



Positive Quality Intervention: Regorafenib in the treatment of Hepatocellular Carcinoma

Description of PQI: Understand how to identify eligible patients and manage adverse effects of Regorafenib (Stivarga®) treatment in Hepatocellular Carcinoma.

Background: Regorafenib is a kinase inhibitor indicated for the treatment of patients (Childs Pugh A) with Hepatocellular Carcinoma (HCC) who have been previously treated with sorafenib. In the phase III – RESORCE Trial, regorafenib was assessed in patients with HCC who have progressed on sorafenib and concluded that there was an improved overall survival compared to placebo (10.6 mo vs. 7.8 mo). This study also portrayed the difficulties of maintaining therapy, as the discontinuation rate due to adverse events within the treatment arm was observed at 25% and 43% due to progression. The most common grade (all grade) adverse events occurring more frequently in the regorafenib group included:

- Hand-foot skin reaction (51%)
- Asthenia/ Fatigue (42%)
- Diarrhea (41%)
- Hypertension (31%)

In addition to regorafenib, other 2nd line options include nivolumab. Patients that are not eligible for nivolumab may include those with comorbidities including but not limited to: pneumonitis; thyroid disorders; renal dysfunction; colitis; previous transplants.

PQI Process:

Consider reviewing all current HCC patients in EMR for appropriateness of regorafenib therapy.

Upon receipt of a new prescription for Regorafenib in HCC:

- If the typical starting dose of 160mg by mouth once a day is written, *consider* initiating dose titration based on the ReDos trial in metastatic colorectal cancer (mCRC) .
 - 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)

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- Coordinate and establish a weekly follow up call with the patient or caregiver for the first 8 weeks
- Monitor baseline LFTs
- CBC with differential and platelets and serum electrolytes at Baseline and Monthly
- Monitor blood pressure weekly for the first 6 weeks of therapy then every Cycle
- Monitor for hand-foot skin reaction (HFSR) weekly for 2 cycles, then every Cycle thereafter
- Monitor for signs/symptoms of cardiac issues, bleeding, GI perforation or fistula, infection, and/ or neurological symptoms.
- Monitor for impaired wound healing. (Hold medication for 2 weeks prior to surgery to allow proper wound healing)
- Consider providing Urea base moisturizer
- Consider use of Anti-Diarrheals

Patient Centered Activities:

- Provide Oral Chemotherapy Education Form
 - Emphasize counseling on side effect table
 - **Can Access Online at www.oralchemoedsheets.com**
 - Educate patients on side effects and report adverse effects to prescriber and recommend dose adjustments in 40 mg increments as tolerated
- Counsel Patient
 - Dosing is once daily for 3 weeks on therapy then 1 week off therapy per cycle
 - STIVARGA (regorafenib) currently comes in a package size of 28 tablets which may or may not be a suitable dispensing amount
 - Medication expires 7 weeks after opening bottle
 - Take dosage with low fat meal (< 600 calories)
 - Examples of Low Fat food choices⁵
 - Dairy and dairy-like products
 - Low-fat (1%) or fat-free (skim) yogurt, cottage cheese, or milk
 - Fat-free American cheese or other types of fat-free cheeses
 - Fish, meat, poultry, and other protein
 - Egg whites or egg substitutes
 - Crab, white fish, shrimp, and light tuna (packed in water)

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- Chicken and turkey breast (without skin), or ground turkey breast
- Beans, peas, and lentils, cooked (or canned) without added fats or fatty meats
- Grains, cereals, and pastas
 - Hot (oatmeal or grits) and cold cereals (except granola types)
 - Whole grain brown Rice or noodles (watch out for fat in added sauces)
 - Whole grain bagels, pita bread, or English muffins
 - Low-fat crackers and breads
 - Soft tortillas – corn or whole wheat
- Fruits- including fresh, frozen, or canned (in their own juice)
- Vegetables- including fresh, frozen, or canned (choose lower-sodium varieties)
- Other foods
 - Broth type soups with a vegetable base
 - Sauces, pudding, or shakes made with skim milk

References:

1. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. Bruix, Jordi et al. The Lancet, Volume 389 , Issue 10064 , 56 - 66
2. Ou FS, Bekaii-Saab T. ReDOS* trial presented at the ASCO GI Cancers Symposium 2018. ReDOS poster from ASCO GI, Jan. 2018.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN guidelines®) for colon cancer v.2.2018. © Page COL-D 9 of 10. National Comprehensive Cancer Network 2018. All rights reserved. Accessed May 10, 2018.
4. Bekaii-Saab T, Ou FS, Ciombor KK, et al. Regorafenib dose optimization study (ReDOS): A phase II randomized study of lower starting dose regorafenib compared to standard dose regorafenib in patients with refractory metastatic colorectal cancer (mCRC). Journal of Clinical Oncology 2016 34:15_suppl, TPS3630-TPS3630

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5. STIVARGA® (Regorafenib) [Prescribing Information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, April 2017.
6. <https://www.cancer.org/healthy/eat-healthy-get-active/take-control-your-w>

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