NCODA Positive Quality Interventions

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Positive Quality Intervention: Acalabrutinib (CALQUENCE) In Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Description:

- The purpose of this PQI is to discuss clinical considerations around the use of acalabrutinib (CALQUENCE®) to optimize outcomes for patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

Background:

- Acalabrutinib is a selective, covalent Bruton tyrosine kinase (BTK) inhibitor that irreversibly binds BTK, blocking B-cell receptor signaling. This inhibits downstream pathways that promote CLL cell proliferation, survival, adhesion, and migration.
- FDA approved indications include:
    - CLL/SLL
        - As monotherapy
        - In combination with obinutuzumab in patients with previously untreated disease until disease progression or unacceptable toxicity
        - In combination with venetoclax in patients with previously untreated disease until disease progression, unacceptable toxicity or completion of 14 cycles of treatment (fixed duration)
    - Mantel cell lymphoma (MCL)
        - As monotherapy for the treatment of adult patients with MCL who have received at least one prior therapy
        - In combination with bendamustine and rituximab for the treatment of adult patients with previously untreated MCL who are ineligible for autologous hematopoietic stem cell transplantation
- The most common adverse reactions (≥ 30%), excluding laboratory abnormalities, are upper respiratory tract infection, diarrhea, headache, and musculoskeletal pain.
- The most common Grade 3 or 4 laboratory abnormalities (≥ 10%) are absolute neutrophil count decreased, uric acid increased, absolute lymphocyte count decreased, and platelets decreased.

PQI Process:

Upon the receipt of a new prescription of acalabrutinib for CLL/SLL:

- Verify dose: acalabrutinib 100 mg by mouth every 12 hours, taken whole with water, with or without food
    - If dose is missed by > 3 hours, skip and take the next at its regularly scheduled time
    - Avoid in patients with severe hepatic impairment
    - No dose adjustment needed in mild to moderate hepatic or renal impairment (use in severe renal impairment or with dialysis has not yet been evaluated)
    - In combination with obinutuzumab
        - Start acalabrutinib at Cycle 1 (each cycle is 28 days)
        - Start obinutuzumab at Cycle 2 for a total of 6 cycles (refer to obinutuzumab prescribing information for recommended dosing)

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        - Administer acalabrutinib **prior** to obinutuzumab when given on the same day
        - Administers until disease progression or unacceptable toxicity
    - In combination with venetoclax
        - Start acalabrutinib at Cycle 1 (each cycle is 28 days)
        - Start venetoclax at Cycle 3 for total of 12 cycles; starting dose venetoclax is 20 mg daily for first week of treatment and increases weekly as per dosing schedule for 5-week ramp up (up to 400 mg daily) as described in the venetoclax PI.
        - Continue treatment with acalabrutinib + venetoclax until disease progression, unacceptable toxicity or completion of 14 cycles of treatment
- Review patient medication list for possible drug-drug interactions
    - Strong CYP3A4 inducer: avoid use; if use cannot be avoided, increase dosage to 200 mg every 12 hours
    - Strong CYP3A4 inhibitor: avoid use; if the inhibitor is a short-term medication (e.g., anti-infectives for up to seven days), stop acalabrutinib and resume after at least 24 hours post inhibitor discontinuation
    - Moderate CYP3A4 inhibitor: reduce acalabrutinib dosage to 100 mg daily
    - Tablet formulation may be co-administered with gastric reducing agents
- Adverse Event Monitoring and Management
    - Infections, including opportunistic infections
        - Monitor for signs/symptoms of infections and treat promptly
        - Consider prophylaxis in patients who are at increased risk for opportunistic infections
    - Hemorrhagic events
        - Monitor for bleeding and manage appropriately
        - Consider the benefit-risk of withholding acalabrutinib for 3-7 days pre- and post-surgery depending on type of surgery and the risk of bleeding
        - Caution in patients on antithrombotic agents
    - Myelosuppression (neutropenia, anemia, thrombocytopenia, and lymphopenia)
        - Monitor complete blood cell counts regularly
    - Cardiac arrhythmia
        - Monitor for symptoms of arrhythmias (ex. palpitations, dizziness, syncope, dyspnea) and manage appropriately
        - Risk of arrhythmias may be increased in patients with cardiac risk factors, hypertension, previous arrhythmias, and acute infection
    - Skin cancer as secondary malignancy
        - Monitor patients for skin cancer and advise protection from sun exposure
    - Hepatotoxicity, including drug-induced liver injury (DILI)
        - Evaluate bilirubin and transaminases at baseline and throughout treatment
        - For patients who develop abnormal liver tests, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity
        - If DILI is suspected, withhold acalabrutinib; upon confirmation of DILI, discontinue acalabrutinib

Table 1. Recommended Dosage Modifications for Adverse Reactions (acalabrutinib monotherapy/in combination with obinutuzumab*)

Event	Adverse Reaction Occurrence	Dosage Modification (Starting dose = 100 mg approximately every 12 hours)
Grade 3 or greater nonhematologic toxicities, Grade 3 thrombocytopenia with bleeding, Grade 4 thrombocytopenia or Grade 4 neutropenia lasting longer than 7 days	First and Second	Interrupt acalabrutinib. Once toxicity has resolved to Grade 1 or baseline level, acalabrutinib may be resumed at normal starting dose.
	Third	Interrupt acalabrutinib. Once toxicity has resolved to Grade 1 or baseline level, acalabrutinib may be resumed at a reduced frequency of 100 mg once daily.
	Fourth	Discontinue acalabrutinib.

*See CALQUENCE PI Table 4 for recommended dosage modifications when given in combination with venetoclax

Patient-Centered Activities:

- Patient Education
  - Provide Patient Education Sheet (PES) and review with patient
    - Acalabrutinib PES
    - Acalabrutinib + Venetoclax PES
  - Instruct patients to report any signs or symptoms of atrial fibrillation or flutter such as palpitations, dizziness, faint feeling, or chest discomfort
  - Counsel patients to report any signs or symptoms of infections including new or worsening cough or shortness of breath, sore throat, chills, notably increased fatigue, or fever of 100.4º F or higher
  - Counsel patients to report any new or uncontrolled bleeding including nosebleed lasting > 5 minutes despite pressure, a cut that won't stop bleeding, heavy gum bleeding when brushing or flossing, or blood in urine or stool
  - Patients should be made aware of the increased bleeding risk associated with acalabrutinib
    - Due to this risk, they may need to hold their medication prior to any procedures
  - Ensure patients have access to supportive care medications for diarrhea such as loperamide
- Patient Assistance: CALQUENCE Co-Pay Savings Program & AstraZeneca Access 360

References:

1. CALQUENCE® (acalabrutinib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2026.
2. Sharman JP, et al. Acalabrutinib with or without obinutuzumab versus chlorambucil and obinutuzumab for treatment-naive chronic lymphocytic leukemia (ELEVATE TN): a randomized, controlled, phase 3 trial. Lancet. 2020 Apr 18;395(10232):1278-1291.
3. Ghia P, et al. ASCEND: Phase III, Randomized Trial of Acalabrutinib Versus Idelalisib Plus Rituximab or Bendamustine Plus Rituximab in Relapsed or Refractory Chronic Lymphocytic Leukemia. J Clin Oncol. 2020 Sept 01;38(25):2849-2861.
4. Byrd J, et al. Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial. J Clin Oncol. 2021 Nov 01;39(31):3441-3452.