MEDIA FACT SHEET

CALQUENCE® (acalabrutinib) 100 mg capsules

ABOUT CALQUENCE® (acalabrutinib)

- CALQUENCE is a kinase inhibitor indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.[1]
    - CALQUENCE is approved under the US Food and Drug Administration (FDA)'s accelerated approval pathway, based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- CALQUENCE is an inhibitor of Bruton tyrosine kinase (BTK). CALQUENCE binds irreversibly to BTK, thereby inhibiting its activity.[1]
    - In B cells, BTK signaling results in the activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis and adhesion.[1]
- Continuous inhibition of BTK is maintained with twice daily oral dosing (100mg capsule).[1]

ACALABRUTINIB CLINICAL TRIAL PROGRAM

- CALQUENCE was approved based on results from the Phase II open-label, single-arm ACE-LY-004 trial. Summary of key efficacy results as assessed by an Independent Review Committee (IRC): The trial showed that 80% of adult patients treated with CALQUENCE achieved an overall response (95% CI: 72, 87), 40% achieved a complete response (95% CI: 31, 49), and 40% achieved a partial response (95% CI: 32, 50).[1]
- The most common adverse reactions (≥20%) were anemia (46%), thrombocytopenia (44%), headache (39%), neutropenia (36%), diarrhea (31%), fatigue (28%), myalgia (21%) and bruising (21%). Hematological events were based on laboratory measurements and adverse reactions.[1]
- Dosage reductions or discontinuations due to any adverse reaction were reported in 1.6% and 6.5% of patients, respectively.[1]
- Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 4.8% of patients.[1]
- Select Important Safety Information
    - Hemorrhage
        - Serious hemorrhagic events, including fatal events, have occurred in the combined safety database of 612 patients with hematologic malignancies treated with CALQUENCE monotherapy. Grade 3 or higher bleeding events, including gastrointestinal, intracranial, and epistaxis, have been reported in 2% of patients. Overall, bleeding events, including bruising and petechiae of any grade, occurred in approximately 50% of patients with hematological malignancies.
        - The mechanism for the bleeding events is not well understood.
        - CALQUENCE may further increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies, and patients should be monitored for signs of bleeding.
        - Consider the benefit-risk of withholding CALQUENCE for 3 to 7 days pre- and post-surgery, depending upon the type of surgery and the risk of bleeding.
        - See additional Important Safety Information.
- ACE-LY-004 was an open-label, single-arm clinical trial of CALQUENCE monotherapy in 124 adult patients with MCL who had received at least one prior therapy.
    - The major efficacy endpoint was overall response rate, and additional efficacy endpoints included duration of response, progress-free survival and overall survival.[1,2]
- Acalabrutinib is also in development for the treatment of multiple B-cell malignancies and other cancers including chronic lymphocytic leukemia, MCL, Waldenström macroglobulinemia, follicular lymphoma, diffuse large B-cell lymphoma, and multiple myeloma.
    - It is also being studied as a monotherapy and in combination trials for the treatment of solid tumors. More than 35 clinical trials across 40 countries with more than 2,500 patients are underway or have completed.[2]

ABOUT MANTLE CELL LYMPHOMA

- MCL is a rare B-cell non-Hodgkin lymphoma and is typically diagnosed at an advanced stage (Stage III or IV in older individuals). By the time MCL is diagnosed, the cancer has usually spread to the gastrointestinal tract and bone marrow.[3]
- MCL is a life-threatening blood cancer with no cure.[4] While MCL patients initially respond to treatment, there is a high relapse rate.[5] Patients who relapse or are refractory to current therapies have a poor prognosis.[6]
- The mean age at diagnosis for MCL is 68 years old, with MCL occurring twice as often in men than women.[5]
- MCL accounts for approximately 3% of new NHL cases in the US, with 3,300 new cases diagnosed each year.[7,8]
- Currently, there is no standard therapy in relapsed or refractory MCL.[5] Currently approved treatment options include chemoimmunotherapy, targeted therapy, and stem cell transplant.

IMPORTANT SAFETY INFORMATION about CALQUENCE® (acalabrutinib)

Hemorrhage

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The mechanism for the bleeding events is not well understood.

CALQUENCE may further increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies, and patients should be monitored for signs of bleeding.

Consider the benefit-risk of withholding CALQUENCE for 3 to 7 days pre- and post-surgery, depending upon the type of surgery and the risk of bleeding.

Infection

Serious infections (bacterial, viral, or fungal), including fatal events and opportunistic infections, have occurred in the combined safety database of 612 patients with hematologic malignancies treated with CALQUENCE monotherapy. Grade 3 or higher infections occurred in 18% of these patients. The most frequently reported Grade 3 or 4 infection was pneumonia. Infections due to hepatitis B virus (HBV) reactivation and progressive multifocal leukoencephalopathy (PML) have occurred.

Monitor patients for signs and symptoms of infection and treat as medically appropriate. Consider prophylaxis in patients who are at increased risk for opportunistic infections.

Cytopenias

In the combined safety database of 612 patients with hematologic malignancies, patients treated with CALQUENCE monotherapy experienced Grade 3 or 4 cytopenias, including neutropenia (23%), anemia (11%), and thrombocytopenia (8%), based on laboratory measurements. Monitor complete blood counts monthly during treatment.

Second Primary Malignancies

Second primary malignancies, including non-skin carcinomas, have occurred in 11% of patients with hematologic malignancies treated with CALQUENCE monotherapy in the combined safety database of 612 patients. The most frequent second primary malignancy was skin cancer, reported in 7% of patients. Advise protection from sun exposure.

Atrial Fibrillation and Flutter

In the combined safety database of 612 patients with hematologic malignancies treated with CALQUENCE monotherapy, atrial fibrillation and atrial flutter of any grade occurred in 3% of patients, and Grade 3 in 1% of patients. Monitor for atrial fibrillation and atrial flutter and manage as appropriate.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) of any grade were anemia,* thrombocytopenia,* headache (39%), neutropenia,* diarrhea (31%), fatigue (28%), myalgia (21%), and bruising (21%).

*Treatment-emergent decreases (all grades) of hemoglobin (46%), platelets (44%), and neutrophils (36%) were based on laboratory measurements and adverse reactions.

The most common Grade ≥ 3 non-hematological adverse reaction (reported in at least 2% of patients) was diarrhea (3.2%).

Dosage reductions or discontinuations due to any adverse reaction were reported in 1.6% and 6.5% of patients, respectively.

Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 4.8% of patients.

DRUG INTERACTIONS

Strong CYP3A Inhibitors: Avoid co-administration with a strong CYP3A inhibitor. If a strong CYP3A inhibitor will be used short-term, interrupt CALQUENCE.

Moderate CYP3A Inhibitors: When CALQUENCE is co-administered with a moderate CYP3A inhibitor, reduce CALQUENCE dose to 100 mg once daily.

Strong CYP3A Inducers: Avoid co-administration with a strong CYP3A inducer. If a strong CYP3A inducer cannot be avoided, increase the CALQUENCE dose to 200 mg twice daily.

Gastric Acid Reducing Agents: If treatment with a gastric acid reducing agent is required, consider using an H2-receptor antagonist or an antacid. Take CALQUENCE 2 hours before taking an H2-receptor antagonist. Separate dosing with an antacid by at least 2 hours.

Avoid co-administration with proton pump inhibitors. Due to the long-lasting effect of proton pump inhibitors, separation of doses may not eliminate the interaction with CALQUENCE.

SPECIFIC POPULATIONS

There is insufficient clinical data on CALQUENCE use in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. Advise women of the potential risk to a fetus.

It is not known if CALQUENCE is present in human milk. Advise lactating women not to breastfeed while taking CALQUENCE and for at least 2 weeks after the final dose.

Please see complete Prescribing Information including Patient Information.

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[1] CALQUENCE® (acalabrutinib) Prescribing Information. AstraZeneca Pharmaceuticals LP, Wilmington, DE.
[2] Data on File. REF US-15441. AstraZeneca Pharmaceuticals LP, Wilmington, DE.
[3] Lymphoma Research Foundation. Mantle Cell Lymphoma. Available from: http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6300157. Accessed August 2017.
[4] Hoster E, Klapper W, Hermine O, et al. Confirmation of the Mantle Cell Lymphoma International Prognostic Index in Randomized Trials of the European Mantle Cell Lymphoma Network. J Clin Oncol. 2014;32:1338-1346.
[5] Cheah CY, Seymour JF, Wang M. Mantle Cell Lymphoma. J Clin Oncol. 34, no. 11 (April 2016) 1256-1269.
[6] Leukemia and Lymphoma Society. Mantle Cell Lymphoma Facts. Available from: https://www.lls.org/sites/default/files/file_assets/mantlecelllymphoma.pdf. Accessed August 2017.
[7] Zhou Y, Wang H, Fang W, et al. 4 Incidence Trends of Mantle Cell Lymphoma in the United States between 1992 and 2004. Cancer. 2008;113:791-798.
[8] Teras LR, DeSantis CE, Cerhan JR, et al. 2016 US lymphoid malignancy statistics by World Health Organization subtypes. CA Cancer J Clin. 2016;66:443-459.