#1 prescribed BTKi for patients starting CLL treatment*[5]

START STRONG

In ELEVATE-TN at ~2.5-year follow-up,† primary endpoint was IRC-PFS with CALQUENCE + obinutuzumab vs GClb

HR‡=0.10 (95% CI: 0.06-0.17); *P*§<0.0001[1,2]

~2.5-YEAR FOLLOW-UP: INTERIM ANALYSIS†

CALQUENCE monotherapy delivered consistent PFS results in 1L CLL patients with del(17p) and/or *TP53*m†[1,2]

Intent-to-treat (secondary endpoint)[1,2]

80% **PFS risk reduction‖ (CALQUENCE:GClb)**

HR=0.20‡ (95% CI: 0.13-0.30; n=356); *P*§<0.0001

del(17p) and/or *TP53*m (exploratory analysis)[2]

77% **PFS risk reduction‖ (CALQUENCE:GClb)**

HR=0.23‡ (95% CI: 0.09-0.61; n=48); descriptive only

Hazard ratios (95% CI) for CALQUENCE:GClb in other cytogenetic/molecular subgroups: 0.11 (0.07-0.19) with u*IGHV* and 0.69 (0.31-1.56) with m*IGHV*; 0.07 (0.02-0.22) with del(11q) and 0.26 (0.16-0.41) without del(11q); 0.23 (0.09-0.61) with del(17p) and/or *TP53* mutation; 0.19 (0.11-0.31) without del(17p) and/or *TP53* mutation; 0.10 (0.03-0.33) with complex karyotype and 0.27 (0.16-0.46) without complex karyotype.[2]

Study not powered to show statistical significance across prespecified subgroups.

~6-YEAR FOLLOW-UP: POST-HOC ANALYSIS¶

Long-term follow-up data for CALQUENCE monotherapy in 1L CLL¶[3]

Intent-to-treat#[3]

5-year PFS rate with CALQUENCE¶

22% with GClb (95% CI: 16.0-29.5)

(95% CI: 65.6-79.3)

del(17p) and/or *TP53*m**[3]

5-year PFS rate with CALQUENCE¶

18% with GClb (95% CI: 6.0-36.3)

(95% CI: 47.2-86.0)

The 74.5-month follow-up data, including estimated PFS rates at 60 months, were descriptive only and not formally tested.

Safety results with CALQUENCE ± obinutuzumab in 1L CLL

- **At 28.3-month median follow-up**[1]
  - **The most common ARs (≥30%)** of Any Grade in patients treated with **CALQUENCE + obinutuzumab (n=178)** were infection (69%), including upper respiratory tract infection (39%); neutropenia (53%); anemia (52%); thrombocytopenia (51%); headache (40%); diarrhea (39%); musculoskeletal pain (37%); fatigue (34%); and bruising (31%). In the **CALQUENCE monotherapy arm (n=179)**, the most common ARs (≥30%) of Any Grade were infection (65%), including upper respiratory tract infection (35%); anemia (53%); headache (39%); diarrhea (35%); musculoskeletal pain (32%); and thrombocytopenia (32%).
  - **Fatal adverse reactions** that occurred in the absence of disease progression and with an onset within 30 days of the last study treatment was 2% for both CALQUENCE + obinutuzumab and CALQUENCE monotherapy. **Serious adverse reactions** were reported in 39% of patients treated with CALQUENCE + obinutuzumab and 32% of patients treated with CALQUENCE monotherapy, most often due to event of pneumonia (2.8% and 7%, respectively)
  - Median duration of exposure was 27.7 months for both CALQUENCE + obinutuzumab and CALQUENCE monotherapy
- Safety results at 74.5-month median follow-up were consistent with the interim analysis[1,4]

*Based on combined IQVIA, SHS, and Ontada datasets through December 2025.[5] †At 28.3-month median follow-up (range: 0.0 to 40.8 months).[1] ‡HR based on stratified Cox proportional-hazards model.[1] §Based on a stratified log-rank test, with an alpha level of 0.012 derived from alpha spending function by the O'Brien-Fleming method.[1] ‖Reduced risk of disease progression or death. ¶At 74.5-month median follow-up (range: 0.0-89.0 months).[4] #HR at 74.5-month median follow-up (range 0.0-89.0 months)=0.24 (95% CI: 0.17-0.32). HR based on stratified Cox proportional-hazards model.[3] **HR at 74.5-month median follow-up (range 0.0-89.0 months)=0.23 (95% CI: 0.10-0.52). HR based on stratified Cox proportional-hazards model.[3]

1L=first-line; ARs=adverse reactions; BTKi=Bruton tyrosine kinase inhibitor; CI=confidence interval; CLL=chronic lymphocytic leukemia; del(11q)=deletion in the 11q chromosome; del(17p)=deletion in the 17p chromosome; GClb=obinutuzumab and chlorambucil; HR=hazard ratio; IRC=Independent Review Committee; PFS=progression-free survival; *TP53*m=tumor protein p53 mutation; u*IGHV*=unmutated immunoglobulin heavy-chain variable region gene.

INDICATION AND USAGE

CALQUENCE is a Bruton tyrosine kinase (BTK) inhibitor indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

IMPORTANT SAFETY INFORMATION ABOUT CALQUENCE® (acalabrutinib) tablets

Serious and Opportunistic Infections

Fatal and serious infections, including opportunistic infections, have occurred in patients with hematologic malignancies treated with CALQUENCE.

Serious or Grade 3 or higher infections (bacterial, viral, or fungal) occurred in 29% of 2,055 patients exposed to CALQUENCE in clinical trials, most often due to respiratory tract infections (18% of all patients, including pneumonia in 14%). These infections predominantly occurred in the absence of Grade 3 or 4 neutropenia, with neutropenic infection reported in 8% of all patients. Opportunistic infections in recipients of CALQUENCE have included, but are not limited to, hepatitis B virus reactivation, fungal pneumonia, *Pneumocystis jirovecii* pneumonia, Epstein-Barr virus reactivation, cytomegalovirus, and progressive multifocal leukoencephalopathy (PML). Consider prophylaxis in patients who are at increased risk for opportunistic infections. Monitor patients for signs and symptoms of infection and treat promptly.

Please see Important Safety Information throughout, and full Prescribing Information, including Patient Information.

CALQUENCE®
acalabrutinib 100 mg tablets

About ELEVATE-TN[1,2,4]

ELEVATE-TN was a Phase 3, randomized, multicenter, open-label study in 535 patients with previously untreated CLL. Patients were randomized 1:1:1 to receive either CALQUENCE + obinutuzumab (n=179), CALQUENCE monotherapy (n=179), or GClb (maximum 6 cycles) (n=177). Patients received CALQUENCE 100 mg BID* until disease progression or unacceptable toxicity. Primary endpoint was IRC-assessed PFS (CALQUENCE + obinutuzumab vs GClb) at interim analysis (28.3-month median follow-up†). Select secondary endpoints at interim analysis were IRC-assessed PFS (CALQUENCE monotherapy vs GClb), IRC-assessed ORR, OS, and safety. After the interim analysis of 28.3 months, PFS and ORR were INV-assessed only.

*Approximately every 12 hours.[1] †At 28.3-month median follow-up (range: 0.0-40.8 months).[1]
BID=twice daily; INV=investigator; ORR=overall response rate; OS=overall survival.

IMPORTANT SAFETY INFORMATION ABOUT CALQUENCE® (acalabrutinib) tablets (cont'd)

Hemorrhage

Fatal and serious hemorrhagic events have occurred in patients treated with CALQUENCE. Major hemorrhage (serious or Grade 3 or higher bleeding or any central nervous system bleeding) occurred in 4.7% of patients, with fatal hemorrhage occurring in 0.1% of 2,055 patients exposed to CALQUENCE in clinical trials. Bleeding events of any grade, excluding bruising and petechiae, occurred in 39% of patients.

Use of antithrombotic agents concomitantly with CALQUENCE may further increase the risk of hemorrhage. In clinical trials, major hemorrhage occurred in 5% of patients taking CALQUENCE without antithrombotic agents and 3.2% of patients taking CALQUENCE with antithrombotic agents. Consider the risks and benefits of antithrombotic agents when co-administered with CALQUENCE. Monitor patients 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.

Cytopenias

CALQUENCE can cause Grade 3 or 4 cytopenias. Grade 3 or 4 cytopenias included absolute neutrophil count decreased (28%), absolute lymphocyte count decreased (10%), hemoglobin decreased (9%), and platelets decreased (9%) in 1,758 patients treated with CALQUENCE alone and in combination with obinutuzumab or venetoclax; Grade 4 neutropenia developed in 14% of patients.

Monitor complete blood counts regularly during treatment. Interrupt treatment, reduce the dose, or discontinue treatment as warranted.

Second Primary Malignancies

Second primary malignancies, including skin cancers and other solid tumors, occurred in 16% of 2,055 patients exposed to CALQUENCE in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer, reported in 9% of patients, followed by other solid tumors in 8% (including melanoma, lung cancer, gastrointestinal cancers, and genitourinary cancers) and hematologic malignancies (1.1%). Fatal second primary malignancies occurred in 0.8% of patients. Monitor patients for the development of second cancers and advise protection from sun exposure.

Cardiac Arrhythmias

Fatal and serious cardiac arrhythmias have occurred in patients treated with CALQUENCE. Grade 3 or 4 atrial fibrillation or flutter was reported in 2.2% of 2,055 patients treated with CALQUENCE, with all grades of atrial fibrillation or flutter reported in 7% of all patients. Grade 3 or higher ventricular arrhythmia events were reported in 0.5% of patients, including fatal cases in 0.3% of all patients. The risk of arrhythmias may be increased in patients with cardiac risk factors, hypertension, previous arrhythmias, and acute infection. Monitor for symptoms of arrhythmia (eg, palpitations, dizziness, syncope, dyspnea) and manage as appropriate.

Hepatotoxicity, Including Drug-Induced Liver Injury

Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of drug-induced liver injury (DILI), has occurred in patients treated with Bruton tyrosine kinase inhibitors, including CALQUENCE.

Evaluate bilirubin and transaminases at baseline and throughout treatment with CALQUENCE. For patients who develop abnormal liver tests after CALQUENCE, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity. If DILI is suspected, withhold CALQUENCE. Upon confirmation of DILI, discontinue CALQUENCE.

ADVERSE REACTIONS

Chronic Lymphocytic Leukemia

The most common adverse reactions (≥30%) of any grade in patients with CLL in the ELEVATE-TN and ASCEND studies exposed to CALQUENCE (n=511) were anemia,* neutropenia,* thrombocytopenia,* headache, upper respiratory tract infection, and diarrhea.

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

In patients with previously untreated CLL in the ELEVATE-TN study exposed to CALQUENCE (n=357), fatal adverse reactions that occurred in the absence of disease progression and with onset within 30 days of the last study treatment were reported in 2% for each treatment arm, most often from infection. Serious adverse reactions were reported in 39% (69/178) of patients in the CALQUENCE plus obinutuzumab arm (n=178) and 32% (57/179) in the CALQUENCE monotherapy arm (n=179), most often due to events of pneumonia (2.8% to 7%).

Adverse reactions led to CALQUENCE dose reduction in 7% and 4% of patients in the CALQUENCE plus obinutuzumab arm and CALQUENCE monotherapy arm, respectively. Adverse reactions led to discontinuation in 11% and 10% of patients, respectively. Increases in creatinine to 1.5 to 3 times ULN occurred in 3.9% and 2.8% of patients in the CALQUENCE combination arm and monotherapy arm, respectively.

In patients with relapsed/refractory CLL in the ASCEND study exposed to CALQUENCE (n=154), serious adverse reactions occurred in 29% of patients. Serious adverse reactions in >5% of patients who received CALQUENCE included lower respiratory tract infection (6%). Fatal adverse reactions within 30 days of the last dose of CALQUENCE occurred in 2.6% of patients, including from second primary malignancies and infection.

Adverse reactions led to CALQUENCE dose reduction in 3.9% of patients, dose interruptions in 34% of patients, most often due to respiratory tract infections followed by neutropenia, and discontinuation in 10% of patients, most frequently due to second primary malignancies followed by infection. Increases in creatinine to 1.5 to 3 times ULN occurred in 1.3% of patients who received CALQUENCE.

DRUG INTERACTIONS

Strong CYP3A Inhibitors: Avoid co-administration of CALQUENCE with a strong CYP3A inhibitor. If these inhibitors will be used short-term, interrupt CALQUENCE. After discontinuation of strong CYP3A inhibitor for at least 24 hours, resume previous dosage of CALQUENCE.

Moderate CYP3A Inhibitors: Reduce the dosage of CALQUENCE to 100 mg once daily when co-administered with a moderate CYP3A inhibitor.

Strong CYP3A Inducers: Avoid co-administration of CALQUENCE with a strong CYP3A inducer. If co-administration is unavoidable, increase the dosage of CALQUENCE to 200 mg approximately every 12 hours.

SPECIFIC POPULATIONS

Based on findings in animals, CALQUENCE may cause fetal harm and dystocia when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. Advise pregnant women of the potential risk to a fetus.

Pregnancy testing is recommended for females of reproductive potential prior to initiating CALQUENCE therapy. Advise female patients of reproductive potential to use effective contraception during treatment with CALQUENCE and for 1 week following the last dose of CALQUENCE.

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

Avoid use of CALQUENCE in patients with severe hepatic impairment (Child-Pugh class C). No dosage adjustment of CALQUENCE is recommended in patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment.

Please see Important Safety Information throughout, and full Prescribing Information, including Patient Information.

You may report side effects related to AstraZeneca products.

References: 1. CALQUENCE® (acalabrutinib) tablets [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2026. **2.** Sharman JP, Egyed M, Jurczak W, et al. Acalabrutinib with or without obinutuzumab versus chlorambucil and obinutuzumab for treatment-naive chronic lymphocytic leukaemia (ELEVATE-TN): a randomised, controlled, phase 3 trial [published correction appears in *Lancet*. 2020;395(10238):1694]. *Lancet*. 2020;395(10232):1278-1291 and supplementary appendix. **3.** Data on File. REF-289865. AstraZeneca Pharmaceuticals LP. **4.** Sharman JP, Egyed M, Jurczak W, et al. Acalabrutinib-obinutuzumab improves survival vs chemoimmunotherapy in treatment-naive CLL in the 6-year follow-up of ELEVATE-TN [article and supplementary appendix published online April 8, 2025]. *Blood*. 2025. **5.** Data on File. US-109123. AstraZeneca Pharmaceuticals LP.

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