A Real-World Study Evaluating Drug Tolerability and Health Care Resource Use with Acalabrutinib Versus Ibrutinib in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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Introduction

- The Bruton tyrosine kinase inhibitors (BTKis) ibrutinib and acalabrutinib are standard of care in first-line and relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).
  - However, ibrutinib has tolerability concerns, including hypertension (HTN) and major adverse cardiovascular events (MACE).
- Acalabrutinib has demonstrated comparable progression-free survival with an improved safety profile, including a lower rate of MACE, versus ibrutinib in R/R CLL/SLL.[1]
- This study used real-world data from US community oncology practices to compare the tolerability and health care resource use (HCRU) of acalabrutinib and ibrutinib in R/R CLL/SLL, which has not been previously evaluated.

Methods

- This retrospective observational study used electronic medical record data from ONCare Alliance, a network of 32 US community oncology practices.
- This study included patients with R/R CLL/SLL who initiated acalabrutinib or ibrutinib monotherapy on or between January 1, 2017 and December 31, 2023.
- Data collected included patient and disease characteristics, tolerability (characterized by occurrence of MACE), and HCRU associated with MACE, including clinic and emergency department visits, hospital admissions, and specialist consultations.
- Time to development of first MACE was evaluated, defined as:
  - atrial fibrillation
  - new/worsening HTN
  - cardiac arrhythmia
  - venous thromboembolic event
  - myocardial infarction
  - transient ischemic attack
  - left ventricular dysfunction
  - valvular heart disease
  - congestive heart failure
  - cerebrovascular accident
  - clinically significant bleeding event
  - ventricular arrhythmia
  - cardiac death
- Time to development of MACE was analyzed using propensity score weighted multivariate Cox proportional hazards analysis.
  - Categorical variables were evaluated using the Yates corrected x^2 test.
- An estimated sample size of 90 patients receiving acalabrutinib and 180 receiving ibrutinib provided 80% power to detect an odds ratio (OR) of up to 0.40 on the primary endpoint[a] using a two-sided test statistic and $p < 0.05$ for statistical significance.
  - Patients were consecutively enrolled to meet the targeted sample size in each group.
- To control for selection bias, propensity scores were used to weight the comparative multivariate analyses.
- There were no adjustments for multiple comparisons or imputations for missing data.

[a]Primary endpoint was time to development of new/worsening HTN (data not reported in this poster).

Results

Figure 1. In total, 90 patients receiving acalabrutinib and 180 patients receiving ibrutinib were included and baseline characteristics were balanced between groups

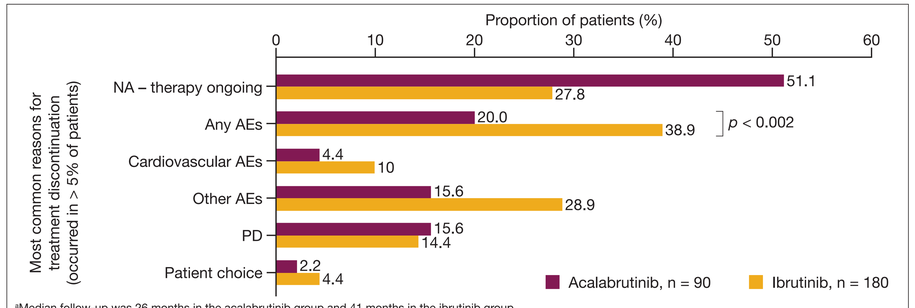
	Acalabrutinib (n = 90)	Ibrutinib (n = 180)
Median age:	75 years	70 years
ECOG PS 0:	42%	36%
ECOG PS 1:	40%	33%
ECOG PS ≥ 2:	8%	8%
Median Charlson comorbidity index:	3	3
Median SBP:	124 mmHg	130 mmHg
Median DBP:	72 mmHg	74 mmHg
History of HTN:	57%	58%

Note: full table of baseline characteristics can be found in Supplementary Table 1.
DBP, diastolic blood pressure; ECOG PS, Eastern Cooperative Oncology Group performance status; HTN, hypertension; SBP, systolic blood pressure.

The median starting daily dose and daily dose at discontinuation for acalabrutinib (both 200 mg) and ibrutinib (both 420 mg) were in line with the product labels.

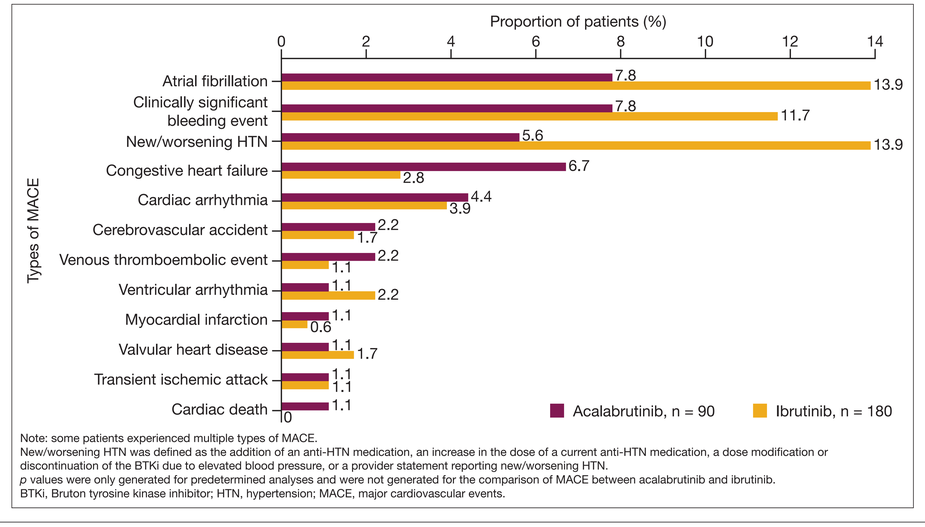
Supportive care during BTKi therapy was comparable between groups (see Supplementary Table 2).

Figure 2. After a median follow-up of 33 months,[a] drug discontinuations were less common with acalabrutinib than with ibrutinib



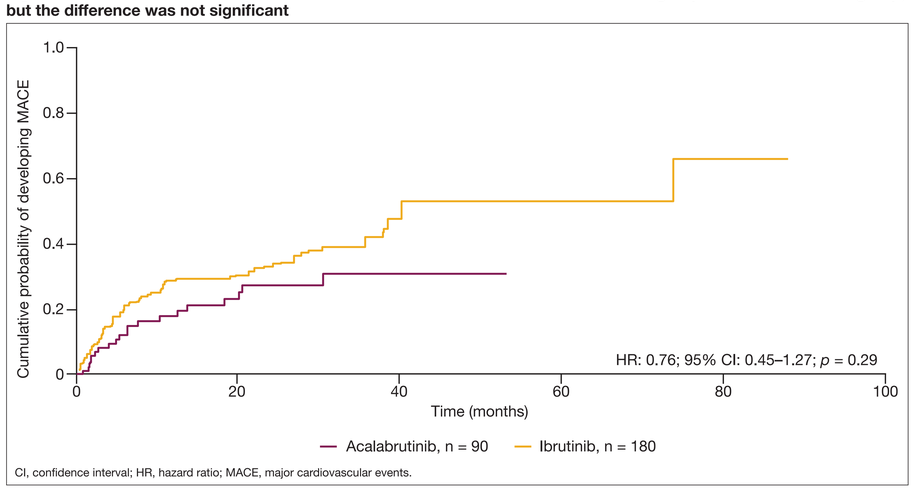
[a]Median follow-up was 26 months in the acalabrutinib group and 41 months in the ibrutinib group.
Other reasons for discontinuation for acalabrutinib versus ibrutinib were other (3.3% vs 6.1%), death (3.3% vs 3.9%), not documented (2.2% vs 0.6%), suboptimal response (2.2% vs 0.0%), physician choice (0.0% vs 2.8%), and completion of planned therapy (0.0% vs 1.1%).
AE, adverse event; NA, not applicable; PD, progressive disease.

Figure 3. Fewer MACE occurred with acalabrutinib than with ibrutinib



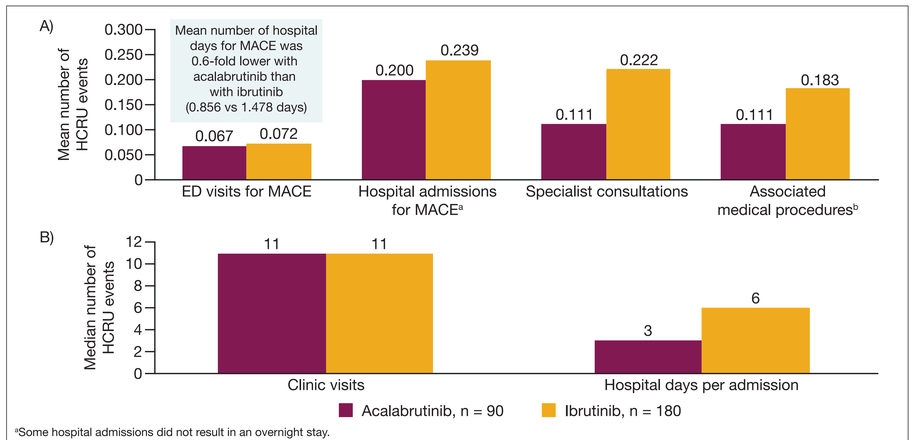
Note: some patients experienced multiple types of MACE.
New/worsening HTN was defined as the addition of an anti-HTN medication, an increase in the dose of a current anti-HTN medication, a dose modification or discontinuation of the BTKi due to elevated blood pressure, or a provider statement reporting new/worsening HTN.
p values were only generated for predetermined analyses and were not generated for the comparison of MACE between acalabrutinib and ibrutinib.
BTKi, Bruton tyrosine kinase inhibitor; HTN, hypertension; MACE, major cardiovascular events.

Figure 4. Median time to development of first MACE was reduced in the acalabrutinib group versus the ibrutinib group, but the difference was not significant



CI, confidence interval; HR, hazard ratio; MACE, major cardiovascular events.

Figure 5. Treatment with acalabrutinib reduced A) mean and B) median HCRU versus ibrutinib



[a]Some hospital admissions did not result in an overnight stay.
[b]Interventions included echocardiograms, cardiac catheterizations, and cardioversion.
p values were only generated for predetermined analyses and were not generated for the comparison of HCRU between acalabrutinib and ibrutinib.
ED, emergency department; HCRU, health care resource use; MACE, major cardiovascular events.

Conclusions

- In patients with R/R CLL/SLL, acalabrutinib monotherapy demonstrated a better tolerability profile and less HCRU due to MACE than ibrutinib.
- This translates to a lower economic burden on the health care system for acalabrutinib than for ibrutinib.

References

1. Byrd JC *et al. J Clin Oncol* 2021;39:3441–52.

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