IN 1L MCL

START STRONG

5.5 years mPFS* with CALQUENCE + BR vs 4.1 years with placebo + BR†[1]

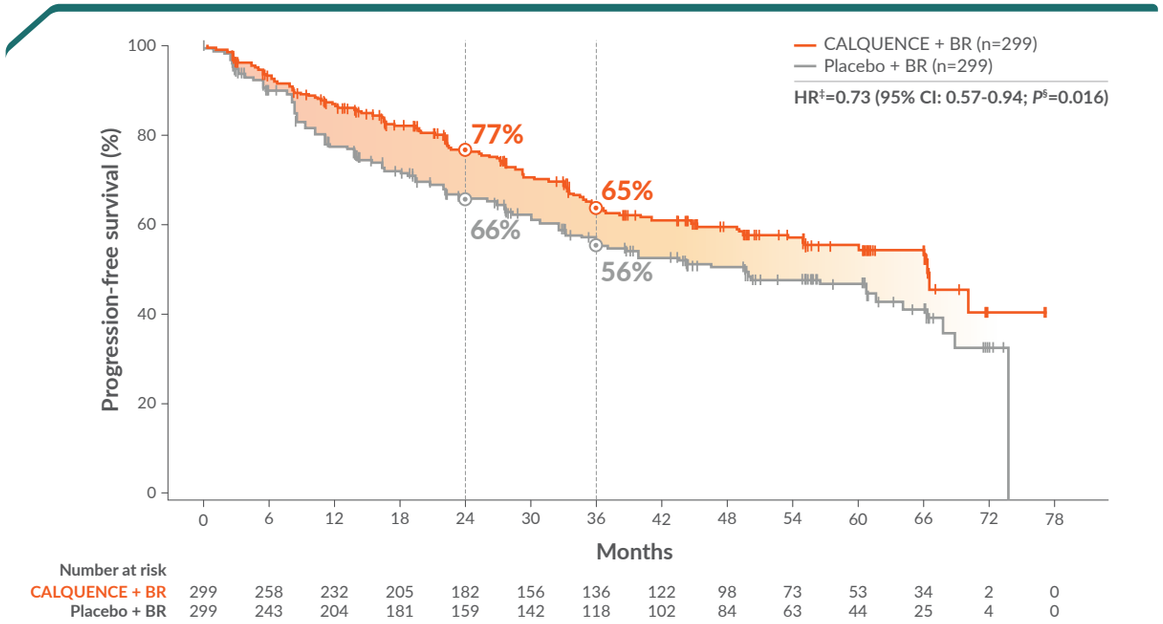
(HR†=0.73 [95% CI: 0.57-0.94]; *P*‡=0.016)

The first and only BTKi approved in 1L MCL: CALQUENCE in combination with bendamustine and rituximab for patients ineligible for auto-HSCT[1]

CALQUENCE + BR significantly improved PFS vs placebo + BR[1,2]

ECHO is the first BTKi-based Phase 3 trial leading to FDA approval in 1L MCL.[1,2] PFS risk reduction was 27% with CALQUENCE + BR (n=299) vs placebo + BR (n=299) (**HR‡=0.73 [95% CI: 0.57-0.94]**; ***P*§=0.016**) at 49.8-month median follow-up.†[1,2]

IRC-assessed PFS‖[1,3]



Number at risk													
CALQUENCE + BR	299	258	232	205	182	156	136	122	98	73	53	34	2	0
Placebo + BR	299	243	204	181	159	142	118	102	84	63	44	25	4	0

- At interim analysis, 110 patients (36.8%) in the CALQUENCE + BR arm and 137 patients (45.8%) in the placebo + BR arm had a PFS event, of which 57 patients (19.1%) and 99 patients (33.1%) had disease progression, respectively[3]

PFS rates at 24 and 36 months are based on Kaplan-Meier estimates and are descriptive only. ECHO was not powered to assess a statistical difference between treatment groups at these time points.[3]

Study design[1,2]: ECHO is a randomized, double-blind, placebo-controlled, multicenter Phase 3 trial evaluating CALQUENCE + BR vs placebo + BR in adult patients with previously untreated MCL (N=598). Patients were randomized 1:1 to receive CALQUENCE + BR (6 cycles)¶ or placebo + BR (6 cycles).¶ Patients achieving a response (PR or CR) received maintenance rituximab (every 2 cycles for a maximum of 2 years). CALQUENCE was continued until disease progression or unacceptable toxicity. Crossover to CALQUENCE monotherapy was permitted for patients in the placebo + BR arm at disease progression.# The primary endpoint was IRC-assessed PFS using the Lugano Classification. Select secondary endpoints included INV-assessed PFS, INV- and IRC-assessed ORR (CR + PR), IRC-assessed DoR, and OS.[2,3]

*At interim analysis, mPFS was 66.4 months with CALQUENCE + BR (95% CI: 55.1-NE) vs 49.6 months (95% CI: 36.0-64.1) with placebo + BR.[1] †At 49.8-month median-follow-up (range: 0.0-77.3 months).[1,3] ‡Based on stratified Cox proportional-hazards model for HR (95% CI).[1] §Estimated based on stratified log-rank test for *P* value, with an alpha level of 0.039 derived by the O'Brien-Fleming method.[1] ‖Stratified by randomization stratification factors: geographic regions (North American, Western Europe, and Other) and simplified MIPI score (low risk [0 to 3], intermediate risk [4 to 5], high risk [6 to 11]).[1] ¶Each cycle was 28 days.[1] #CALQUENCE 100 mg BID, orally until disease progression or unacceptable toxicity.[1]

1L=first-line; auto-HSCT=autologous hematopoietic stem cell transplantation; BID=twice daily; BR=bendamustine + rituximab; BTKi=Bruton tyrosine kinase inhibitor; CI=confidence interval; CR=complete response; DoR=duration of response; FDA=Food and Drug Administration; HR=hazard ratio; IRC=independent review committee; INV=investigator; MCL=mantle cell lymphoma; MIPI=Mantle Cell Lymphoma International Prognostic Index; mPFS=median progression-free survival; NE=not evaluable; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; PR=partial response.

INDICATION AND USAGE

CALQUENCE in combination with bendamustine and rituximab is indicated for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are ineligible for autologous hematopoietic stem cell transplantation (HSCT).

SELECT SAFETY INFORMATION

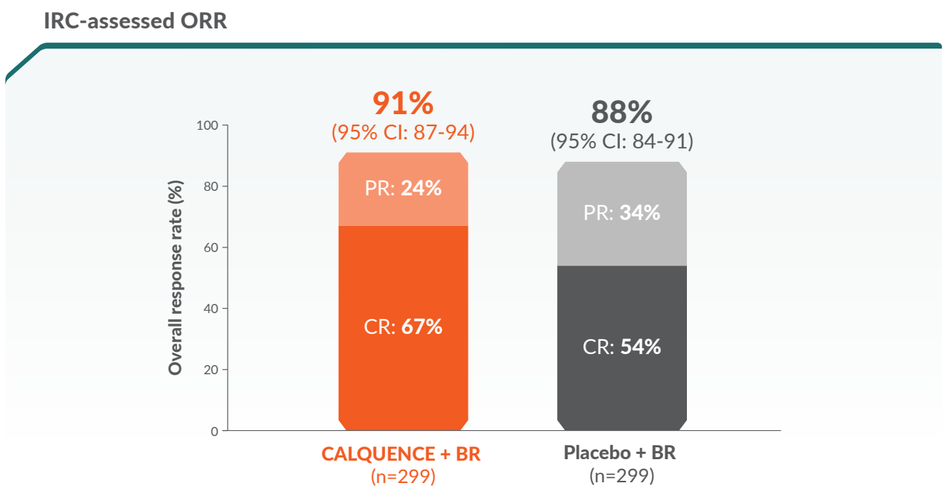
Serious adverse events, including fatal events, have occurred with CALQUENCE, including serious and opportunistic infections, hemorrhage, cytopenias, second primary malignancies, cardiac arrhythmias, and hepatotoxicity, including drug-induced liver injury. The most common adverse reactions (≥30%) are diarrhea, upper respiratory tract infection, headache, musculoskeletal pain, lower respiratory tract infection, and fatigue. The most common Grade 3 or 4 laboratory abnormalities (≥10%) are absolute neutrophil count decreased, absolute lymphocyte count decreased, platelets decreased, and hemoglobin decreased.

Please see full Important Safety Information on following pages, and accompanying full Prescribing Information, including Patient Information.

CALQUENCE®
acalabrutinib 100 mg tablets

9 out of 10 patients responded to CALQUENCE + BR*[1,2]

67% of patients had CR with CALQUENCE + BR and 54% with placebo + BR



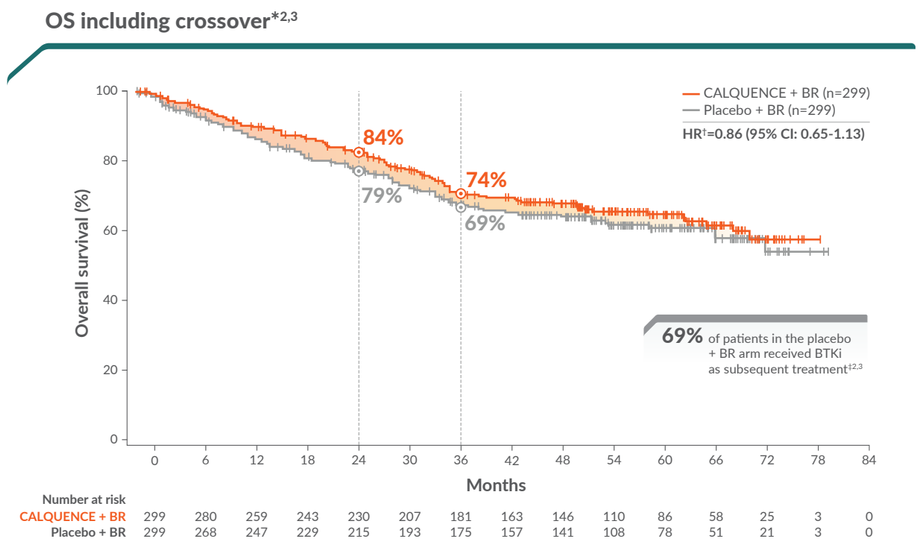
The difference in ORR between the two arms was not statistically significant.

- In patients who responded, median DoR was 64 months (range: 0.0-74.5; 95% CI: 52.5-NE) with CALQUENCE + BR (n=272) and 54 months (range: 0.0-70.5; 95% CI: 37.6-66.1) with placebo + BR (n=263)[3]

*Includes PR + CR.

Overall survival data[2]

mOS not yet reached in either arm at the time of PFS analysis[3]



- At interim analysis, there were a total of 203 deaths: 97 (32%) patients in the CALQUENCE + BR arm and 106 (35%) patients in the placebo + BR arm[1]

OS data are immature. The estimated OS rates at 24 and 36 months are based on Kaplan-Meier estimates.[3] OS analysis was descriptive in nature.

*Crossover to CALQUENCE monotherapy was permitted for patients in the placebo + BR arm at disease progression.[1,2]
†Based on stratified or unstratified log-rank test, by randomization stratification factors as recorded in Interactive Voice/Web Response System if stratified.
‡51 patients in the placebo + BR treatment arm who experienced progressive disease crossed over to receive CALQUENCE monotherapy 100 mg BID, orally until disease progression or unacceptable toxicity.[1,4]
mOS=median overall survival.

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 32% of 1,764 patients exposed to CALQUENCE in clinical trials, most often due to respiratory tract infections (19% of all patients, including pneumonia in 9%). These infections predominantly occurred in the absence of Grade 3 or 4 neutropenia, with neutropenic infection reported in 2.7% 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 4.4% of patients, with fatal hemorrhage occurring in 0.2% of 1,764 patients exposed to CALQUENCE in clinical trials. Bleeding events of any grade, excluding bruising and petechiae, occurred in 40% of patients.

Use of antithrombotic agents concomitantly with CALQUENCE may further increase the risk of hemorrhage. In clinical trials, major hemorrhage occurred in 7% of patients taking CALQUENCE without antithrombotic agents and 4% 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 (26%), platelets decreased (10%), hemoglobin decreased (10%), and absolute lymphocyte count decreased (10%) in patients treated with CALQUENCE alone or in combination with obinutuzumab; 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 18% of 1,764 patients exposed to CALQUENCE in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer, reported in 10% of patients, followed by other solid tumors in 9% (including melanoma, lung cancer, gastrointestinal cancers, and genitourinary cancers) and hematologic malignancies (1%). 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 2.6% of 1,764 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 0.6% 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.

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

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

Previously Untreated Mantle Cell Lymphoma

The most common adverse reactions (≥15%) of any grade in patients with previously untreated MCL who received CALQUENCE plus BR were rash (47%), COVID-19 (38%), fatigue (37%), diarrhea (37%), pneumonia (31%), headache (31%), upper respiratory tract infection (30%), pyrexia (29%), cough (27%), vomiting (26%), constipation (25%), hemorrhage (20%), edema (20%), secondary primary malignancy (19%), dizziness (18%), arthralgia (18%), and dyspnea (17%).

Grade 4 laboratory abnormalities in >15% of patients treated with CALQUENCE plus BR include lymphocytes decreased (26%), absolute neutrophils decreased (36%), and uric acid increased (17%).

Serious adverse reactions occurred in 69% of patients who received CALQUENCE plus BR. Serious adverse reactions reported in ≥2% of patients were pneumonia (23%; includes COVID-19 pneumonia), COVID-19 (20%; includes COVID-19 pneumonia), second primary malignancy (7%), pyrexia (6%), rash (3.4%), febrile neutropenia (3.4%), atrial fibrillation (3%), sepsis (2.7%), and anemia (2.4%). Fatal adverse reactions that occurred within 30 days of the last study treatment were reported in 12% who received CALQUENCE plus BR including COVID-19 (6%; includes COVID-19 pneumonia), pneumonia (1%), second primary malignancy (0.7%), sepsis (0.3%), and pneumonitis (0.3%).

Adverse reactions led to permanent discontinuation of CALQUENCE in 43%, dosage interruptions in 74%, and dosage reductions in 10% of patients. Adverse reactions that resulted in dosage modification in >10% included infections, cytopenias, rashes, and gastrointestinal toxicity. Adverse reactions which resulted in permanent discontinuation of CALQUENCE in ≥4% of patients included COVID-19 (includes COVID-19 pneumonia) and neutropenia.

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.

You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933. If you prefer to report these to the FDA, call 1-800-FDA-1088.

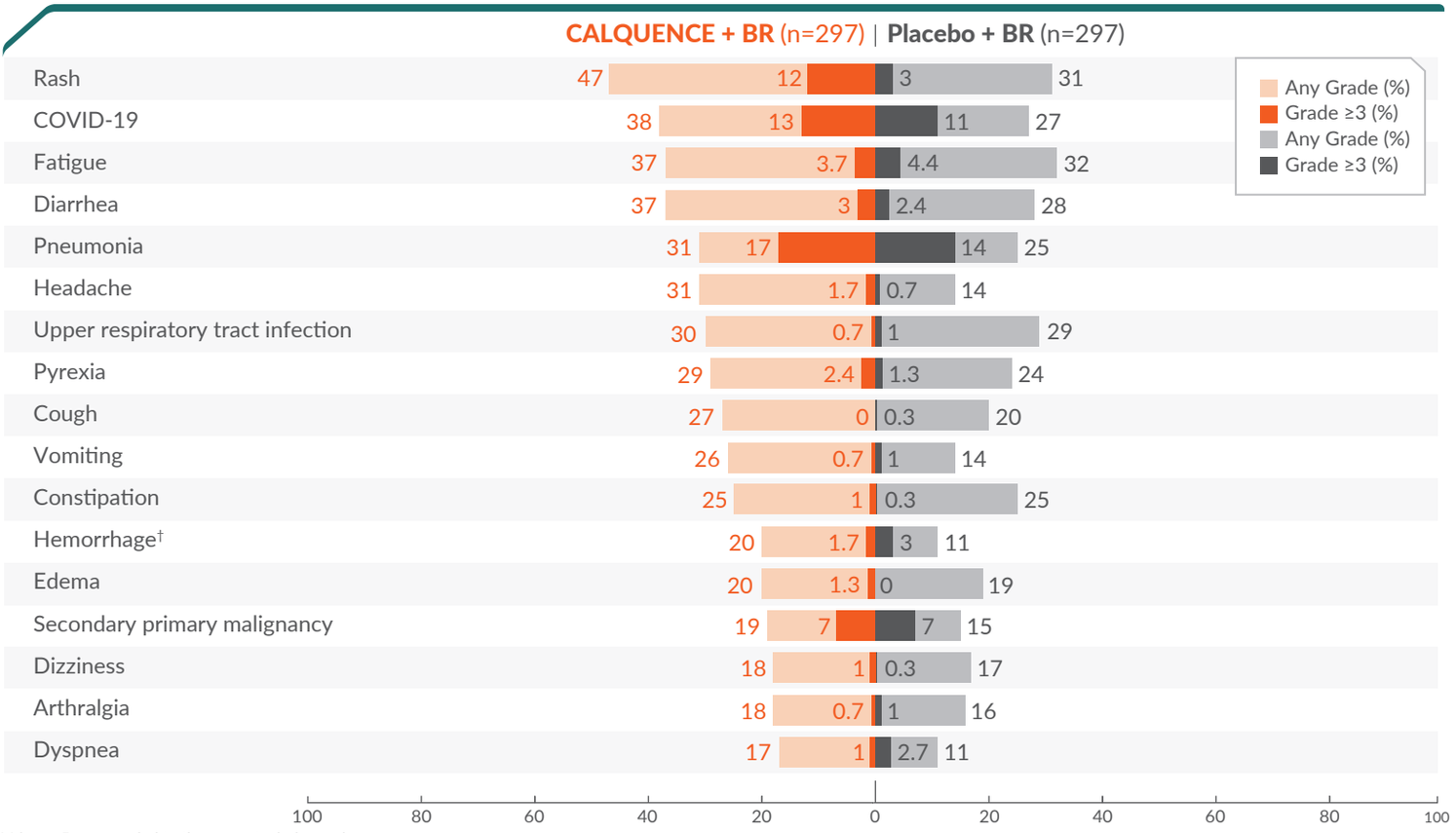
References: 1. CALQUENCE® (acalabrutinib) tablets [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025. **2.** Wang M, Mayer J, Belada D, et al. Acalabrutinib plus bendamustine and rituximab in untreated mantle cell lymphoma (MCL): results from the phase 3, double-blind, placebo-controlled ECHO trial. Presented at: European Hematology Association (EHA) annual meeting; June 13-16, 2024; Madrid, Spain. **3.** Data on File. REF-255868. AstraZeneca Pharmaceuticals LP. **4.** Wang M, et al. Abstract LBA3439 presented at: 2024 EHA Congress; June 13-16, 2024; Madrid, Spain.

CALQUENCE®
acalabrutinib 100 mg tablets

Safety was consistent with the established profile of CALQUENCE*[1,2]

Most ARs were Grade 1 and 2 in the CALQUENCE + BR arm

Most common ARs (≥15% All Grades)



Values >5 are rounded to the nearest whole number.

- The median duration of exposure was 28.6 months with CALQUENCE + BR and 24.6 months with placebo + BR[1,3]
- Adverse reactions leading to discontinuation: 43% (n=127) with CALQUENCE + BR and 31% (n=92) with placebo + BR[1,2]

Low rates of select cardiovascular adverse events[2]

	CALQUENCE + BR (n=297)		Placebo + BR (n=297)	
	Any Grade (%)	Grade ≥3 (%)	Any Grade (%)	Grade ≥3 (%)
Atrial fibrillation	6	3.7	4.4	1.7
Hypertension	12	5	16	8
Major bleeding‡	2.4	2.0	5	3.4

Values >5 are rounded to the nearest whole number.

In a pooled analysis of 1764 patients treated with CALQUENCE, Grade 3 or 4 atrial fibrillation or flutter was reported in 2.6% of patients and All Grades in 7% of all patients. Grade 3 or higher ventricular arrhythmia events were reported in 0.6% of patients, including fatal cases in 0.3% of all patients.[1]

The first and only BTKi approved in 1L MCL:
CALQUENCE + BR for patients ineligible for auto-HSCT[1]

LEARN MORE

*Except COVID-19.[2]
†Hemorrhage includes all terms containing hematoma, hemorrhage, and related terms indicative of bleeding.[1]
‡Defined as a hemorrhagic event that is serious, or Grade ≥3 in severity, or that is a CNS hemorrhage (any severity Grade).[2]
ARs=adverse reactions; CNS=central nervous system.

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