Written by: Jennifer M. Hasiak O'Doherty, PharmD
Hematology & Oncology Consultants, P.C.
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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. 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 and tipiracil:

- Verify the dose is correct
  - 35 mg/m^2 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^3 and ANC > 1500mm^3 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^2 orally two times daily
    - Consider reduction to 15 mg/m^2 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^3 or febrile neutropenia
  - Platelets less than 50,000/mm^3 or Grade 3 or 4 non-hematological adverse reactions
  - After recovery, resume after reducing the dose by 5 mg/m^2/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^3) 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[2]

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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^2 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.