Written By: Joshua Nubla
NCODA
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Positive Quality Intervention: Avapritinib (Ayvakit®) Management for Gastrointestinal Stromal Tumor

Description: This PQI will discuss the initiation and management of patients receiving avapritinib.

Background: Avapritinib is a tyrosine kinase inhibitor indicated for the treatment of adults with unresectable or metastatic GIST harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations. Avapritinib was approved in January 2020 and is the first therapy approved for patients with GIST with a PDGFRA exon 18 mutation. The NAVIGATOR trial included patients with a confirmed diagnosis of GIST and received 300 mg or 400 mg orally once daily until disease progression or unacceptable toxicity. Patients starting at 400 mg were later reduced to 300 mg due to toxicity. The primary endpoint was overall response rate (ORR), and 43 patients who had exon 18 PDGFRA mutations were included in the ORR analysis. For GIST patients with PDGFRA exon 18 mutations, ORR was 84% with complete response in 7% of patients and partial response in 77% of patients. Patients with PDGFRA D842V mutations had an ORR of 89% (CR 8% and PR 82%; n=38). There were 22 patients with a PDGFRA exon 18 mutation with a duration of response ≥ 6 months (61%) and 20 patients with a PDGFRA D842V mutation with a duration of response ≥ 6 months (59%). Dose reduction due to an adverse reaction occurred in 49% of patients who received avapritinib with a median time to dose reduction of 9 weeks. The most common adverse reactions (≥ 20%) were edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation, abdominal pain, constipation, rash, and dizziness.[1]

PQI Process:

- Confirm diagnosis and verify genetic testing for PDGFRA exon 18 and PDGFRA D842V mutations

Upon receiving a prescription for avapritinib:

- Verify dose – Usual dose 300 mg orally once daily on empty stomach (1 hour before/2 hours after)
    - No dose adjustment needed with mild/moderate renal or mild/moderate hepatic impairment
    - Dose modifications:

First dose reduction	200 mg once daily
Second dose reduction	100 mg once daily
Third dose reduction	Permanently discontinue in patients unable to tolerate 100 mg daily

- Assess patient for antiemetic regimen; consider regular option for patient use as needed
- Check for drug interactions
    - Avoid avapritinib administration with strong or moderate CYP3A inhibitors.
    - If combination with moderate CYP3A4 is unavoidable, reduce dose of avapritinib to 100 mg once daily
    - Avoid avapritinib administration with strong or moderate CYP3A inducers
- Dose modifications for specific adverse reactions:
    - Intracranial Hemorrhage
        - Grade 1 or 2:
            - First Occurrence: Hold until resolution and resume at reduced dose
            - Subsequent Occurrence: Discontinue
        - Grade 3 or 4: Permanently discontinue

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PQI Process Continued:

- Central Nervous System Effects:
  - Grade 1:
    - Continue at same dose or hold until improvement to baseline or resolution
    - Resume at same dose or reduced dose
  - Grade 2 or 3:
    - Hold until improvement to baseline, grade 1, or resolution
    - Resume at same or reduced dose
  - Grade 4: Discontinue
- Other adverse reactions at Grade 3 or 4:
  - Hold until improvement to less than or equal to Grade 2
  - Resume at same or reduced dose, as clinically appropriate

Patient Centered Activities:

- Provide Oral Chemotherapy Education (OCE) Sheet
- Counsel patient that medication should be taken on empty stomach
- Educate patient that a missed dose needs to be taken within 8 hours of the regular dosing time
- Counsel patient on potential drug interactions with avapritinib
- Monitor patient for central nervous side effects such as dizziness, trouble sleeping, changes in mood or behavior as well as any neurological signs and symptoms related with intracranial hemorrhage
  - Educate the patient and their caregiver network to be alert for cognitive changes such as memory loss, forgetfulness and confusion
- Monitor patient for laboratory changes associated with common adverse reactions such as decreased hemoglobin and increased bilirubin

Supplemental Information:

- Patient Support Program: YourBlueprint (https://www.yourblueprint.com/hcp/)
  - Dedicated Case Manager available at 1-888-258-7768 (1-888-BLUPRNT)
  - Monday-Friday 8AM-8PM ET
- Co-Pay Assistance Program
  - Eligible, commercially insured patients may reduce their out-of-pocket costs ($0 per month)

References:

1. AYVAKIT® (avapritinib) [prescribing information]. Cambridge, MA: Blueprint Medicines Corporation.
2. Heinrich MC, Jones RL, von Mehren M et al. Avapritinib in advanced PDGFRA D842V-mutant gastrointestinal stromal tumour (NAVIGATOR): a multicentre, open-label, phase 1 trial. Lancet Oncol. 2020 Jul;21(7):935-946.