Now with up to 53 months of long-term data[1]

CALQUENCE CONFIDENCE

In previously untreated CLL

90% RISK REDUCTION IN DISEASE PROGRESSION OR DEATH[2]

CALQUENCE + obinutuzumab vs obinutuzumab + chlorambucil*
HR=0.10 (95% CI: 0.06-0.17), *P*<0.0001

*Median progression-free survival (PFS) was not reached with CALQUENCE + obinutuzumab vs 22.6 months (95% CI: 20-28) with obinutuzumab + chlorambucil.[2]
CI=confidence interval; CLL=chronic lymphocytic leukemia; HR=hazard ratio.

CALQUENCE®
(acalabrutinib) 100 mg capsules

INDICATION AND USAGE

CALQUENCE is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

IMPORTANT SAFETY INFORMATION ABOUT CALQUENCE® (acalabrutinib) capsules

Serious and Opportunistic Infections

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

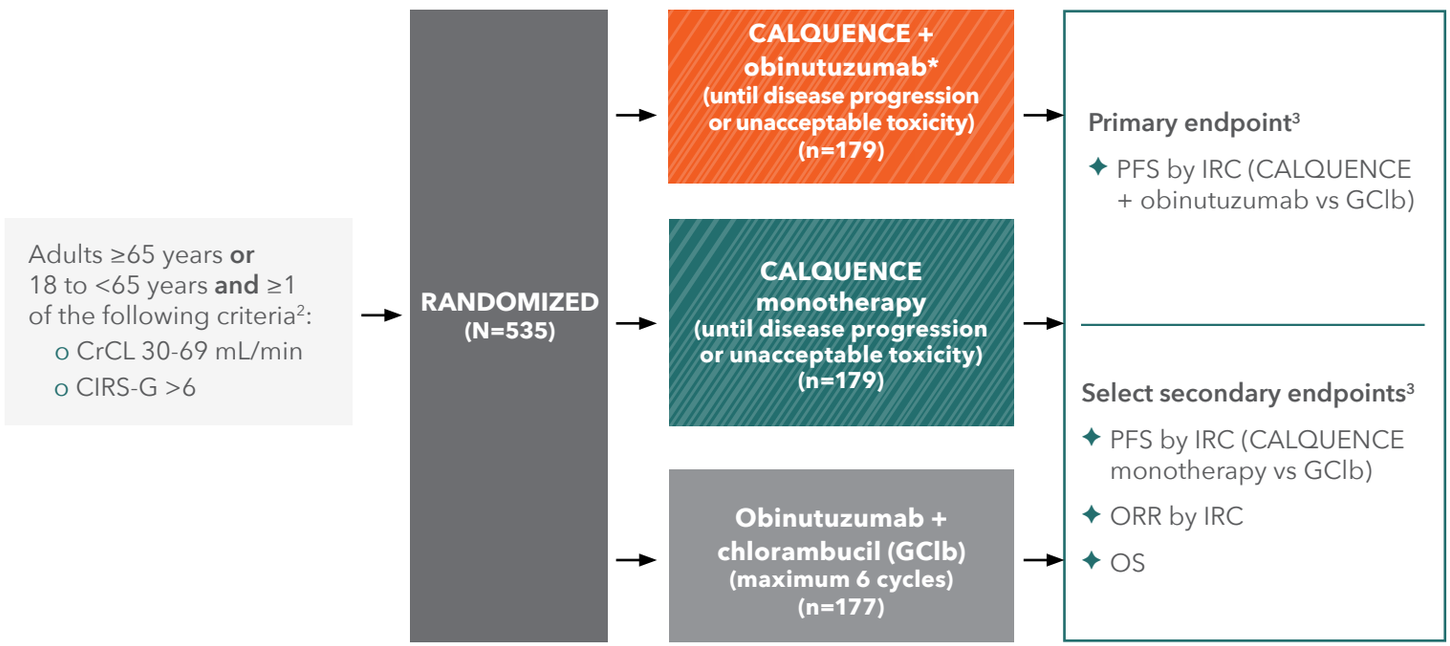
Serious or Grade 3 or higher infections (bacterial, viral, or fungal) occurred in 19% of 1029 patients exposed to CALQUENCE in clinical trials, most often due to respiratory tract infections (11% of all patients, including pneumonia in 6%). These infections predominantly occurred in the absence of Grade 3 or 4 neutropenia, with neutropenic infection reported in 1.9% of all patients. Opportunistic infections in recipients of CALQUENCE have included, but are not limited to, hepatitis B virus reactivation, fungal pneumonia, *Pneumocystis jiroveci* 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 on pages 16-17, and full Prescribing Information, including Patient Information.

TABLE OF CONTENTS

CALQUENCE®
(acalabrutinib) 100 mg capsules

ELEVATE-TN: a Phase 3, open-label, randomized, multicenter trial in patients with previously untreated CLL[2,3]



- **Patients who received antithrombotic agents other than warfarin or equivalent agents were allowed[2]**
- **Patients with controlled, asymptomatic arrhythmias were allowed[3]**

Patients received CALQUENCE 100 mg approximately every 12 hours until disease progression or unacceptable toxicity for either CALQUENCE + obinutuzumab or CALQUENCE monotherapy.[2]

*For CALQUENCE + obinutuzumab, obinutuzumab was given 28 days after the first dose of CALQUENCE (Cycle 2, Day 1), and was given for up to 6 cycles.[2] Refer to the obinutuzumab Prescribing Information for recommended obinutuzumab dosing information.

CIRS-G=Cumulative Illness Rating Scale-Geriatric; CrCL=creatinine clearance; IRC=Independent Review Committee; ORR=overall response rate; OS=overall survival.

IMPORTANT SAFETY INFORMATION (Cont'd)

Hemorrhage

Fatal and serious hemorrhagic events have occurred in patients with hematologic malignancies treated with CALQUENCE. Major hemorrhage (serious or Grade 3 or higher bleeding or any central nervous system bleeding) occurred in 3.0% of patients, with fatal hemorrhage occurring in 0.1% of 1029 patients exposed to CALQUENCE in clinical trials. Bleeding events of any grade, excluding bruising and petechiae, occurred in 22% of patients.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

Patient characteristics were generally well balanced across all 3 arms of the clinical trial

SELECT DEMOGRAPHICS AND BASELINE CHARACTERISTICS IN ELEVATE-TN[3,4]

Characteristic	CALQUENCE + obinutuzumab (n=179)	CALQUENCE monotherapy (n=179)	GClb (n=177)
Age, years; median (range)	70 (41-88)	70 (44-87)	71 (46-91)
Male; %	62	62	60
ECOG performance status; %			
0-1	94	92	94
2	6	8	6
Rai stage III or IV; %	48	49	44
CYTOGENETICS/FISH CATEGORY; %			
17p deletion	10	9	9
11q deletion	17	17	19
TP53 mutation	12	11	12
Unmutated IGHV	58	67	66

ECOG=Eastern Cooperative Oncology Group; FISH=fluorescence in situ hybridization.

IMPORTANT SAFETY INFORMATION (Cont'd)

Hemorrhage (Cont'd)

Use of antithrombotic agents concomitantly ith CALQUENCE may further increase the risk of hemorrhage. In clinical trials, major hemorrhage occurred in 2.7% of patients taking CALQUENCE without antithrombotic agents and 3.6% 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 3-7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

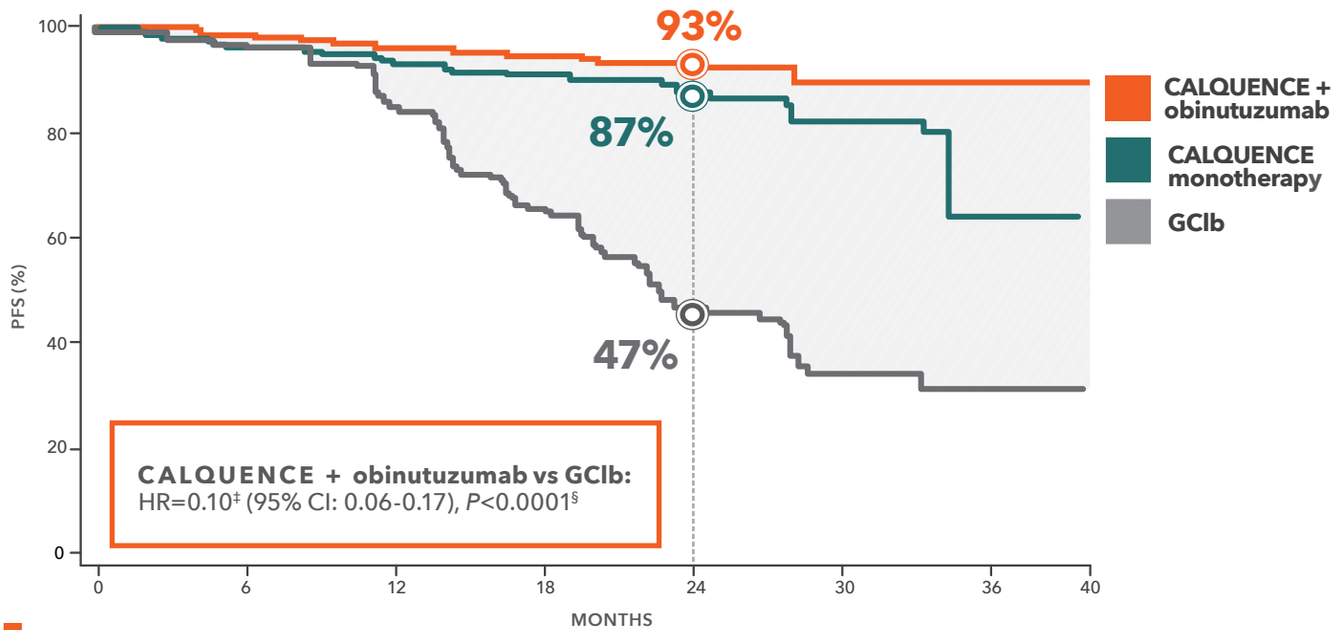
Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

Unprecedented PFS: 90% risk reduction in disease progression or death with CALQUENCE + obinutuzumab vs GClb

At median 28.3-month follow-up (range: 0.0 to 40.8 months), median PFS was not reached with CALQUENCE + obinutuzumab vs 22.6 months (95% CI: 20-28) with GClb*[2]

IRC-ASSESSED PROGRESSION-FREE SURVIVAL[†2,3]



93% estimated PFS at 24 months for CALQUENCE + obinutuzumab‖[3]

CALQUENCE monotherapy: strong results with a single agent[2]

- 80% relative risk reduction in disease progression or death vs GClb (HR=0.20‡ [95% CI: 0.13-0.30], *P*<0.0001§)
- Median PFS was not reached (95% CI: 34-NE) vs 22.6 months (95% CI: 20-28) with GClb

*Per 2008 International Workshop on CLL (IWCLL) criteria.[2] †At the time of analysis, the number of events in each arm was 14 (8%) for CALQUENCE + obinutuzumab, 26 (15%) for CALQUENCE monotherapy, and 93 (53%) for GClb.[2] ‡Based on a stratified Cox proportional-hazards model. Both hazard ratios are compared with the GClb arm.[2] §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.[2] ‖Estimated 24-month PFS: CALQUENCE + obinutuzumab, 93% (95% CI: 87-96); CALQUENCE monotherapy, 87% (95% CI: 81-92); GClb, 47% (95% CI: 39-55).[3]
NE=not estimable.

IMPORTANT SAFETY INFORMATION (Cont'd)

Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (23%), anemia (8%), thrombocytopenia (7%), and lymphopenia (7%), developed in patients with hematologic malignancies treated with CALQUENCE. Grade 4 neutropenia developed in 12% of patients. Monitor complete blood counts regularly during treatment. Interrupt treatment, reduce the dose, or discontinue treatment as warranted.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE®
(acalabrutinib) 100 mg capsules

Safety and tolerability consistent with the established profile of CALQUENCE

*COMMON ADVERSE REACTIONS (≥15%, ANY GRADE) WITH CALQUENCE IN ELEVATE-TN**[2]

Adverse reaction	CALQUENCE + obinutuzumab (n=178)		CALQUENCE monotherapy (n=179)		GClb (n=169)	
	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)
Infection†	69	22‡	65	14‡	46	13‡
Upper respiratory tract infection†	39	2.8	35	0	17	1.2
Lower respiratory tract infection†	24	8	18	4.5	7	1.8
Urinary tract infection	15	1.7	15	2.8	5	0.6
Neutropenia†	53	37	23	13	78	50
Anemia†	52	12	53	10	54	14
Thrombocytopenia†	51	12	32	3.4	61	16
Lymphocytosis†	12	11	16	15	0.6	0.6
Headache	40	1.1	39	1.1	12	0
Dizziness	20	0	12	0	7	0
Diarrhea	39	4.5	35	0.6	21	1.8
Nausea	20	0	22	0	31	0
Musculoskeletal pain†	37	2.2	32	1.1	16	2.4
Arthralgia	22	1.1	16	0.6	4.7	1.2
Fatigue†	34	2.2	23	1.1	24	1.2
Bruising†	31	0	21	0	5	0
Rash†	26	2.2	25	0.6	9	0.6
Hemorrhage†	20	1.7	20	1.7	6	0

*The median duration of exposure to CALQUENCE in the CALQUENCE + obinutuzumab and CALQUENCE monotherapy arms was 27.7 months (range: 0.3 to 40 months).[2] †Includes multiple adverse drug reaction terms (see full Prescribing Information).[2] ‡Includes 3 fatal cases in the CALQUENCE + obinutuzumab arm, 3 fatal cases in the CALQUENCE monotherapy arm, and 1 fatal case in the GClb arm.[2]

ALT=alanine aminotransferase; AST=aspartate aminotransferase.

IMPORTANT SAFETY INFORMATION (Cont'd)

Second Primary Malignancies

Second primary malignancies, including skin cancers and other solid tumors, occurred in 12% of 1029 patients exposed to CALQUENCE in clinical trials. The most frequent second primary malignancy was skin cancer, reported in 6% of patients. Monitor patients for skin cancers and advise protection from sun exposure.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

Other clinically relevant adverse reactions (<15%, any grade) in recipients of CALQUENCE included[2]:

- Neoplasms: second primary malignancy (10%), including non-melanoma skin cancer (5%)
- Infection: herpesvirus infection (6%)
- Cardiac disorders: atrial fibrillation or flutter (3.6%), hypertension (5%)

SELECT NON-HEMATOLOGIC LABORATORY ABNORMALITIES (≥15%, ANY GRADE), NEW OR WORSENING FROM BASELINE WITH CALQUENCE IN ELEVATE-TN*[2]

	CALQUENCE + obinutuzumab (n=178)		CALQUENCE monotherapy (n=179)		GClb (n=169)	
Laboratory abnormality†	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)
Uric acid increase	29	29	22	22	37	37
ALT increase	30	7	20	1.1	36	6
AST increase	38	5	17	0.6	60	8
Bilirubin increase	13	0.6	15	0.6	11	0.6

Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 3.9% and 2.8% of patients in the CALQUENCE + obinutuzumab and CALQUENCE monotherapy arms, respectively.[2]

10% to 11% of patients taking CALQUENCE discontinued treatment due to adverse reactions at median 28.3-month follow-up[2]

*The median duration of exposure to CALQUENCE in the CALQUENCE + obinutuzumab and CALQUENCE monotherapy arms was 27.7 months (range: 0.3 to 40 months).[2] †Excludes electrolytes.[2]

ALT=alanine aminotransferase; AST=aspartate aminotransferase.

IMPORTANT SAFETY INFORMATION (Cont'd)

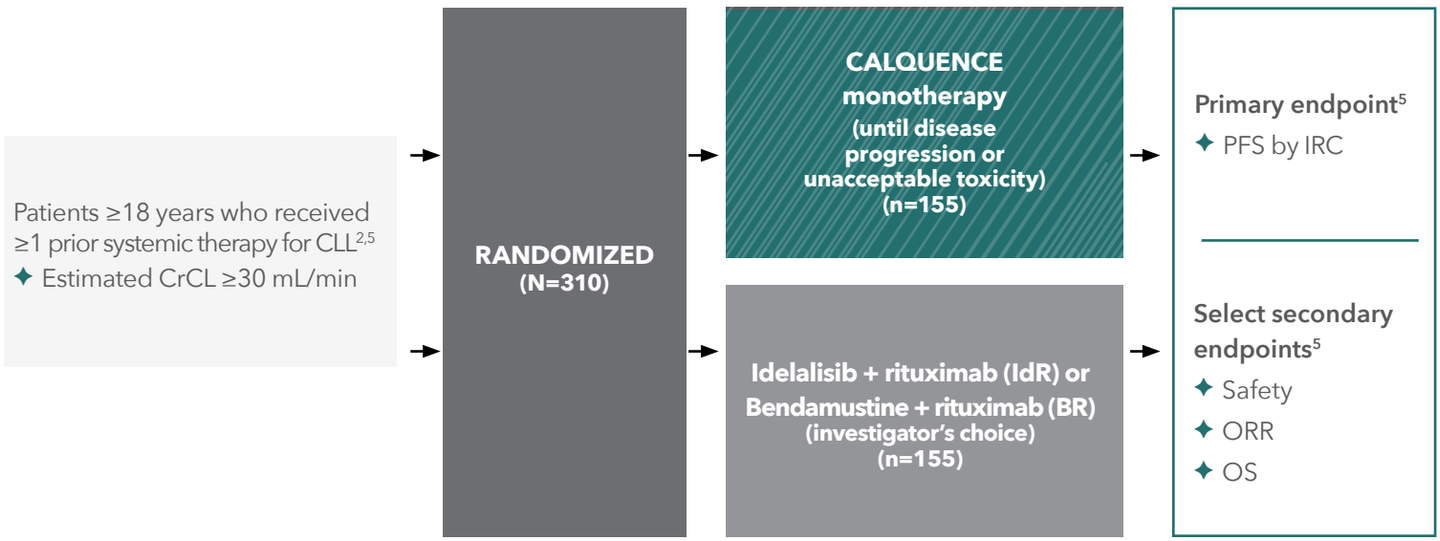
Atrial Fibrillation and Flutter

Grade 3 atrial fibrillation or flutter occurred in 1.1% of 1029 patients treated with CALQUENCE, with all grades of atrial fibrillation or flutter reported in 4.1% of all patients. The risk may be increased in patients with cardiac risk factors, hypertension, previous arrhythmias, and acute infection. Monitor for symptoms of arrhythmia (e.g., palpitations, dizziness, syncope, dyspnea) and manage as appropriate.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

ASCEND: a Phase 3, open-label, randomized, multicenter trial in patients with relapsed/refractory CLL[2,5]



- **Patients who received antithrombotic agents other than warfarin or equivalent agents were allowed[2]**
- **Patients with controlled, asymptomatic arrhythmias were allowed[5]**

Patients were randomized 1:1 to receive CALQUENCE 100 mg approximately every 12 hours until disease progression or unacceptable toxicity

OR

Investigator's choice of:

- Idelalisib 150 mg orally approximately every 12 hours until disease progression or unacceptable toxicity in combination with 8 infusions of rituximab (375 mg/m^2 intravenously on Day 1 of Cycle 1, followed by 500 mg/m^2 every 2 weeks for 4 doses and then every 4 weeks for 3 doses), with a 28-day cycle length, or
- Bendamustine 70 mg/m^2 intravenously (Days 1 and 2 of each 28-day cycle) in combination with rituximab (375 mg/m^2 intravenously on Day 1 of Cycle 1, then 500 mg/m^2 on Day 1 of subsequent cycles), for up to 6 cycles[2]

The interim analysis had a median follow-up of 16.1 months (range: 0.03 to 22.4 months).[2]
The final analysis had a median follow-up of 22.1 months (range: 0.5 to 29.1 months) in the CALQUENCE arm and 21.9 months (range: 0.0-27.7 months) in the IdR or BR arm.[5]

IMPORTANT SAFETY INFORMATION (Cont'd)

ADVERSE REACTIONS

The most common adverse reactions (≥ 30%) of any grade in patients with CLL 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 exposed to CALQUENCE, 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% of patients in the CALQUENCE plus obinutuzumab arm and 32% in the CALQUENCE monotherapy arm, most often due to events of pneumonia (7% and 2.8%, respectively).

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

Patient characteristics were generally well balanced across both arms of the clinical trial

SELECT DEMOGRAPHICS AND BASELINE CHARACTERISTICS IN ASCEND[5,7,8]

Characteristic	CALQUENCE (n=155)	IdR or BR (n=155)
Age, years; median (range)	68 (32-89)	67 (34-90)
Male; %	70	65
ECOG performance status; %		
0-1	88	86
2	12	14
Rai stage III or IV; %	42	41
Median number of prior CLL therapies (range)	1 (1-8)	2 (1-10)
Number of prior CLL therapies; %		
1	53	43
2	26	30
3	11	15
≥4	10	12
PREVIOUS THERAPY		
Purine analogues (eg, fludarabine, cladribine)	70%	67%
Alkylators other than bendamustine (eg, chlorambucil)	86%	85%
Bendamustine	30%	31%
Anti-CD20 monoclonal antibodies	84%	77%
Stem cell transplant	1%	1%
Other*	6%	4%
CYTOGENETICS/FISH CATEGORY; %		
17p deletion	18	14
11q deletion	25	29
TP53 mutation	26	22
Unmutated IGHV	77	82

*Other prior therapies included anti-CD52 antibody (n=6), anti-CD19 antibody (n=3), immunomodulatory agent (n=2), anti-PD-L1 antibody (n=1), anti-CD23 antibody (n=1), autologous dendritic cell vaccine (n=1), and hydroxycarbamide (n=1).[5]

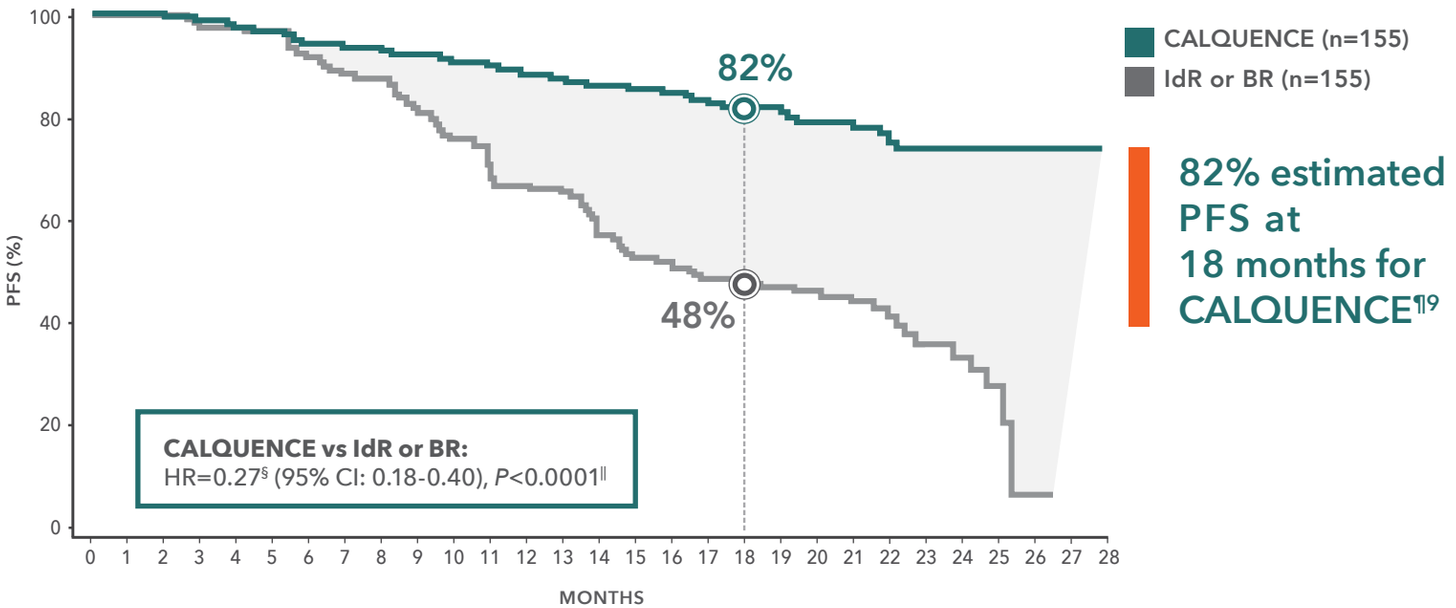
Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

73% risk reduction in disease progression or death with CALQUENCE vs IdR or BR

At median 22.1-month follow-up (range: 0.5 to 29.1 months), median PFS was not reached with CALQUENCE vs 16.8 months (95% CI: 14.1-22.4) with IdR or BR*†[6,9]

FINAL ANALYSIS: INVESTIGATOR-ASSESSED PROGRESSION-FREE SURVIVAL‡[9]



82% estimated PFS at 18 months for CALQUENCE¶[9]

At the interim analysis, median PFS was not reached with CALQUENCE vs 16.5 months (95% CI: 14.0-17.1) with IdR or BR at a median 16.1-month follow-up*[5]

- 69% risk reduction in disease progression or death with CALQUENCE vs IdR or BR (HR=0.31§ [95% CI: 0.20-0.49], *P*<0.0001#)[2]
- There was no statistically significant difference in ORR between the 2 treatment arms at the interim or the final analysis[2,9]

*Per 2008 IWCLL criteria.[2,9] †The final analysis had a median follow-up of 22.1 months (range: 0.5 to 29.1 months) in the CALQUENCE arm and 21.9 months (range: 0.0-27.7 months) in the IdR or BR arm.[5] ‡At the time of the final analysis, the number of events in each arm was 35 (23%) for CALQUENCE and 90 (58%) for IdR or BR.[5] §Based on a stratified Cox proportional-hazards model.[2,9] ‖Based on a stratified log-rank test, stratified by randomization stratification factors as recorded in an interactive voice/web response system.[9] ¶Estimated 18-month PFS: CALQUENCE, 82% (95% CI: 75-87); IdR or BR, 48% (95% CI: 40-56).[9] #Based on a stratified log-rank test. The prespecified type I error rate (α) is 0.012 derived from a Lan-DeMets alpha spending function with O'Brien-Fleming boundary.[2]

IMPORTANT SAFETY INFORMATION (Cont'd)

ADVERSE EVENTS (Cont'd)

Adverse reactions led to CALQUENCE dose reduction in 7% and 4% of patients in the CALQUENCE plus obinutuzumab arm (N=178) and CALQUENCE monotherapy arm (N=179), respectively. Adverse events led to discontinuation in 11% and 10% of patients, respectively.

In patients with relapsed/refractory CLL exposed to CALQUENCE, 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.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

At the interim analysis (median 16.1-month follow-up), safety and tolerability were consistent with the established profile of CALQUENCE

*COMMON ADVERSE REACTIONS (≥15%, ANY GRADE) WITH CALQUENCE IN ASCEND**[2]

Adverse reaction	CALQUENCE (n=154)		IdR (n=118)		BR (n=35)	
	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)
Infection†	56	15‡	65	28‡	49	11
Lower respiratory tract infection†	23	6	26	15	14	6
Upper respiratory tract infection†	29	1.9	26	3.4	17	2.9
Neutropenia†	48	23	79	53	80	40
Anemia†	47	15	45	8	57	17
Thrombocytopenia†	33	6	41	13	54	6
Lymphocytosis†	26	19	23	18	2.9	2.9
Headache	22	0.6	6	0	0	0
Diarrhea†	18	1.3	49	25	14	0
Hemorrhage†	16	1.3	5	1.7	6	2.9
Fatigue†	15	1.9	13	0.8	31	6
Musculoskeletal pain†	15	1.3	15	1.7	2.9	0

*The median duration of exposure to CALQUENCE was 15.7 months.[2] †Includes multiple adverse drug reaction terms (see full Prescribing Information).[2] ‡Includes 1 fatal case in the CALQUENCE monotherapy arm and 1 fatal case in the IdR arm.[2]

IMPORTANT SAFETY INFORMATION (Cont'd)

ADVERSE EVENTS (Cont'd)

Adverse reactions led to CALQUENCE dose reduction in 3.9% of patients (N=154), dosage 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 1.5 to 3 times the upper limit of normal occurred in 1.3% of patients who received CALQUENCE.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information

CALQUENCE® (acalabrutinib) 100 mg capsules

Other clinically relevant adverse reactions (<15%, any grade) in recipients of CALQUENCE included[2]:

- Skin and subcutaneous disorders: bruising (10%), rash (9%)
- Neoplasms: second primary malignancy (12%), including non-melanoma skin cancer (6%)
- Musculoskeletal and connective tissue disorders: arthralgia (8%)
- Cardiac disorders: atrial fibrillation or flutter (5%), hypertension (3.2%)
- Infection: herpesvirus infection (4.5%)

SELECT NON-HEMATOLOGIC LABORATORY ABNORMALITIES (≥10%, ANY GRADE), NEW OR WORSENING FROM BASELINE WITH CALQUENCE IN ASCEND*[2]

	CALQUENCE (n=154)		IdR (n=118)		BR (n=35)	
Laboratory abnormality†	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)
Uric acid increase	15	15	11	11	23	23
ALT increase	15	1.9	59	23	26	2.9
AST increase	13	0.6	48	13	31	2.9
Bilirubin increase	13	1.3	16	1.7	26	11

Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 1.3% of patients who received CALQUENCE.[2]

Safety and tolerability results in the final analysis were consistent with those of the interim analysis[9]

In the final analysis, at median 22-month follow-up, the most common adverse reactions (≥20%) of any grade in patients receiving CALQUENCE were headache, neutropenia, diarrhea, and upper respiratory tract infection.[9]

Serious adverse reactions in >5% of patients who received CALQUENCE included pneumonia (6%).[9]

10% and 16% of patients discontinued CALQUENCE due to adverse reactions at median 16.1-month and 22-month follow-ups, respectively[2,9]

*The median duration of exposure to CALQUENCE was 15.7 months.[2] †Excludes electrolytes.[2]

IMPORTANT SAFETY INFORMATION (Cont'd)

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 approximately every 12 hours.

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.

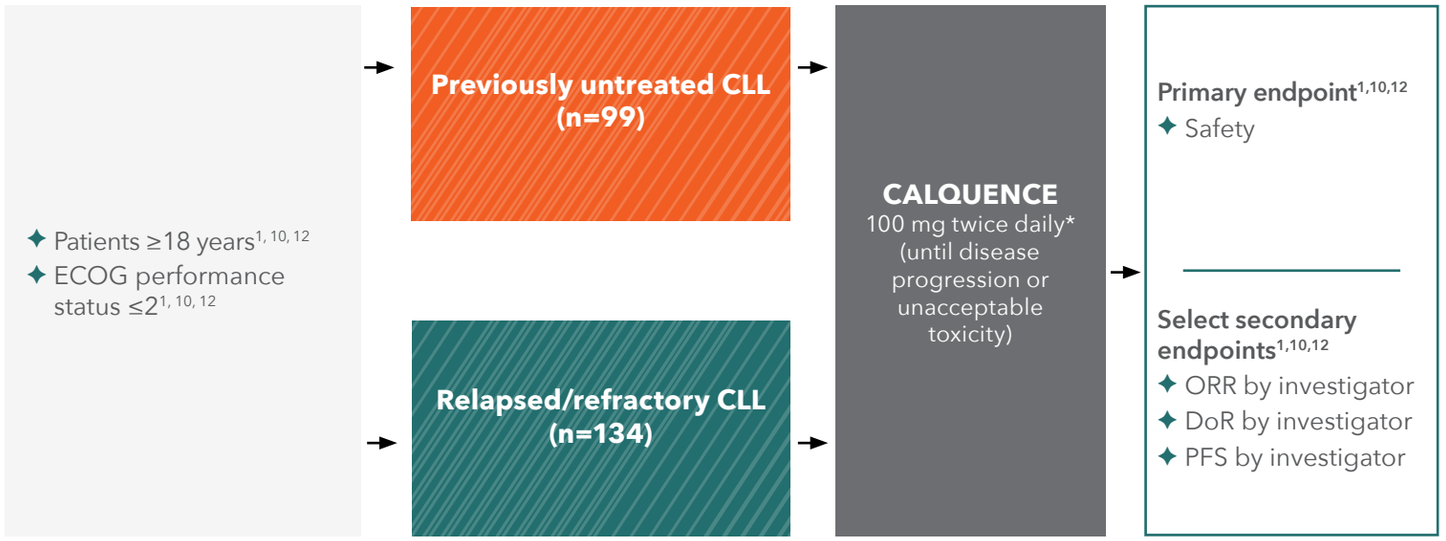
Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

LONG-TERM STUDY

A multi-cohort trial of patients with CLL

Phase 1/2 single-arm study included expansion phases[1,10-11]:



*Patients initially receiving 200 mg once daily (previously untreated, n=37; relapsed/refractory, n=33) were switched to 100 mg twice daily per protocol amendment based on the increased BTK occupancy with 100 mg twice daily dosing vs 200 mg once daily.[1,10]
AEs=adverse events; DoR=duration of response.

- **Patients who received antithrombotic agents other than warfarin or equivalent agents were allowed[1,10]**
- **Patients with controlled, asymptomatic arrhythmias were allowed[1,10]**

IMPORTANT SAFETY INFORMATION (Cont'd)

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.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

Select demographics and baseline characteristics[1,10,12]

Characteristic	Previously untreated (n=99)	Relapsed/refractory (n=134)
Age, years; median (range)	64 (33-85)	66 (42-85)
Male; %	67%	74%
ECOG performance status 0-1; %	100%	97%
Bulky disease ≥5 cm; %	53%	47%
Prior therapies; median (range)	-	2 (1-13)
TYPE OF PRIOR SYSTEMIC THERAPY; %		
Nucleoside analog (eg, fludarabine, cladribine)	-	58%
Alkylating agent (eg, bendamustine, chlorambucil)	-	69%
Anti-CD20	-	95%
PRIOR IBRUTINIB THERAPY		
Duration of prior ibrutinib therapy; median, months (range)	-	-
Time from ibrutinib end to acalabrutinib start; median, days (range)	-	-
CYTOGENETICS/FISH CATEGORY; %		
17p deletion	10%	23%
Unmutated IGHV	62%	73%
COMORBIDITIES; %		
Cardiac disorders*	24%	29%
Atrial fibrillation	8%	9%
Hypertension	55%	50%

*Includes multiple cardiac disorder terms.[12]

IMPORTANT SAFETY INFORMATION (Cont'd)

SPECIFIC POPULATIONS (Cont'd)

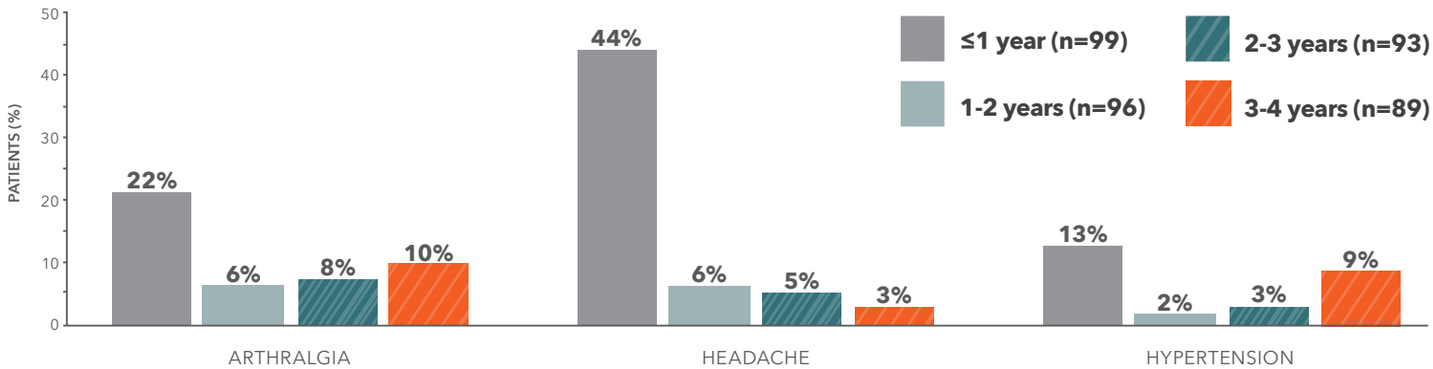
Pregnancy testing is recommended for females of reproductive potential prior to initiating CALQUENCE therapy. Advise female patients of reproductive potential to use effective contraception during treatment with CALQUENCE and for at least 1 week following the last dose of CALQUENCE.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

Rates of most adverse events decreased after the first year

SELECT TREATMENT-EMERGENT ADVERSE EVENTS BY YEARLY INTERVALS[1]



Only 6% of patients discontinued treatment due to AEs[1]

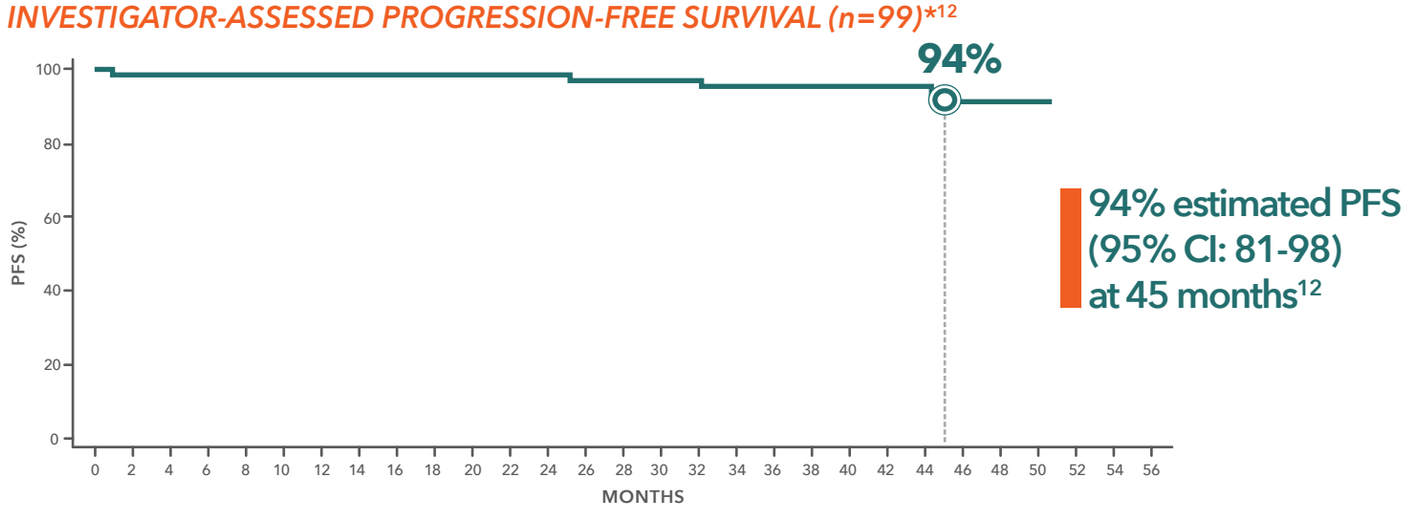
No patients discontinued CALQUENCE due to atrial fibrillation, hypertension, or bleeding events. No ventricular tachyarrhythmias were reported.[1]

Most common adverse events (≥30%) were diarrhea, headache, upper respiratory tract infection, arthralgia, contusion, weight increased, nausea, and cough. Serious adverse events were reported in 38 patients and included pneumonia (4%), influenza (3%), sepsis (3%), and sinusitis (2%). Grade ≥3 atrial fibrillation occurred in 2 patients and Grade ≥3 bleeding events occurred in 3 patients. Hypertension occurred in 22 patients (Grade ≥3 in 11 patients).[1,12]

Long-term efficacy over 4 years

Median PFS was not reached at median 53-month follow-up (range: 1 to 59 months)[1,12]

*INVESTIGATOR-ASSESSED PROGRESSION-FREE SURVIVAL (n=99)**[12]



*At the time of analysis, the number of events was 4 (4%).[12]

IMPORTANT SAFETY INFORMATION (Cont'd)

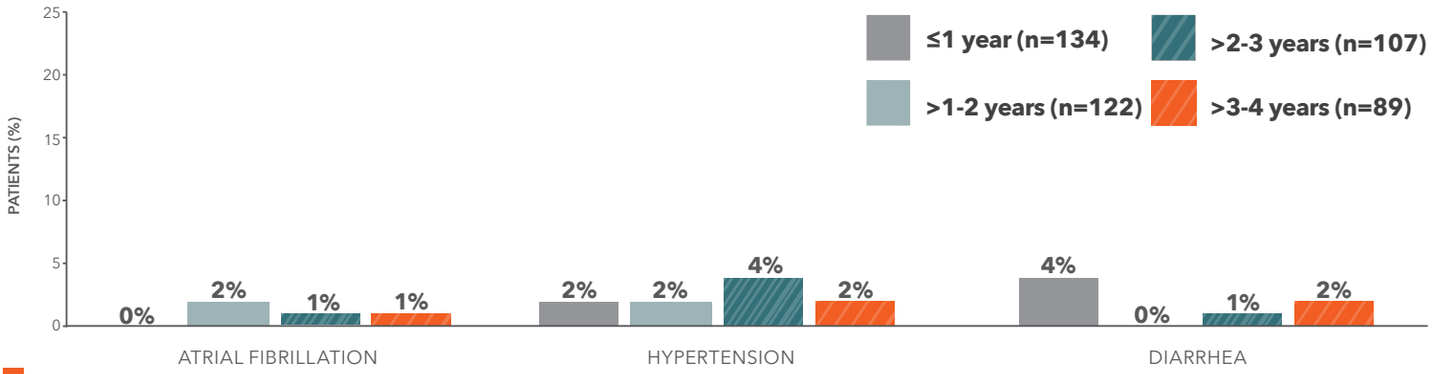
SPECIFIC POPULATIONS (Cont'd)
It is not known if CALQUENCE is present in human milk. Advise lactating women not to breastfeed while taking CALQUENCE and for at least 2 weeks after the final dose.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

Frequency of severe AEs was low and consistent over time

SELECT TREATMENT-EMERGENT GRADE ≥3 ADVERSE EVENTS BY YEARLY INTERVALS[10,13]



Consistently low rates of grade ≥3 atrial fibrillation and hypertension over time[10,13]

13% of patients discontinued treatment due to AEs.[10]

Most common adverse events were diarrhea, headache, upper respiratory tract infection, and fatigue. Grade ≥3 AEs occurred in 89 patients (66%) and included neutropenia (14%), pneumonia (11%), hypertension (7%), anemia (7%), and diarrhea (5%). Grade ≥3 infections occurred in 23% of patients. Grade 3 atrial fibrillation occurred in 3 patients and major bleeding events (Grade ≥3, serious AEs, and/or any central nervous system hemorrhage) occurred in 7 patients.[10]

High response rates regardless of high-risk features*

INVESTIGATOR-ASSESSED OVERALL RESPONSE RATES[10]

	% (95% CI)	Number of responders/patients
ORR: CR + PR + PRL	94 (89-97)	126/134
CR	4 (-)	6/134
PR + PRL	90 (-)	120/134
ORR BY HIGH-RISK SUBGROUP: CR + PR + PRL		
17p deletion	93 (76-99)	25/27
11q deletion	95 (76-100)	20/21
Unmutated IGHV	95 (88-99)	77/81

*At median 41-month follow-up (range: 0.2 to 58 months).[10]
PRL=partial response with lymphocytosis.

IMPORTANT SAFETY INFORMATION (Cont'd)

SPECIFIC POPULATIONS (Cont'd)

Avoid administration of CALQUENCE in patients with severe hepatic impairment. Dose modifications are not required for patients with mild or moderate hepatic impairment.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing Information, including Patient Information.

CALQUENCE® (acalabrutinib) 100 mg capsules

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

CALQUENCE is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

IMPORTANT SAFETY INFORMATION ABOUT CALQUENCE® (acalabrutinib) capsules

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 19% of 1029 patients exposed to CALQUENCE in clinical trials, most often due to respiratory tract infections (11% of all patients, including pneumonia in 6%). These infections predominantly occurred in the absence of Grade 3 or 4 neutropenia, with neutropenic infection reported in 1.9% of all patients. Opportunistic infections in recipients of CALQUENCE have included, but are not limited to, hepatitis B virus reactivation, fungal pneumonia, *Pneumocystis jiroveci* 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 with hematologic malignancies treated with CALQUENCE. Major hemorrhage (serious or Grade 3 or higher bleeding or any central nervous system bleeding) occurred in 3.0% of patients, with fatal hemorrhage occurring in 0.1% of 1029 patients exposed to CALQUENCE in clinical trials. Bleeding events of any grade, excluding bruising and petechiae, occurred in 22% of patients.

Use of antithrombotic agents concomitantly with CALQUENCE may further increase the risk of hemorrhage. In clinical trials, major hemorrhage occurred in 2.7% of patients taking CALQUENCE without antithrombotic agents and 3.6% 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 3-7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (23%), anemia (8%), thrombocytopenia (7%), and lymphopenia (7%), developed in patients with hematologic malignancies treated with CALQUENCE. Grade 4 neutropenia developed in 12% 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 12% of 1029 patients exposed to CALQUENCE in clinical trials. The most frequent second primary malignancy was skin cancer, reported in 6% of patients. Monitor patients for skin cancers and advise protection from sun exposure.

Atrial Fibrillation and Flutter

Grade 3 atrial fibrillation or flutter occurred in 1.1% of 1029 patients treated with CALQUENCE, with all grades of atrial fibrillation or flutter reported in 4.1% of all patients. The risk may be increased in patients with cardiac risk factors, hypertension, previous arrhythmias, and acute infection. Monitor for symptoms of arrhythmia (e.g., palpitations, dizziness, syncope, dyspnea) and manage as appropriate.

ADVERSE REACTIONS

The most common adverse reactions (≥ 30%) of any grade in patients with CLL 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 exposed to CALQUENCE, 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% of patients in the CALQUENCE plus obinutuzumab arm and 32% in the CALQUENCE monotherapy arm, most often due to events of pneumonia (7% and 2.8%, respectively).

CALQUENCE®
(acalabrutinib) 100 mg capsules

Adverse reactions led to CALQUENCE dose reduction in 7% and 4% of patients in the CALQUENCE plus obinutuzumab arm (N=178) and CALQUENCE monotherapy arm (N=179), respectively. Adverse events led to discontinuation in 11% and 10% of patients, respectively. Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 3.9% and 2.8% of patients in the CALQUENCE combination arm and monotherapy arm, respectively.

In patients with relapsed/refractory CLL exposed to CALQUENCE, 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 (N=154), dosage 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 1.5 to 3 times the upper limit of normal occurred in 1.3% of patients who received CALQUENCE.

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 approximately every 12 hours.

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

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 at least 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 at least 2 weeks after the final dose.

Avoid administration of CALQUENCE in patients with severe hepatic impairment. Dose modifications are not required for patients with mild or moderate hepatic impairment.

Please see full Prescribing Information, including Patient Information.

You may report side effects related to AstraZeneca products by clicking here.

References: 1. Byrd JC, Woyach JA, Furman RR, et al. Acalabrutinib in treatment-naïve chronic lymphocytic leukemia: mature results from phase 2 study demonstrating durable remissions and long-term tolerability. Poster presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 29–31, 2020 (Virtual Meeting). **2.** CALQUENCE [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2019. **3.** 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. **4.** Data on File, REF-64711. AstraZeneca Pharmaceuticals LP. **5.** Ghia P, Pluta A, Wach M, 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;38(25):2849-2861. **6.** ACE-CL-309 Clinical Study Report Efficacy Addendum. AstraZeneca Pharmaceuticals. **7.** Eichhorst B, Robak T, Montserrat E, et al. Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2015;26(Suppl 5):v78-v84. **8.** Weide R, Feiten S, Chakupurakal G, et al. Survival improvement of patients with chronic lymphocytic leukemia (CLL) in routine care 1995–2017. *Leuk Lymphoma.* 2020;61(3):557-566. **9.** Ghia P, Pluta A, Wach M, et al. Acalabrutinib vs idelalisib plus rituximab or bendamustine plus rituximab in relapsed/refractory chronic lymphocytic leukemia: ASCEND final results. Poster presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 29-31, 2020 (Virtual Meeting). **10.** Byrd JC, Wierda WG, Schuh A, et al. Acalabrutinib monotherapy in patients with relapsed/refractory chronic lymphocytic leukemia: updated phase 2 results. *Blood.* 2020;135(15):1204-1213. **11.** ACP-196 (acalabrutinib), a novel Bruton tyrosine kinase (Btk) inhibitor, for treatment of chronic lymphocytic leukemia. ClinicalTrials.gov identifier: NCT02029443. https://www.clinicaltrials.gov/ct2/show/NCT02029443. **12.** Data on File, REF-91068. AstraZeneca Pharmaceuticals LP. **13.** Furman RR, Wierda W, Schuh A, et al. Acalabrutinib monotherapy in patients with relapsed/refractory chronic lymphocytic leukemia: 42-month follow-up of a phase 2 study. Poster presented at: American Society of Hematology (ASH) Annual Meeting. December 7-10, 2019. Orlando, Florida.

AstraZeneca

CALQUENCE®
(acalabrutinib) 100 mg capsules