Written By: Andrew Kowalski, PharmD
Osama Abdelghany, PharmD, MHA, BCOP
Smilow Cancer Hospital at Yale New Haven Health

Positive Quality Intervention: Copanlisib (Aliqopa®) for the Management of Relapsed/Refractory Follicular Lymphoma

Description: There are a number of treatment options for patients with follicular lymphoma that have relapsed or are refractory to first line options. The purpose of this PQI is to discuss appropriate patient identification and clinical considerations around the use of copanlisib for the treatment of adults who have received at least two other previous therapies.

Background: Non-Hodgkin's lymphoma includes both aggressive and indolent malignancies. Follicular lymphoma is the most common subtype of indolent Non-Hodgkin's Lymphoma. Copanlisib is an intravenous phosphatidylinositol 3-kinase (PI3K) inhibitor. PI3K pathways are often hyperactive in B-Cell malignancies. A phase II study in follicular lymphoma demonstrated an overall response rate of 59% with copanlisib. In 168 adults with exposure to copanlisib, the most common treatment related adverse events in any grade were hyperglycemia (54%), leukopenia (36%), fatigue (36%), diarrhea (36%), and hypertension (35%). Grade 3+ adverse events were observed for hyperglycemia (39%), leukopenia (27%), hypertension (27%) and infections (14%).

November 13, 2023 – Bayer announced it will work with the FDA on a voluntary withdrawal of the Aliqopa® (copanlisib) U.S. New Drug Application for adult patients with relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies.

PQI Process: Upon receipt of an order for copanlisib

- Ensure patient is an appropriate candidate for copanlisib and has received at least two prior therapies
- Discuss potential risks of copanlisib therapy
    - Increased risk of infection
        - Monitor for signs and symptoms of infection, including pneumocystis jirovecii pneumonia (PJP)
        - For suspected PJP infection of any grade: hold copanlisib; if infection is confirmed, treat until resolution, then resume copanlisib at previous dose with concomitant PJP prophylaxis
- Hyperglycemia[2]
    - Check blood glucose prior to copanlisib infusion and withhold dose unless the following parameters have been met:
        - Fasting plasma glucose ≤ 160 mg/dL OR random glucose ≤ 200 mg/dL
        - If pre/post-dose blood glucose ≥ 500 mg/dL then withhold until above parameters have been met and reduce copanlisib from 60 mg to 45 mg
        - On subsequent occurrences, reduce to 30 mg when above parameters have been met
        - If persistent, discontinue
    - Nondiabetic patients
        - Consider checking HbA1c prior to copanlisib treatment and re-checking once treatment is discontinued
            - Patients who develop an increase in HbA1c during copanlisib treatment should be re-tested in 3 months to determine if HbA1c has returned to baseline

        - Post-infusion monitoring is not needed for nondiabetic patients
        - Insulin is discouraged in nondiabetic patients due to the increased risk of hypoglycemia
        - Encourage adequate hydration
    - Prediabetic/diabetic patients
        - Check HbA1c prior and consider consulting with an endocrinologist prior to treatment
        - Post-infusion blood glucose should be checked, and monitoring should occur
            - Post-dose blood glucose ≥ 500 mg/dL consider reduction to 45 mg with subsequent infusion
        - When a meal is consumed within 8 hours post-infusion ensure low carbohydrate diet
    - Hypertension:
        - Monitor blood pressure at least pre- and post-dose; it may be necessary to monitor more frequently as clinically indicated
        - In clinical trials, blood pressure remained elevated 6-8 hours post infusion
        - Hold, reduce dose, or discontinue based on the severity and persistence of hypertension
- Drug-Drug Interactions
    - Avoid concomitant use of strong CYP3A4 inhibitors
        - If concurrent therapy cannot be avoided, reduce the copanlisib dose to 45 mg
- Reconstitution:
    - Add 4.4 mL of sterile NS and gently shake for 30 seconds, then let stand for 1 minute
        - If particulates remain, gently shake again and let sit for 1 minute
    - Final concentration 15 mg/mL
- Storage:
    - Reconstituted or diluted solution: 2-8 C° up to 24 hours
    - Avoid exposure to direct sunlight
- Administration: Infuse over 1 hour

Patient-Centered Activities:

- Educate patients on copanlisib therapy and recommend appropriate interventions:
    - Hyperglycemia: Monitor patients for signs of confusion, feeling sleepy, increased thirst, increased hunger, passing urine more often, flushing, fast breathing, or breath that smells like fruit
    - Hypertension: Monitor patients for signs/symptoms of high blood pressure like very bad headache or dizziness, passing out, or change in eyesight
    - Diarrhea
        - Monitor bowel movements occurring each day
        - Recommend to patients to drink 8–10 glasses of water each day
        - Antidiarrheal medications may be used to help control symptoms
        - See **Oncolytic Induced Diarrhea** PQI and provide Oral Chemotherapy Education Supplemental Sheet
    - Allergic or cutaneous reactions**:** Monitor for signs of rash, hives, itching, red/swollen/blistered/peeling skin with/without fever, wheezing, tightness in the chest/throat, trouble breathing/swallowing/talking, unusual hoarseness, or swelling of the mouth/face/lips/tongue/throat
    - Infections and pneumonitis: Monitor for any signs of lung or breathing problems like shortness of breath, fever, chills, very bad sore throat, ear or sinus pain, cough, increased sputum or change in color of sputum, pain with passing urine, mouth sores, or wound that will not heal
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Dreyling M, et al. Phase II study of copanlisib, a PI3K inhibitor, in relapsed or refractory, indolent or aggressive lymphoma. *Annals of Oncology*. 2017; 28: 2169-78.

doi:10.1093/annonc/mdx289.
2. Aliqopa® (copanlisib) [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.