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Positive Quality Intervention: Metastatic Colorectal Cancer-Trifluridine and Tipiracil

Description of PQI: To increase awareness and management of adverse effects related to trifluridine/tipiracil treatment in metastatic colorectal cancer

Background: 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). 98% of patients were refractory to or failing on a fluoropyrimidine-based therapy in a prior treatment regimen. 42% of patients in the Trifluridine and Tipiracil arm went on to receive subsequent therapy at the end of the trial.

Dose limiting effects:

- **Risk of Infection- neutropenia (Grade 3/4: 38%)**
- Decreased appetite (Grade 3/4: 4%)
- Diarrhea (Grade 3/4: 3%)
- Nausea/Vomiting (Grade 3/4: 2%)

It is not recommended to start at a lower dose to prevent dose limiting toxicities.

When to watch for side events: Cycle 1-3 are the cycles to watch out for the most.

- 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. (**http://ascopubs.org/doi/abs/10.1200/JCO.2017.35.4_suppl.775)

National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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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

PQI process:

- 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.
- 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.
- Instruct patient to report any adverse effects
    - **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
        - Grade 3 or 4 non-hematological adverse reactions

- **After recovery, resume Trifluridine and Tipiracil after reducing the dose by 5 mg/m2/dose from the previous dose level for the following <u>only if there is more than a week delay of the next cycle:</u>**
  - Febrile neutropenia
  - Uncomplicated grade 4 neutropenia (which has recovered to greater than or equal to 1,500/mm3) or thrombocytopenia

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
  - 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