

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 5 mg (*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 $\geq 1,500/\text{mm}^3$ and platelets $\geq 75,000/\text{mm}^3$
 - Hold treatment for ANC $< 500/\text{mm}^3$, febrile neutropenia, or platelets $< 50,000 \text{ mm}^3$
- Kidney function
 - CrCl 15-29 mL/min – Dose adjust to 20 mg/m² BID with food on days 1-5 and 8-12 of 28 day cycle
 - Consider dose reduction to 15 mg/m² BID if unable to tolerate 20 mg/m²
- 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

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 3.11.22*

- 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/m² (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/m²/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/m²/dose.
 - Do not escalate dose after it has been reduced