CALQUENCE
STRENGTH TO GO THE DISTANCE

IN PREVIOUSLY UNTREATED CLL

90%

RISK REDUCTION IN DISEASE PROGRESSION OR DEATH[1]

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.[1]
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).

Select Safety Information

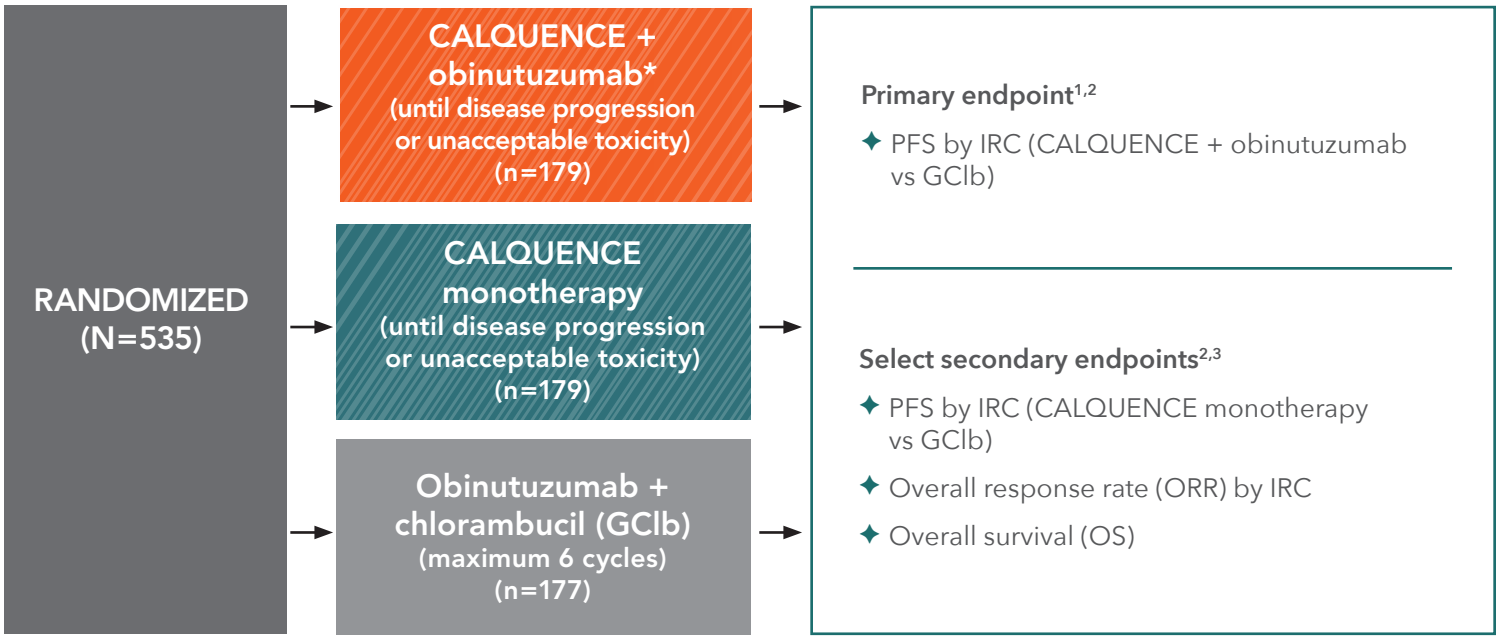
Serious and Opportunistic Infections

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.

ELEVATE-TN: a Phase 3, open-label, randomized, multicenter trial in patients with previously untreated CLL[1,2]



Patients received CALQUENCE 100 mg approximately every 12 hours until disease progression or unacceptable toxicity for either CALQUENCE + obinutuzumab or CALQUENCE monotherapy.[1]

*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.[1]

Key inclusion criteria[1,2]:

- Age:
  - ≥65 years **or**
  - 18 to <65 years **and** ≥1 of the following criteria:
    - CrCL 30-69 mL/min
    - CIRS-G >6

Key exclusion criteria[1,2]:

- Any prior systemic treatment for CLL
- Required or was receiving anticoagulation with warfarin or equivalent vitamin K antagonists within 7 days of first dose of study drug
  - Novel antithrombotic treatments were allowed

CIRS-G=Cumulative Illness Rating Scale-Geriatric; CrCL=creatinine clearance; IRC=Independent Review Committee.

Select Safety Information

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.

Please see Important Safety Information throughout and on pages 16-17, and full Prescribing 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[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 stages 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
Complex karyotype (≥3 abnormalities)	16	17	18

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

Select Safety Information

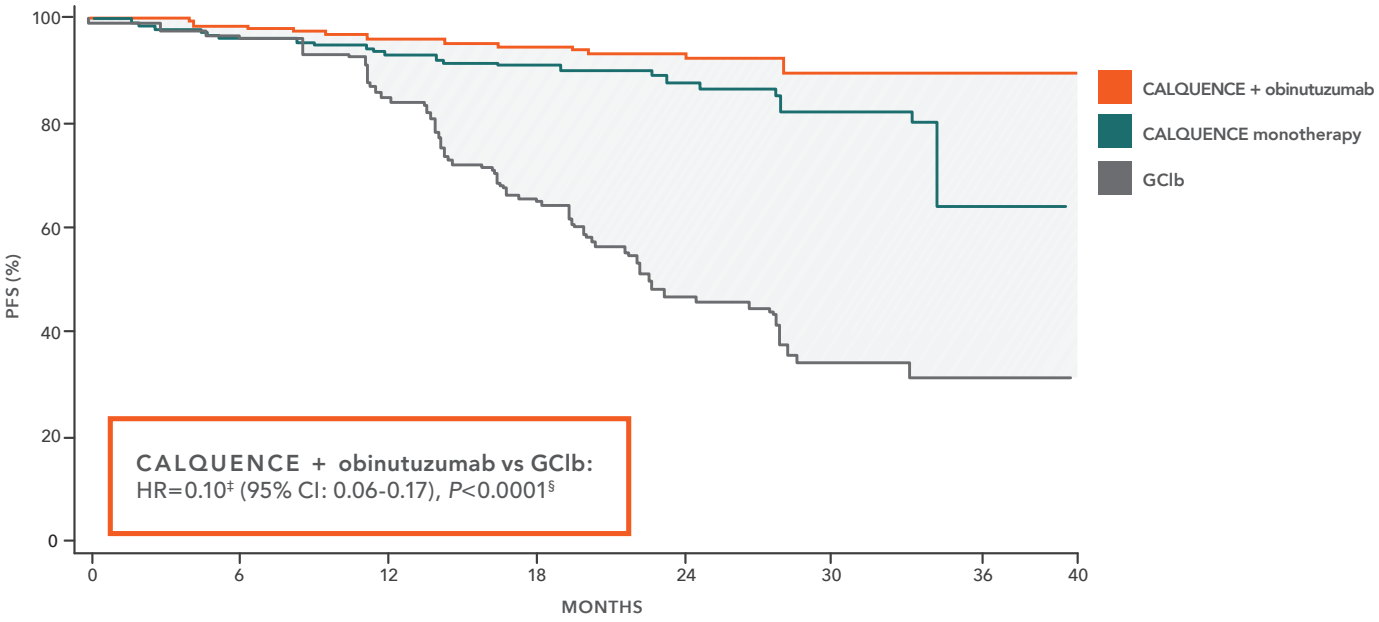
Cytopenias
Grade 3 or 4 cytopenias, including neutropenia (23%), anemia (8%), thrombocytopenia (7%), and lymphopenia (7%), developed in patients with hematologic malignancies treated with CALQUENCE. Grade 4 neutropenia developed in 12% of patients. Monitor complete blood counts regularly during treatment.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

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*[1]

IRC-ASSESSED PROGRESSION-FREE SURVIVAL†[1,4]



CALQUENCE monotherapy[1]:

- 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

ORR[1]:

- 94% ORR in the CALQUENCE + obinutuzumab arm (168/179; 95% CI: 89-97, *P*<0.0001¶); CR/CRi: 14%; PR/nPR: 81%
- CALQUENCE monotherapy: 86% ORR (153/179; 95% CI: 80-90, *P*=0.0763¶); CR/CRi: 1%; PR/nPR: 85%
- GClb: 79% ORR (139/177; 95% CI: 72-84, N/A); CR/CRi: 5%; PR/nPR: 74%

*Per 2008 International Workshop on CLL (IWCLL) criteria.[1]
†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.[1]
‡Based on a stratified Cox proportional-hazards model. Both hazard ratios are compared with the GClb arm.[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]
¶Based on a stratified Cochran-Mantel-Haenszel test for the comparison with the GClb arm.[1]
CR=complete response; CRi=complete response with incomplete blood count recovery; NE=not estimable; nPR=nodular partial response; PR=partial response.

Select Safety Information

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.

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*[1]

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

SELECT NON-HEMATOLOGIC LABORATORY ABNORMALITIES (≥15%, ANY GRADE), NEW OR WORSENING FROM BASELINE WITH CALQUENCE IN ELEVATE-TN*[1]

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

*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).[1]

†Includes multiple adverse drug reaction terms (see full Prescribing Information).[1]

‡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.[1]

§Excludes electrolytes.[1]

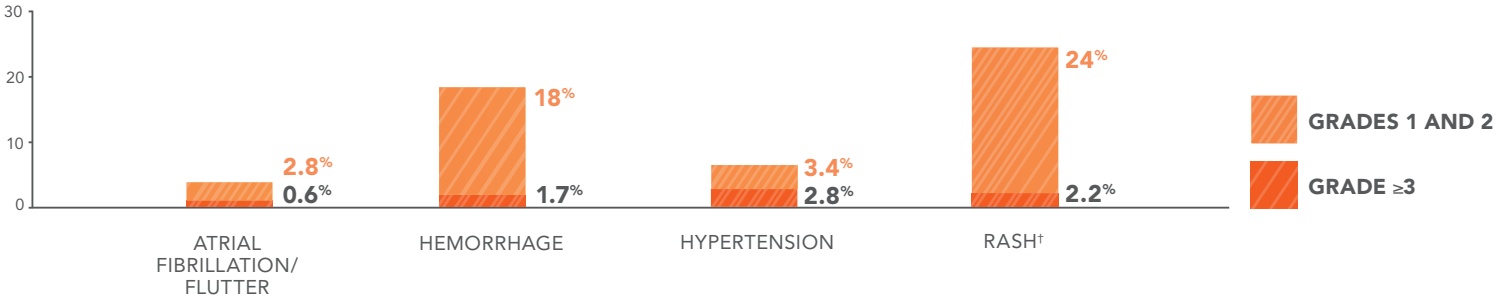
ALT=alanine aminotransferase; AST=aspartate aminotransferase.

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

CALQUENCE® (acalabrutinib) 100 mg capsules

Most adverse reactions were Grade 1 or 2

SELECT ADVERSE REACTIONS FOR CALQUENCE + OBINUTUZUMAB (n=178)*[1,4]



Other clinically relevant adverse reactions (<15%, any grade) in recipients of CALQUENCE (CALQUENCE + obinutuzumab and as monotherapy) included[1]:

- 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%)

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 and monotherapy arms, respectively.[1]

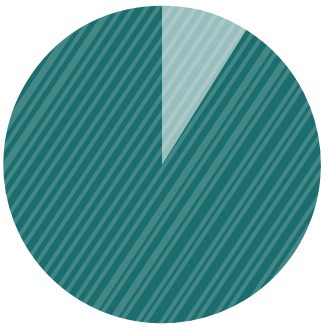
In the CALQUENCE + obinutuzumab and CALQUENCE monotherapy arms, fatal adverse reactions that occurred in the absence of disease progression and with onset within 30 days of the last study treatment were reported in 2% for each treatment arm, most often from infection. Serious adverse reactions were reported in 39% of patients in the CALQUENCE + obinutuzumab arm and 32% in the CALQUENCE monotherapy arm, most often due to events of pneumonia (7% and 2.8%, respectively).[1]

Few patients discontinued CALQUENCE due to adverse reactions at median 28.3-month follow-up[1]

CALQUENCE + OBINUTUZUMAB

11% discontinued therapy due to adverse reactions

CALQUENCE MONOTHERAPY



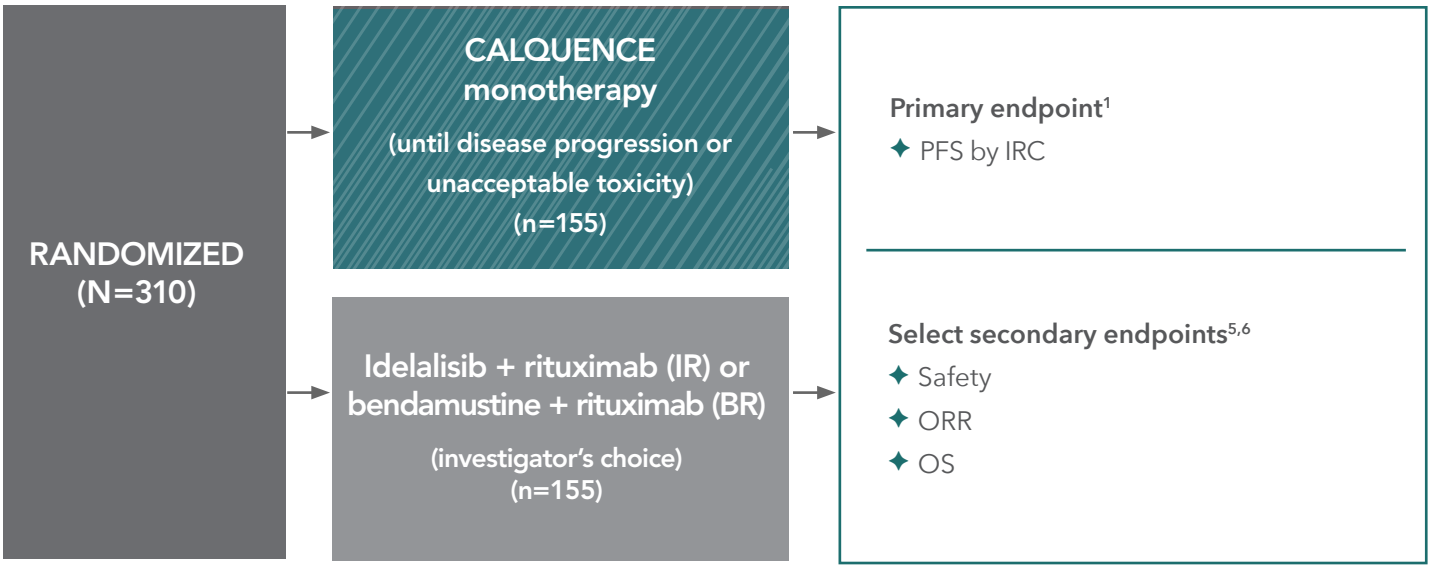
10% discontinued therapy due to adverse reactions

*Infusion-related reactions were reported in 14% of patients in the CALQUENCE + obinutuzumab arm and 39% of patients in the GClb arm.[4]
†Excludes dermatitis and other related terms.[1]

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

CALQUENCE® (acalabrutinib) 100 mg capsules

ASCEND: a Phase 3, open-label, randomized, multicenter trial in patients with relapsed/refractory CLL[1,5]



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[1]

Key inclusion criteria[1,5]:

- Age ≥18 years
- Received ≥1 prior systemic therapy for CLL
- Estimated CrCL ≥30 mL/min

Key exclusion criteria[1,5]:

- Significant cardiovascular disease within 6 months of screening
- Required or was receiving anticoagulation with warfarin or equivalent vitamin K antagonists within 7 days of first dose of study drug
  - Novel antithrombotic treatments were allowed

Select Safety Information

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.

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

SELECT DEMOGRAPHICS AND BASELINE CHARACTERISTICS IN ASCEND[4]

Characteristic	CALQUENCE (n=155)	IR or BR (n=155)
Age, years; median (range)	68 (32-89)	67 (34-90)
Male; %	70	65
ECOG performance status; %		
0-1	88	87
2	12	14
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	16
≥4	10	12
Rai stages III or IV; %	42	41
CYTOGENETICS/FISH CATEGORY; %		
17p deletion	18	14
11q deletion	25	28
TP53 mutation	25	22
Unmutated IGHV	76	81
Complex karyotype (≥3 abnormalities)	32	30

Select Safety Information

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).

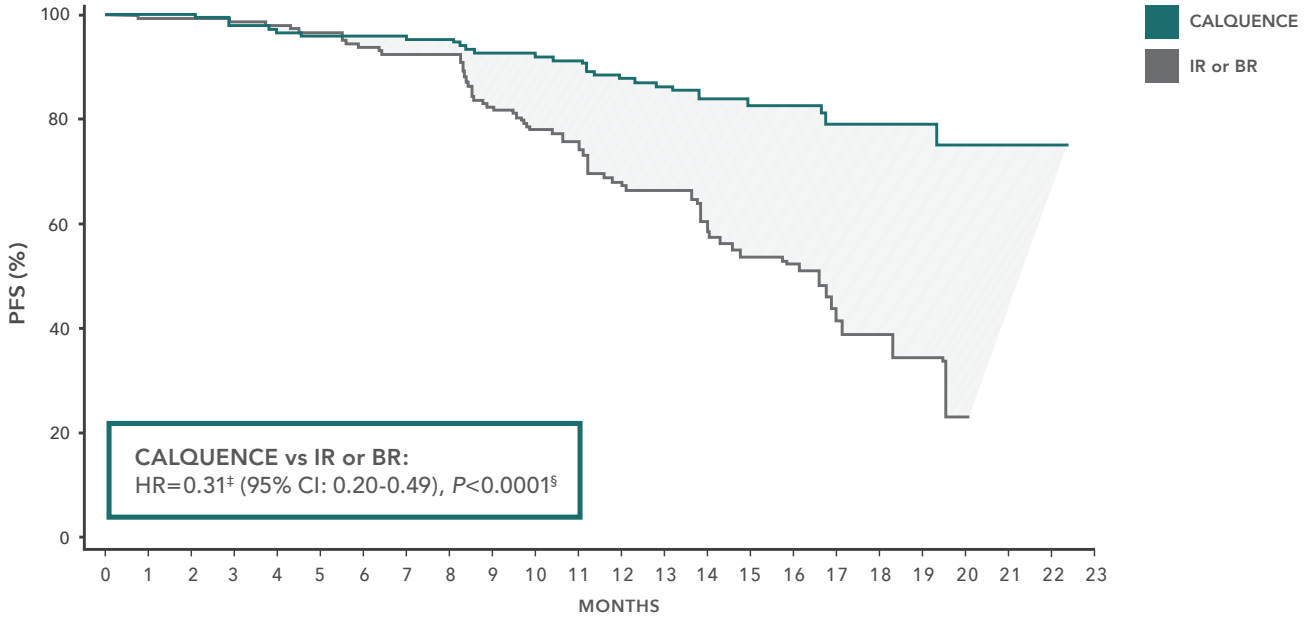
Adverse reactions led to CALQUENCE dose reduction in 7% and 4% of patients in the CALQUENCE plus obinutuzumab arm (N=178) and CALQUENCE monotherapy arm (N=179), respectively. Adverse events led to discontinuation in 11% and 10% of patients, respectively. Increases in creatinine 1.5 to 3 times the upper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

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

69% risk reduction in disease progression or death with CALQUENCE vs IR or BR

At median 16.1-month follow-up (range: 0.03 to 22.4 months), median PFS was not reached with CALQUENCE vs 16.5 months (95% CI: 14.0-17.1) with IR or BR*[1]

IRC-ASSESSED PROGRESSION-FREE SURVIVAL†[1,4]



✦ CALQUENCE: 81% ORR (95% CI: 74-87; CR/CRi: 0%; PR/nPR: 81%)[1] ✦ IR or BR: 75% ORR (95% CI: 68-82; CR/CRi: 1%; PR/nPR: 74%)[1]

CALQUENCE is the first and only BTKi monotherapy to demonstrate superior PFS against standard-of-care combinations, including novel agents, in relapsed/refractory CLL[1]

*Per 2008 IWCLL criteria.[1]

†At the time of analysis, the number of events in each arm was 27 (17%) for CALQUENCE and 68 (44%) for IR or BR.[1]

‡Based on a stratified Cox proportional-hazards model.[1]

§Based on a stratified log-rank test. The pre-specified type I error rate (α) for this interim analysis is 0.012 derived from a Lan-DeMets alpha spending function with O'Brien-Fleming boundary.[1]

Select Safety Information

ADVERSE REACTIONS (Cont'd)

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.

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

Safety and tolerability consistent with the established profile of CALQUENCE

COMMON ADVERSE REACTIONS (≥15%, ANY GRADE) WITH CALQUENCE IN ASCEND*[1]

Adverse reaction	CALQUENCE (n=154)		IR (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

SELECT NON-HEMATOLOGIC LABORATORY ABNORMALITIES (≥10%, ANY GRADE), NEW OR WORSENING FROM BASELINE WITH CALQUENCE IN ASCEND*[1]

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

*The median duration of exposure to CALQUENCE was 15.7 months.[1]

†Includes multiple adverse drug reaction terms (see full Prescribing Information).[1]

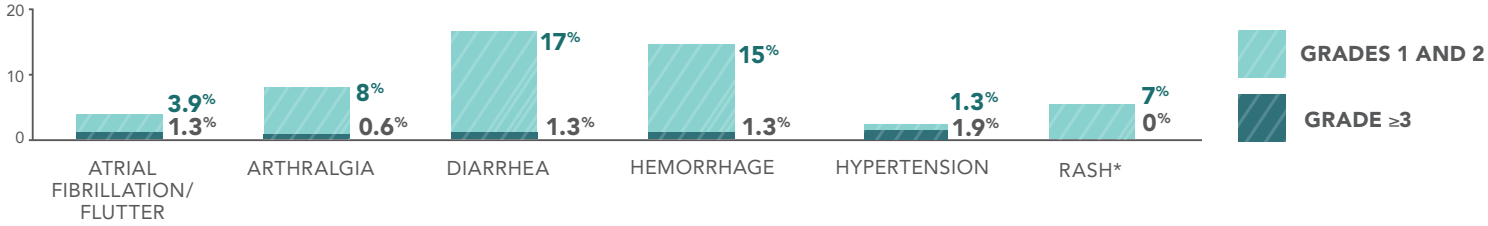
‡Includes 1 fatal case in the CALQUENCE monotherapy arm and 1 fatal case in the IR arm.[1]

§Excludes electrolytes.[1]

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

Most adverse reactions were Grade 1 or 2

SELECT ADVERSE REACTIONS FOR CALQUENCE (n=154)[1,4]



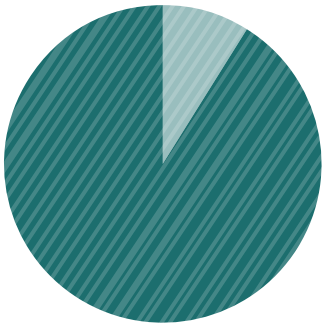
Clinically relevant adverse reactions (<15%, any grade) in recipients of CALQUENCE included[1]:

- 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%)

Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 1.3% of patients who received CALQUENCE.[1]

In the CALQUENCE arm, 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.[1]

Few patients discontinued CALQUENCE due to adverse reactions at median 16.1-month follow-up[1]



10% discontinued therapy due to adverse reactions

*Excludes dermatitis and other related terms.[1]

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

Continuous BTK inhibition through twice-daily dosing

CALQUENCE maintained a median steady-state BTK occupancy of ≥95% in peripheral blood over 12 hours, inactivating BTK throughout the recommended dosing interval[1]

BTK OCCUPANCY OVER 12 HOURS

Taking CALQUENCE[1]

Not actual capsule size.

One 100-mg capsule of CALQUENCE is taken orally twice daily

Take approximately every 12 hours until disease progression or unacceptable toxicity

CALQUENCE can be taken with or without food

Capsule should be swallowed whole with water, and should not be opened, broken, or chewed

Select Safety Information

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.

Taking CALQUENCE + obinutuzumab

CALQUENCE + OBINUTUZUMAB DOSING SCHEDULE[1]

If given on the same day, administer CALQUENCE prior to obinutuzumab. In the ELEVATE-TN trial, obinutuzumab was given 28 days after the first dose of CALQUENCE (Day 1 of Cycle 2), and was given for up to 6 cycles.[1]

Refer to the obinutuzumab Prescribing Information for recommended obinutuzumab dosing information.

Select Safety Information

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 Important Safety Information throughout and on pages 16-17, and full Prescribing Information.

CALQUENCE: a strong focus on patient education

CALQUENCECares™

CALQUENCECares™ offers your patients education and support throughout treatment with CALQUENCE

Encourage your patients to enroll for personalized education and support, including:

- Information about CLL and treatment with CALQUENCE
- Trained nurses and pharmacists who are available to help at 1-800-236-9933
- Regular mailings or e-mails with tips and information on managing treatment

Patients can register online at **CALQUENCECaresCLL.com**

AstraZeneca Access 360™

Helping patients access the care they need

The AstraZeneca Access 360™ program provides personal support to connect patients to affordability programs and streamline access and reimbursement for CALQUENCE

Access 360 provides:

- Assistance with understanding patient insurance coverage and pharmacy options
- Prior authorization support
- Claims and appeal process support
- Eligibility requirements and enrollment assistance for specialty Patient Savings Programs
- Referrals to patient assistance programs
- Referrals to nurse assistance or educational support programs, if applicable

To learn more about the AstraZeneca Access 360™ program, please call **1-844-ASK-A360 (1-844-275-2360)**, Monday–Friday, 8 AM–8 PM ET, or visit **MyAccess360.com**.

CALQUENCE Patient Savings Program for eligible commercially insured patients

The goal of the CALQUENCE Patient Savings Program is to assist eligible patients with their out-of-pocket costs for CALQUENCE.

Most eligible patients will pay $0 per month and may have access to up to $26,000 per year to assist with CALQUENCE out-of-pocket costs. There are no income requirements to participate in the program.

For additional information, please visit **astrazenecaspecialtysavings.com** or call Access 360 at **1-844-ASK-A360 (1-844-275-2360)**.

Eligibility requirements

- Must be a resident of the United States or Puerto Rico
- Patients must have commercial health insurance that covers medication costs for CALQUENCE, but not the full cost to the patient

Patients are ineligible if prescriptions are paid by any state or other federally funded programs, including, but not limited to, Medicare Part B, Medicare Part D, Medicaid, Medigap, VA or TRICARE, or where prohibited by law. Eligibility rules apply. Additional restrictions may apply.

The CALQUENCE Patient Savings Program covers the cost of the drug only, and does not cover costs for office visits, or any other associated costs.

Offer is invalid for claims and transactions more than 120 days from the date of service.

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

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).

Please see additional Important Safety Information on page 17, and full Prescribing Information.

ADVERSE REACTIONS (Cont'd)

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 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, either visit **www.FDA.gov/medwatch** or call 1-800-FDA-1088.*

References: 1. CALQUENCE [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2019. **2.** Elevate CLL TN: study of obinutuzumab + chlorambucil, acalabrutinib (ACP-196) + obinutuzumab, and acalabrutinib in subjects with previously untreated CLL. ClinicalTrials.gov identifier: NCT02475681. https://clinicaltrials.gov/ct2/show/NCT02475681. Updated October 14, 2019. Accessed November 14, 2019. **3.** Sharman JP, Banerji V, Fogliatto LM, et al. ELEVATE TN: phase 3 study of acalabrutinib combined with obinutuzumab (O) or alone vs O plus chlorambucil (Clb) in patients (pts) with treatment-naive chronic lymphocytic leukemia (CLL). Abstract for: American Society of Hematology Annual Meeting; December 7-10, 2019; Orlando, FL. **4.** Data on File, REF-64711. AstraZeneca Pharmaceuticals LP. **5.** A study of acalabrutinib vs investigator's choice of idelalisib plus rituximab or bendamustine plus rituximab in R/R CLL. ClinicalTrials.gov identifier: NCT02970318. https://clinicaltrials.gov/ct2/show/NCT02970318. Updated August 16, 2019. Accessed November 14, 2019. **6.** Ghia P, Pluta A, Watch M, et al. ASCEND phase 3 study of acalabrutinib vs investigator's choice of rituximab plus idelalisib (IDR) or bendamustine (BR) in patients with relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL). Presented at: 24th European Hematology Society Congress; June 13-16, 2019; Amsterdam, the Netherlands.