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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 has relapsed or is 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 a variety of 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%), and hypertension (27%) and infections (14%).

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: Withhold copanlisib; if infection is confirmed, treat infection until resolution, then resume copanlisib at previous dose with concomitant PJP prophylaxis
    - Hyperglycemia
        - Monitor blood glucose at least pre- and post-dose. It may be necessary to monitor more frequently as clinically indicated
        - In clinical trials, copanlisib induced hyperglycemia peaked 5-8 hours post-infusion and remained elevated 24 hours post-infusion
        - Pre-dose fasting blood glucose ≥160 mg/dL or random (non-fasting) blood glucose ≥200 mg/dL:
            - Withhold copanlisib until fasting glucose is ≤160 mg/dL or a random (non-fasting) blood glucose is ≤200 mg/dL
        - Pre-dose or post-dose blood glucose ≥500 mg/dL:
            - First occurrence: Withhold copanlisib until fasting blood glucose is ≤160 mg/dL, or a random (non-fasting) blood glucose is ≤200 mg/dL. Reduce dose from 60 mg to 45 mg

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PQI Process Continued:

- Subsequent occurrences: Withhold copanlisib until fasting blood glucose is ≤160 mg/dL, or a random (non-fasting) blood glucose is ≤200 mg/dL. Reduce dose from 45 mg to 30 mg. If hyperglycemia is persistent at the 30 mg dose, discontinue copanlisib

- 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
  - Withhold, reduce dose, or discontinue copanlisib depending on the severity and persistence of hypertension **review prescribing information for full details*
- Drug-Drug Interactions
  - Copanlisib is a major substrate of CYP3A4
  - Avoid concomitant use of strong CYP3A4 inhibitors
    - Potential: If concurrent therapy cannot be avoided, reduce the copanlisib dose to 45 mg

Patient Centered Activities:

- Educate patients on copanlisib therapy and recommend appropriate interventions:
  - Hyperglycemia
    - Monitor patients for signs of confusion, feeling sleepy, more thirst, more 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

Patient Centered Activities Continued:

- 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 or other

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trouble breathing, fever, chills, very bad sore throat, ear or sinus pain, cough, more sputum or change in color of sputum, pain with passing urine, mouth sores, or wound that will not heal

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. 2019.

Supplemental Information:

Select treatment options include:

- Cyclophosphamide, vincristine, prednisone (CVP) + obinutuzumab or rituximab
- Rituximab, Lenalidomide +/- rituximab, Ibritumomab tiuxetan, Idelalisib (refractory to alkylator and rituximab)
- Copanlisib (refractory to two prior therapies), Duvelisib (refractory to two prior therapies)

Administration/Storage:

- Reconstitute
  - Add 4.4 mL of sterile NS. 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 degrees C up to 24 hours
  - Avoid exposure to direct sunlight
- Administration
  - Infuse over 1 hour