National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Updated 12/20/2019

Positive Quality Intervention: Regorafenib in Metastatic Colorectal Cancer

Description:
Management of adverse effects related to Regorafenib (Stivarga®) treatment in metastatic colorectal cancer. Optimal dosing and follow up are essential to help patients benefit fully while taking this medication.

Background:
Regorafenib is a multikinase inhibitor that has shown an overall survival benefit (**6.4 months**, regorafenib + supportive care **versus 5.0 months,** placebo + supportive care; CORRECT Trial) in the third line setting. Keeping patients on therapy can be challenging due to the adverse effect profile* of multikinase inhibitors.
The **ReDOS trial** evaluated the dose escalation strategy in regorafenib patients and efficacy. A strategy with weekly dose escalation of regorafenib from 80 mg to 160 mg/day (Arm A) was found to be superior to a starting dose of 160 mg/day (Arm B). A trend for improved OS was seen in the dose escalation arm. The dose escalation strategy did not appear to compromise QOL. Patients started on 80mg for the first week with weekly dose escalations in the absence of significant drug-related toxicities. Median Overall Survival (OS) was improved in Arm A vs. Arm B (9.8 months vs. 6.0 months; HR 0.72, 95% CI, p=0.12). Median Progression Free Survival (PFS) was 2.8 months for Arm A vs. 2.0 months for Arm B (HR 0.84, CI 95%, p=0.38).

PQI Process:
Upon receipt of a new prescription for regorafenib:

- If the typical starting dose of 160mg po QD is written, exercise clinical judgement and contact prescriber to discuss and potentially start patient on a dose escalation schedule such as the one described (**ReDOS trial strategy)**:
  - Document follow up schedule and dose escalation in EMR
  - Initiate patient at 80mg for the first week of cycle #1
  - If no significant drug-related toxicities, escalate to 120mg for the second week of cycle #1, otherwise hold therapy at current dose
  - If no significant drug-related toxicities, escalate to 160mg for the third week of cycle #1, otherwise hold therapy at current dose
  - For following cycles, start therapy at current tolerated dose (no dose escalation)
- Coordinate and establish a weekly follow up call with the patient or caregiver for the first 8 weeks
- Monitor LFTs at baseline, every 2 weeks (for first 2 months), and then at least monthly thereafter
- Educate patients on side effects and report adverse effects to prescriber and recommend dose adjustments in 40 mg increments as tolerated[2]

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Patient Centered Activities:

- Provide Oncology Chemotherapy Education (OCE) sheet
- Provide patient starter kit
- Ensure patient knows dosing schedule (once daily for 3 weeks on and 1 week off)
- Ensure patient knows to take dose with a low-fat meal (<600 calories and 30% fat)
- Only open 1 bottle of Regorafenib at a time. **Medication expires 7 weeks after bottle is opened**
- Ensure patient or caregiver is able to take and record blood pressure at home weekly
- Consider Anti Diarrheals and Moisturizing cream i.e Urea 20%

Copay Assistance:

- Commercial patients can enroll in a $0 copay card assistance program (online enrollment- www.zerocopaysupport.com)

Supplemental Information:

*Dose limiting side effects include (percentage refers to all grades)[1]:
Skin and subcutaneous tissue adverse events, including palmar-plantar erythrodysesthesia (Hand and Foot syndrome) 72%, diarrhea 43%, hypertension 30%, fatigue 64%, increased LFTs (AST-65%, ALT-45%, Bilirubin-45%). The median time to first adverse event was 2 weeks with worst incidences occurring at 3 weeks. The worst severity of diarrhea occurred at 4 weeks. Increases in LFTs usually occur within the first 8 weeks of therapy.

References:

1. Grothey A, Van Cutsem E, Sobrero A, et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): an international, multicentre, randomised, placebo-controlled, phase 3 trial. Lancet 2013;381(9863):303-312
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4. Bekaii-Saab TS, Ou F-S, Ahn DH, et al. Regorafenib dose-optimisation in patients with refractory metastatic colorectal cancer (ReDOS): a randomised, multicentre, open-label, phase 2 study [published online June 28, 2019]. *Lancet Oncol*. doi: 10.1016/S1470-2045(19)30272-4.