – 1.98</td>
<td>130</td>
<td>65</td>
<td>3</td>
</tr>
<tr>
<td>1.99 – 2.14</td>
<td>140</td>
<td>70</td>
<td>2</td>
</tr>
<tr>
<td>2.15 – 2.29</td>
<td>150</td>
<td>75</td>
<td>1</td>
</tr>
<tr>
<td>≥ 2.30</td>
<td>160</td>
<td>80</td>
<td>0</td>
</tr>
</tbody>
</table>