National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Positive Quality Intervention: Trifluridine and Tipiracil for Metastatic Colorectal Cancer

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

Background: Trifluridine/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. RECOURSE 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/tipiracil:

- Verify the dose is correct
  - 35 mg/m2 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/mm3 and ANC $\geq$ 1500mm3
- 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
  - No dose adjustment necessary for the initial start of Trifluridine and Tipiracil in patients with mild to moderate renal impairment. Dose adjustments for moderate impairment may be needed in subsequent cycles—monitor closely.
- 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 $\geq$1,500/mm3) or thrombocytopenia

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Timing of presentation of adverse events:

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

- Cycle 1 being the most prominent for grade 3 or greater diarrhea, nausea, or vomiting
- Even If grade 3/4 non-hematological events occur, but they resolve with supportive care, continue at the same dose

Neutropenia:

- **Dose holidays are preferred for neutropenia.**
- Retrospective data shows neutropenia at the 1-month mark showed trend towards overall survival benefit[2].

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/m2 twice daily rounded to nearest 5 mg increment and do not exceed 80 mg/dose or 160mg/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 restrictions 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