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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.[1] 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.[2]

PQI Process:

- Identify patients with metastatic gastric or 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)
- Consider conversation with care team with trifluridine/tipiracil as potential oral oncolytic option
  Upon receiving a prescription for trifluridine and tipiracil:
- Verify appropriateness of treatment (indication, prior lines of treatment)
- Verify correct dose: rounded to nearest 5mg *(see dosing in Supplemental Information*)
- Check complete blood counts prior to Day 1 and on Day 15 of each cycle
  - Do not initiate cycle until ANC ≥ 1,500/mm^3 and platelets ≥ 75,000/mm^3
  - Hold treatment for ANC < 500/mm^3, febrile neutropenia, or platelets < 50,000 mm^3
- Kidney function
  - CrCl 15-29 mL/min – Dose adjust to 20 mg/m^2 BID with food on days 1-5 and 8-12 of 28 day cycle
    - Consider dose reduction to 15 mg/m^2 BID if unable to tolerate 20 mg/m^2
- Liver function
  - Do not initiate therapy in patients with moderate to severe hepatic impairment (bilirubin >1.5 ULN and any AST elevation)
- The most common grade 3 or worse adverse effect is neutropenia (38%)
  - In the TAGS trial, the majority of episodes were managed by delaying the next dose
  - 16% of subjects in that trial were managed with granulocyte colony-stimulating factor
- Consider antiemetic and antidiarrheal medications to manage potential patient adverse effects

Patient Centered Activities:

- Provide Oncology Chemotherapy Education (OCE) sheet and counsel on potential side effects
- Counsel patient on dosing schedule and administration (*see Supplemental Information*)
  - 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

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  - 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 (dosage calculator and calendar creator at http://www.lonsurfhcp.com/dosing/dosage-calculator)
- 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. Shitara K. et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2018 Nov;19(11):1437-1448. doi: 10.1016/S1470-2045(18)30739-3.
2. NCCN Guidelines Gastric Cancer.
3. Lonsurf® (trifluridine/tipiracil) [package insert].

Supplemental Information

Dosing and Administration:

- 35 mg/m^2 (based on trifluridine) twice daily on days 1 to 5 and 8 to 12 of a 28-day cycle
- Round to the nearest 5 mg (available in 15 mg and 20 mg tablets)
- Maximum dose 80 mg trifluridine/dose (160 mg/day)
- Administer with food and swallow tablets whole, within 1 hour after completion of morning and evening meals
- If treatment held for neutropenia, thrombocytopenia, or other Grade 3/4 adverse effect, after recovery, reduce dose by 5 mg/m^2/dose if:
  - Patient had febrile neutropenia, uncomplicated Grade 4 neutropenia or thrombocytopenia that resulted in > 1 week delay in start of next cycle
  - Nonhematologic grade 3 or 4 adverse reaction, except for grade 3 or 4 nausea/vomiting controlled by antiemetics or grade 3 diarrhea responsive to antidiarrheal medication
  - Maximum of 3 dose reductions. Permanently discontinue if unable to tolerate 20 mg/m^2/dose.
  - Do not escalate dose after it has been reduced