

## Positive Quality Intervention: Trifluridine and Tipiracil (Lonsurf®) for Metastatic Colorectal Cancer

**Description:** This PQI will highlight strategies for appropriate dosing and management of adverse effects related to trifluridine and tipiracil treatment in metastatic colorectal cancer.

**Background:** Trifluridine and Tipiracil is indicated for the treatment of patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy. RECURSE trial showed a survival benefit of 7.1 months (trifluridine and tipiracil) versus 5.3 months (placebo). Grade 3 and greater adverse effects occurred due to neutropenia (38%), decreased appetite (4%), diarrhea (3%) and nausea/vomiting (2%).

**PQI process:** Upon receiving a prescription for trifluridine and tipiracil:

- Verify the dose is correct
  - 35 mg/m<sup>2</sup> based on trifluridine component (maximum, 80 mg) 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
  - It is not recommended to start at a lower dose to prevent dose limiting toxicities.
- 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/mm<sup>3</sup> and ANC > 1500mm<sup>3</sup> 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/m<sup>2</sup> orally two times daily
    - Consider reduction to 15 mg/m<sup>2</sup> 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/mm<sup>3</sup> or febrile neutropenia
  - Platelets less than 50,000/mm<sup>3</sup> or Grade 3 or 4 non-hematological adverse reactions
  - After recovery, resume after reducing the dose by 5 mg/m<sup>2</sup>/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/mm<sup>3</sup>) or thrombocytopenia

### Timing of presentation of adverse events:

- Cycles 1-3 are the cycles with the highest incidence of adverse events

### Neutropenia:

- Dose holidays are preferred for neutropenia
- Retrospective data shows neutropenia at the 1-month mark showed trend towards overall survival benefit<sup>2</sup>

**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.

### Patient Centered Activities:

- Provide [Oncology Chemotherapy Education \(OCE\)](#) sheet
- Provide Loperamide
- Ensure patient has anti-nausea medications
- Storage: If medication is stored outside of original container, throw medication away after 30 days
- Handling: trifluridine and tipiracil is a cytotoxic drug – follow applicable special handling and disposal procedures
- Provide Starter Kits
  - Contact your sales representative or call 1-844-824-4648
  - Visit [TaihoPatientSupport.com](#)

### Co-Pay Assistance:

- Patients with commercial paying insurance are eligible for co-pay support
- Patients pay no more than Zero dollars (\$0) per treatment cycle of trifluridine and tipiracil
- Information regarding the program can be found at:
  - Call 1-844-824-4648
  - [TaihoPatientSupport.com](#)

### Dosing Guideline Summary:

- Starting dosage: 35 mg/m<sup>2</sup> twice daily rounded to nearest 5 mg increment and do not exceed 80 mg/dose or 160 mg/day
- Active treatment days: Days 1 to 5 and 8 to 12 of each 28 day treatment cycle
- Administration: take within 1 hour after completion of morning and evening meals to lessen the negative effect on neutrophil counts
  - Absence of food does not affect AUC but can cause CMAX to spike leading to adverse effects
  - No restriction on food type

### References:

1. Lonsurf® (trifluridine/tipiracil) [package insert]. Princeton, NY: Taiho Oncology, Inc.; 2019.
2. Atsushi Ohtsu, Takayuki Yoshino, et. Al On Behalf of the RECOURSE Study Group. Onset of neutropenia as an indicator of treatment response in the phase 3 RECOURSE trial of trifluridine/tipiracil (TAS-102) versus placebo in patients with metastatic colorectal cancer. *Journal of Clinical Oncology* 2017 35:4\_suppl, 775-775.

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