Written By: Rob Walchack, PharmD, BCOP
Cleveland Clinic Main Campus

Avapritinib (Ayvakit®) for Indolent Systemic Mastocytosis

Description:
This PQI will discuss the use of oral avapritinib in patients with indolent systemic mastocytosis (ISM).

Background:
Avapritinib is a highly selective and potent tyrosine kinase inhibitor that blocks D816V-mutated KIT and D842V platelet-derived growth factor receptor alpha (PDGFRA), which are mutations that confer resistance to other kinase inhibitors. It is approved in patients with:[1,2]

- Indolent systemic mastocytosis
- Additional indications – see prescribing information[1]

Overall, avapritinib is well-tolerated. Most common adverse events (< 20%):[1]

- Flushing, edema (peripheral, facial, and periorbital), and insomnia
- Increased alkaline phosphatase

PQI Process:

- Confirm diagnosis for ISM
- Avapritinib 25 mg by mouth once daily on an empty stomach (**note:** dosing differs for GIST and AdvSM indications).
- Avapritinib is associated with moderate to high emetic risk, however, the incidence appears to be dose-dependent, as incidence is lower in the treatment of ISM (13%) compared to the treatment of AdvSM (24%) and GIST (64%)
    - Consider use of an antiemetic to be given as needed for nausea/vomiting
- Avapritinib is not recommended for patients with platelet counts <50,000/mm^3
- Assess for potential drug interactions
    - Avoid concomitant use of strong/moderate CYP3A inhibitors and/or inducers.
- No dose modifications are recommended for adverse reactions
    - Dose modifications for renal impairment
        - No dose adjustment is recommended for patients with mild to moderate renal impairment (creatinine clearance 30-89 mL/min)
        - Not studied in patients with creatinine clearance < 30 mL/min
    - Dose modifications for hepatic impairment
        - No dose adjustment is recommended for patients with mild to moderate hepatic impairment
        - Severe hepatic impairment (Child-Pugh Class C): 25 mg orally every other day
- No specific laboratory parameter monitoring is recommended for treatment of patients with ISM

Patient-Centered Activities:

- Provide Patient Education Sheet
- Administer avapritinib on an empty stomach ≥1 hour before or ≥2 hours after a meal.
    - Do not make up for a missed dose within 8 hours of the next scheduled dose.
    - Do not retake dose if vomited; continue with next scheduled dose.
- Discuss the most common side effects: nausea/vomiting/diarrhea or constipation, anorexia, abdominal pain, edema (peripheral, facial, periorbital), photosensitivity (rash, flushing, hair color changes), ↑ tearing, fatigue, headache, insomnia, dizziness.
- Report any signs of intracranial bleeding immediately.
- Educate the patient on the risk of photosensitivity reactions, importance of limiting ultraviolet exposure during treatment and 1 week after treatment; use sunscreen and protective clothing
- Use effective contraception during treatment and for 6 weeks after; applies to both sexes.
- Counsel patients on potential drug interactions.
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. AYVAKIT® (avapritinib) [prescribing information].
2. Gotlib J, Castells M, Oude Elberink H, et al. Avapritinib versus placebo in indolent systemic mastocytosis. *NEJM Evid.* 2023;2(6).
3. National Comprehensive Cancer Network. (Version 1.2023). Retrieved May 25, 2023, from https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf.
4. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(20): 2391-2405.
5. FDA approves Ayvakit (avapritinib) as the first and only treatment for indolent systemic mastocytosis. News release. Blueprint Medicines Corporation. May 22, 2023. Accessed May 25, 2023. https://ir.blueprintmedicines.com/news-releases/news-release-details/fda-approves-ayvakitr-avapritinib-first-and-only-treatment.