CLL

#1 prescribed BTKi for patients starting CLL treatment*[8]

START STRONG

NOW APPROVED
Fixed-duration† CALQUENCE + venetoclax[1]

Primary endpoint: IRC-assessed PFS with CALQUENCE + venetoclax vs FCR/BR
HR‡=0.65; 95% CI: 0.49-0.87; *P*§=0.0038‖[1,2]

AMPLIFY: ~3.5-YEAR FOLLOW-UP

CALQUENCE + venetoclax: The first and only all-oral fixed-duration regimen in 1L CLL†[1]

3-Year Estimated PFS¶[1,2]

77%

(95% CI: 71-81)

Low Rates of Select Cardiovascular AEs¶[2]

n=291

ATRIAL FIBRILLATION OR FLUTTER	HYPERTENSION	MAJOR HEMORRHAGE
Any Grade	Any Grade	Any Grade
0.7%	4.1%	1%
(Grade ≥3: 0.3%)	(Grade ≥3: 2.7%)	(Grade ≥3: 1%)

The estimated rate at 3 years was descriptive only and not formally tested.[1,2]

In a pooled analysis of 2055 patients exposed to CALQUENCE, Grade ≥3 infections occurred in 29%, with neutropenic infection in 8%; major hemorrhage occurred in 4.7%, with fatal hemorrhage in 0.1%; fatal second primary malignancies occurred in 0.8%; Grade 3/4 atrial fibrillation or flutter in 2.2% and Grade ≥3 ventricular arrhythmia in 0.5%, including fatal cases in 0.3%. Among 1758 patients, Grade 3/4 cytopenias included absolute neutrophil count decreased (28%), absolute lymphocyte count decreased (10%), hemoglobin decreased (9%), and platelets decreased (9%), with Grade 4 neutropenia in 14%.[1]

National Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

NCCN CATEGORY 1 PREFERRED

Acalabrutinib (CALQUENCE) is the only BTKi recommended by the National Comprehensive Cancer Network® (NCCN®) as a **Category 1 Preferred option** for **fixed-duration† use** in **1L CLL patients** without del(17p) and/or *TP53*m[3]

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
Category 1=Based upon high-level evidence (≥1 randomized Phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate. Preferred intervention=Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.

*Based on combined IQVIA, SHS, and Ontada datasets through December 2025.[8] †Designed to be completed in fourteen 28-day cycles (2 cycles of CALQUENCE monotherapy followed by 12 cycles of CALQUENCE + venetoclax, starting venetoclax using a 5-week ramp-up as per dose schedule), unless disease progression or unacceptable toxicity warrants earlier discontinuation.[1] ‡Based on a stratified Cox proportional-hazards model.[1,2] §Based on a stratified log-rank test, with an alpha level of 0.0469 derived from an alpha spending function by the O'Brien-Fleming method.[1] ‖At 42.6-month median follow-up.[1] ¶At 40.8-month median follow-up (range: 0.0-59.0 months).[2]

1L=first-line; AEs=adverse events; BR=bendamustine + rituximab; BTKi=Bruton tyrosine kinase inhibitor; CI=confidence interval; CLL=chronic lymphocytic leukemia; del(17p)=deletion in the 17p chromosome; FCR=fludarabine + cyclophosphamide + rituximab; HR=hazard ratio; IRC=Independent Review Committee; PFS=progression-free survival; *TP53*m=tumor protein p53 mutation.

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.

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

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

CALQUENCE®
acalabrutinib 100 mg tablets

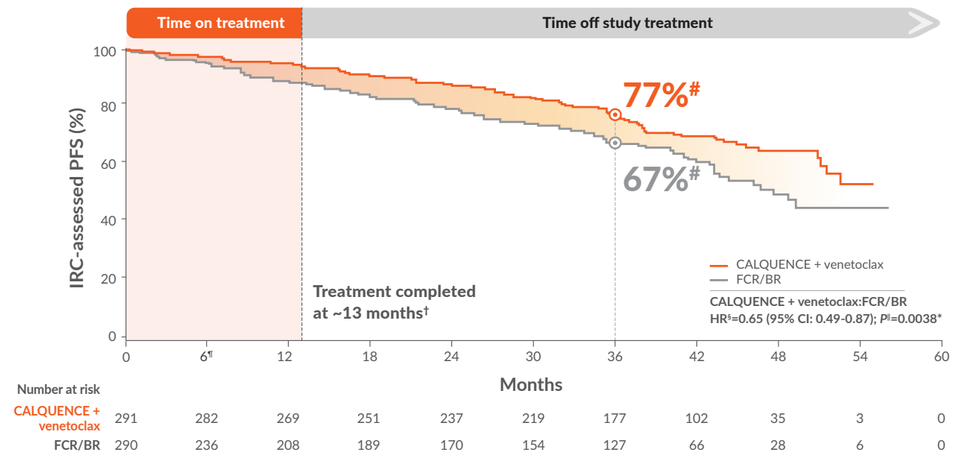
AMPLIFY: ~3.5-YEAR FOLLOW-UP

Durable PFS without long-term treatment*†[1,2]

35% PFS risk reduction‡ with CALQUENCE + venetoclax vs FCR/BR

HR§=0.65 (95% CI: 0.49-0.87); P‖=0.0038*

IRC-assessed PFS (primary endpoint)[1,2]



Number at risk											
CALQUENCE + venetoclax	291	282	269	251	237	219	177	102	35	3	0
FCR/BR	290	236	208	189	170	154	127	66	28	6	0

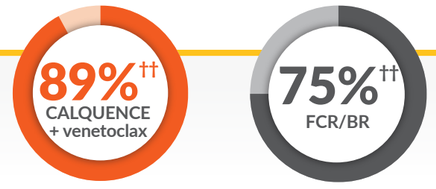
The estimated PFS rates at 36 months were descriptive only and not formally tested.

At 3 years, ~89% of patients who received CALQUENCE + venetoclax did not require subsequent treatment**[4]

TTNT (secondary endpoint)**[2]

- TTNT was defined as the time from randomization to institution of non–protocol-specified treatment for CLL or death[2]

The analysis, including the estimated TTNT rate at 3 years, was descriptive only and not formally tested.



IRC-assessed ORR (secondary endpoint)*[1,2]

- IRC-assessed ORR (PR‡‡/CR§§) in patients receiving CALQUENCE + venetoclax or FCR/BR was 93% (84%/9%) and 75% (69%/5%), respectively‖‖

The analysis was descriptive only and not formally tested.

Study design: AMPLIFY is an open-label, randomized, multicenter Phase 3 trial evaluating CALQUENCE + venetoclax vs FCR/BR in adult patients with previously untreated CLL (N=867). Patients were randomized 1:1:1 to receive CALQUENCE¶¶ (maximum 14 cycles##) + venetoclax*** (maximum 12 cycles##) (n=291), FCR/BR††† (maximum 6 cycles§§) (n=290), or an investigational combination regimen (CALQUENCE + venetoclax + obinutuzumab) not approved for use by the FDA (n=286).‡‡‡[1] The primary endpoint was IRC-assessed PFS (CALQUENCE + venetoclax vs FCR/BR). Select secondary endpoints included OS, ORR, and TTNT.[1,2]

*At 42.6-month median follow-up.[1] †Designed to be completed in fourteen 28-day cycles.[1] ‡Reduced risk of disease progression or death.[1] §Based on a stratified Cox proportional-hazards model.[1] ‖Based on a stratified log-rank test, with an alpha level of 0.0469 derived from an alpha spending function by the O'Brien-Fleming method.[1] ¶Treatment with FCR/BR was completed after ~6 months.[1] #Estimated PFS rate at 3 years.[1,2] **At 40.8-month median follow-up (range: 0.0-59.0 months).[2] ††Estimated TTNT rate at 3 years.[4] ‡‡Includes PR and nPR.[2] §§Includes CR and CRi.[2] ‖‖ORR is defined as patients who achieve CR, CRi, nPR, or PR per IRC and investigator assessment.[1,2] ¶¶CALQUENCE 100 mg PO BID was initiated on Cycle 1 Day 1 for a total of 14 cycles or until disease progression or unacceptable toxicity.[1] ##1 cycle=28 days (4 weeks or ~1 month).[1] ***Venetoclax was initiated on Cycle 3 Day 1, with a 5-week dose ramp-up starting at 20 mg and increasing weekly to 50 mg, 100 mg, 200 mg, and finally 400 mg QD. Venetoclax was administered for a total of 12 cycles.[1] †††Investigator's choice of FCR or BR.[1] ‡‡‡Please see Section 5.1 of the US Prescribing Information.[3]
BID=twice daily; CR=complete response; CRi=complete response with incomplete blood count recovery; FDA=Food and Drug Administration; ORR=overall response rate; OS=overall survival; nPR=nodular partial response; PO=by mouth; PR=partial response; QD=once daily; TTNT=time to next treatment; uMRD=undetectable measurable residual disease.

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

Cytopenias (cont'd)

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.

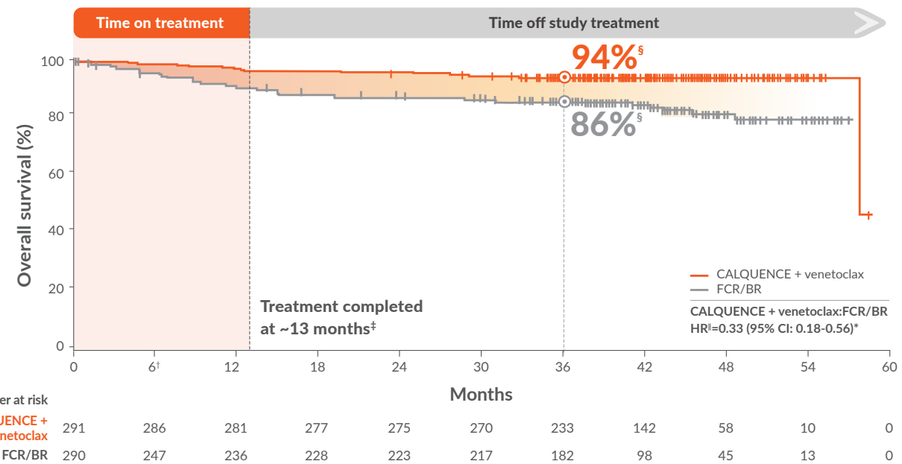
Hepatotoxicity, Including Drug-Induced Liver Injury

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.

AMPLIFY: ~3.5-YEAR FOLLOW-UP

~94% OS rate with CALQUENCE + venetoclax at 3 years*[2]

OS (secondary endpoint)[2]



Number at risk											
CALQUENCE + venetoclax	291	286	281	277	275	270	233	142	58	10	0
FCR/BR	290	247	236	228	223	217	182	98	45	13	0

OS data were immature at the time of primary analysis; hence, the HR is not stable and subject to change as more events occur.

The estimated OS rates at 36 months were descriptive only and not formally tested.

At 41-month median follow-up, a total of 60 death events were reported: 18 (6%) in the CALQUENCE + venetoclax arm and 42 (14%) in the FCR/BR arm.[1]

ARs with CALQUENCE + venetoclax were mostly Grade 1 or 2¶[1,2]

- **The most common ARs** (≥15%, Any Grade/Grade ≥3) with CALQUENCE + venetoclax (n=291) were headache (35%/1.4%), diarrhea (33%/1.7%), musculoskeletal pain# (25%/0.7%), COVID-19 (21%/6%), fatigue** (18%/0.3%), bruising†† (17%/0%), rash‡‡ (16%/1%), and nausea (15%/0%)[1]
- **Select events of clinical interest** (Any Grade/Grade ≥3) with CALQUENCE + venetoclax included cardiac events (any) (9%/1.7%), atrial fibrillation or flutter (0.7%/0.3%), hypertension (4.1%/2.7%), hemorrhage (32%/1.0%), major hemorrhage (1.0%/1.0%), infection (51%/12%), SPM (5%/1.7%), and TLS§§ (0.3%/0.3%), with 0 cases of clinical TLS[2,5]
- **Serious adverse reactions** occurred in 25% of patients receiving CALQUENCE + venetoclax. The most common serious adverse reactions (≥2%) were COVID-19 including COVID-19 pneumonia (9%), second primary malignancies (2.7%), and neutropenia (2.1%). **Fatal adverse events** occurred in 3.4% of patients. The most common fatal adverse events included COVID-19 and COVID-19 pneumonia[1]
- **Laboratory abnormalities** (≥20%, Any Grade) in patients with previously untreated CLL who received CALQUENCE + venetoclax (n=291) included neutrophils decreased (78%), glucose increased (74%), lymphocytes decreased (56%), platelets decreased (43%), hemoglobin decreased (35%), calcium decreased (30%), ALT increased (26%), urate increased (25%), LDH increased (24%), AST increased (22%), potassium increased (22%), ALP increased (20%), and glucose decreased (20%)[1]
- **Neutropenia rates** (Any Grade/Grade ≥3) with CALQUENCE + venetoclax were 31%/27%, and febrile neutropenia rates were 1.7%/1.7%[2]
- **The median duration of exposure** was 12.9 months (range: 1 to 18 months) with CALQUENCE, 11.1 months (range: 2 to 14 months) with venetoclax, and 5.6 months (range: 1-11 months) in the FCR/BR group[1,2]

Low discontinuation rate due to ARs¶[1,2]

n=23/291 n=28/259

Values >5 are rounded to the nearest whole number.

*At 40.8-month median follow-up.[2] †Treatment with FCR/BR was completed after ~6 months.[1] ‡Designed to be completed in fourteen 28-day cycles.[1] §Estimated OS rate at 3 years.[2] ‖Based on a stratified Cox proportional-hazards model.[2] ¶At 42.6-month median follow-up.[1] #Includes back pain, bone pain, musculoskeletal chest pain, musculoskeletal pain, musculoskeletal discomfort, myalgia, neck pain, pain in extremity, spinal pain, non-cardiac chest pain, and pain in the jaw.[1] **Includes fatigue and asthenia.[1] ††Includes increased tendency to bruise, contusion, and ecchymosis.[1] ‡‡Includes rash and dermatitis.[1] §§TLS observed with CALQUENCE + venetoclax (n=1, during venetoclax ramp-up) was limited to laboratory TLS only; no clinical TLS was observed.[2,5]
ALP=alkaline phosphatase; ALT=alanine transferase; AST=aspartate transferase; COVID-19=coronavirus disease 2019; LDH=lactate dehydrogenase; SPM=second primary malignancy; TLS=tumor lysis syndrome.

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

CALQUENCE®
acalabrutinib 100 mg tablets

With CALQUENCE + venetoclax all-oral fixed-duration* therapy, give your 1L CLL patients the chance for[1]:

- Treatment-free period without daily reminders of disease or treatment[6]
- No ongoing treatment exposure[6]
- No ongoing out-of-pocket costs, potentially limiting financial impact†[6]

With all-oral CALQUENCE + venetoclax

- No infusion-related reactions[1]
- No travel or time required for infusion[7]

See how you can offer your eligible patients with 1L CLL a chance to start strong at CALQUENCEhcp.com

*Designed to be completed in fourteen 28-day cycles (2 cycles of CALQUENCE monotherapy followed by 12 cycles of CALQUENCE + venetoclax, starting venetoclax using a 5-week ramp-up as per dose schedule), unless disease progression or unacceptable toxicity warrants earlier discontinuation.[1] †After completing CALQUENCE + venetoclax treatment per the recommended dosing.[1]
AV=CALQUENCE plus venetoclax.

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

Hepatotoxicity, Including Drug-Induced Liver Injury (cont'd)
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

In patients with previously untreated CLL in the AMPLIFY study who received CALQUENCE plus venetoclax (AV) (n=291), the most common adverse reactions (≥15%) of any grade were headache (35%), diarrhea (33%), musculoskeletal pain (25%), COVID-19 (21%), fatigue (18%), bruising (17%), rash (16%), and nausea (15%).

The most common laboratory abnormalities (≥15%) of any grade in patients with previously untreated CLL who received AV were neutrophils decreased (78%), glucose increased (74%), lymphocytes decreased (56%), platelets decreased (43%), hemoglobin decreased (35%), calcium decreased (30%), ALT increased (26%), urate increased (25%), LDH increased (24%), potassium increased (22%), AST increased (22%), ALP increased (20%), glucose decreased (20%), creatinine increased (19%), and sodium increased (15%). Grade 4 laboratory abnormalities in >15% of patients treated with AV include absolute neutrophil count decreased (15%).

Serious adverse reactions occurred in 25% of patients receiving AV. The most common serious adverse reactions (≥2%) were COVID-19 including COVID-19 pneumonia (9%), second primary malignancies (2.7%), and neutropenia (2.1%). Fatal adverse events occurred in 3.4% of patients. The most common fatal adverse events included COVID-19 and COVID-19 pneumonia.

Treatment discontinuation of CALQUENCE due to adverse reactions occurred in 8% of patients receiving AV. The most common adverse reaction (≥2%) leading to treatment discontinuation was COVID-19 pneumonia (2.1%). Dose reduction of CALQUENCE occurred in 6% of patients. Neutropenia was the only adverse reaction leading to dose reduction that occurred in ≥1% of patients.

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.

Of patients that received AV in AMPLIFY, 33% (97/291) were ≥65 years, and 4.5% (13/291) were ≥75 years of age. In patients ≥65 years and <65 years of age, the fatal adverse reactions were 5% and 2.6%, respectively.

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.** Brown JR, Seymour JF, Jurczak W, et al. Fixed-duration acalabrutinib combinations in untreated chronic lymphocytic leukemia and supplementary materials [appendix and protocol]. *N Engl J Med*. 2025;392(8):748-762. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma V.2.2026. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed January 5, 2026. To view the most recent and complete version of the guideline, go online to NCCN.org **4.** Ghia P, Eichhorst B, Wrobel T, et al. Impact of prognostic mutations on outcomes with fixed-duration acalabrutinib-venetoclax combinations versus chemoimmunotherapy: an exploratory analysis from AMPLIFY. Abstract abs25-8313. Presented at: American Society of Hematology (ASH) Annual Meeting; December 6-9, 2025; Orlando, FL. **5.** Seymour J, Aw A, Ribrag V, et al. Safety analysis of fixed-duration acalabrutinib-venetoclax combinations vs chemoimmunotherapy: a post hoc analysis from the phase 3 AMPLIFY trial. Poster 1424. Presented at: XXI International Workshop on CLL (iwCLL); September 12-15, 2025; Krakow, Poland. **6.** Davids MS, Ryan CE, Lampson BL, et al. Phase II study of acalabrutinib, venetoclax, and obinutuzumab in a treatment-naïve chronic lymphocytic leukemia population enriched for high-risk disease. *J Clin Oncol*. 2025;43(7):788-799. **7.** CLL Society. Targeted oral treatment options. Accessed October 6, 2025. https://cllsociety.org/resource-library/Targeted-Oral-Treatment-Options-CLLS-Resource-Library.pdf **8.** Data on File. US-109123. AstraZeneca Pharmaceuticals LP.

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