National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Positive Quality Intervention: Regorafenib in the treatment of Hepatocellular Carcinoma

Description of PQI: Understand how to effectively manage adverse effects of Regorafenib 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 sofarenib 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 this study, median time to progression (regorafenib vs placebo) was 3.2 vs 1.5 months. The rates of grade ≥3 adverse events were 79.7% with regorafenib and 58.5% with placebo.

There is an ongoing study in metastatic colorectal cancer or mCRC (ReDos) that is currently evaluating the efficacy of starting regorafenib at lower doses compared to the standard dose.

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.

Dosing Guideline Background:

1. 160 mg (four 40mg tabs) once daily for the first 21 days of a 28-day cycle
2. Consider dose titration (Redos)
3. Take at the same time each day. Swallow tablet whole with water after a low-fat meal (containing <600 calories and <30% fat).

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

- If the typical starting dose of 160mg by mouth once a day is written consider initiating dose titration based on the mCRC ReDos trial.
    - 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 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
- Counsel patient regarding safety risk on proper amount of dose per cycle based on regimen changes understanding your organization's dispensing protocol and that STIVARGA (regorafenib) currently comes in a package size of 28 tablets which may or may not be a suitable size.

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
    - Medication expires 7 weeks after opening bottle

- Take dosage with low fat meal (< 600 calories)
    - Examples of Low Fat food choices[5]
        - 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)
            - 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:

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