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

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Introduction

- The development of Bruton tyrosine kinase inhibitors (BTKis) was a major advance in chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).
- The first-generation BTKi ibrutinib showed sustained 8-year progression-free survival in first-line (1L) CLL/SLL.[1]
  - However, ibrutinib has tolerability concerns, including hypertension (HTN) and major adverse cardiovascular events (MACE).
- The second-generation BTKi acalabrutinib demonstrated durable disease response with an improved safety profile versus ibrutinib in relapsed/refractory CLL/SLL.[2]
- No randomized controlled trial has compared acalabrutinib with ibrutinib in 1L CLL/SLL.
- This study used real-world data from US community practices to compare tolerability and health care resource use (HCRU) of acalabrutinib and ibrutinib in 1L CLL/SLL.

Methods

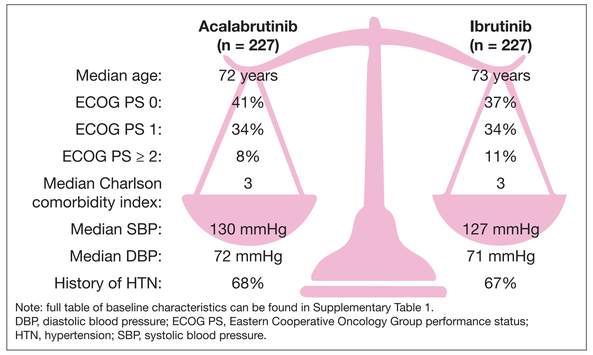
- This retrospective observational study used electronic medical record data from ONCare Alliance, a network of 32 US community oncology practices.
- This study included patients with CLL/SLL who initiated 1L acalabrutinib or ibrutinib monotherapy on or between January 1, 2017 and December 31, 2023.
- 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:

• new/worsening HTN	• atrial fibrillation
• atrial flutter	• valvular heart disease
• congestive heart failure	• cardiac arrhythmia
• ventricular arrhythmia	• myocardial infarction
• cerebrovascular accident	• clinically significant bleeding event
• transient ischemic attack	• venous thromboembolic event
• left ventricular dysfunction	• cardiac death

- Time to development of MACE was analyzed using multivariate Cox regression, with $p < 0.05$ to retain.
- To control for selection bias, propensity scores were used to weight the comparative multivariate analyses.
- An estimated sample size of 454 patients (227 per arm) provided sufficient statistical power.
  - Patients were consecutively enrolled to meet the targeted sample size in each group.
- There were no adjustments for multiple comparisons or imputations for missing data.

Results

Figure 1. In total, 454 patients (227 per group) were included and baseline characteristics were balanced between groups

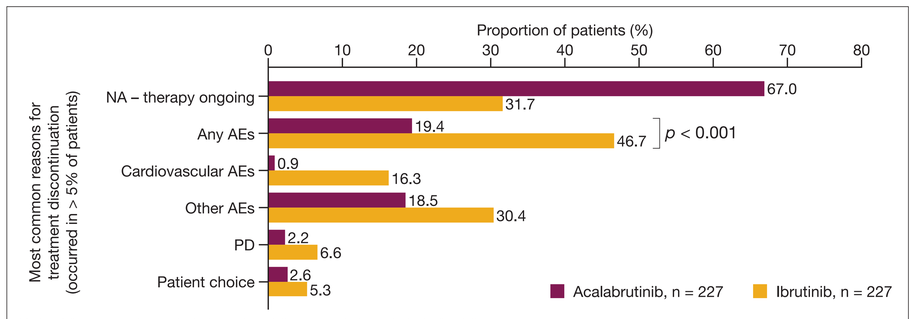


Note: full table of baseline characteristics can be found in Supplementary Table 1.
DBP, diastolic blood pressure; ECOG PS, Eastern Cooperative Oncology Group performance status; HTN, hypertension; SBP, systolic blood pressure.

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.

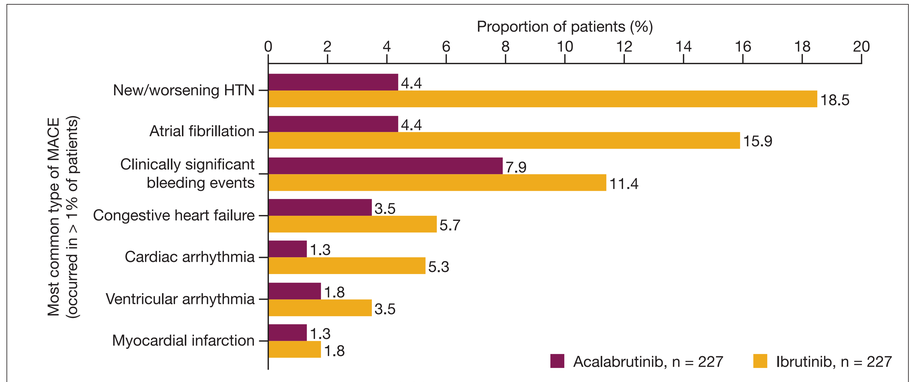
Supportive care during BTKi therapy was comparable between groups (see Supplementary Table 2).

Figure 2. After a median follow-up of 28 months,[a] drug discontinuations due to intolerability were less common with acalabrutinib than with ibrutinib



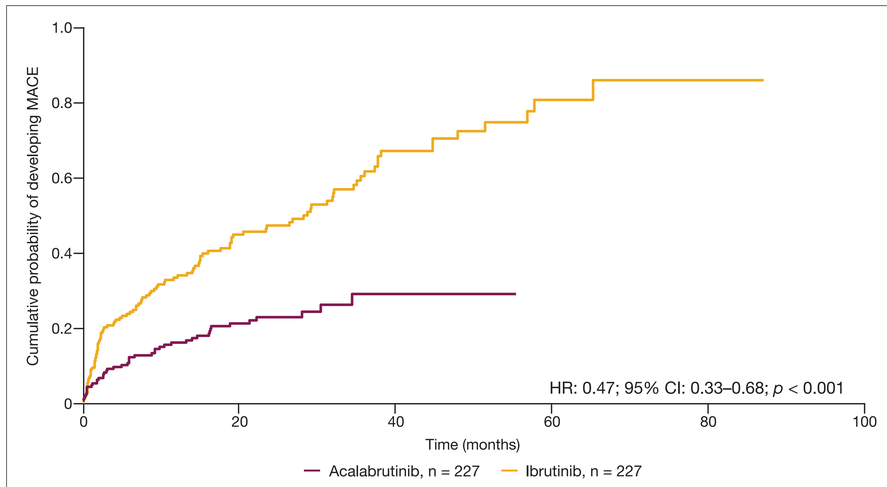
[a]Median follow-up was 25 months in the acalabrutinib group and 40 months in the ibrutinib group.
Other reasons for discontinuation for acalabrutinib versus ibrutinib were physician choice (1.8% vs 3.1%), other (2.6% vs 2.2%), suboptimal response (1.3% vs 1.8%), death (2.2% vs 1.3%), and not documented (0.9% vs 1.3%).
AE, adverse event; NA, not applicable; PD, progressive disease.

Figure 3. Fewer MACE occurred with acalabrutinib than with ibrutinib



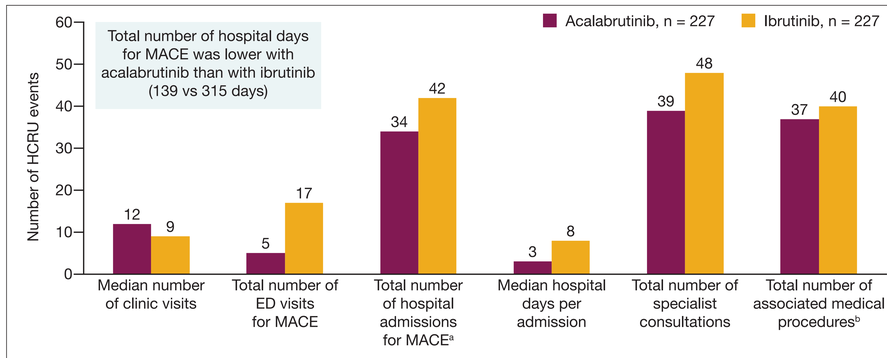
Note: some patients experienced multiple types of MACE. Other types of MACE with acalabrutinib versus ibrutinib were cerebrovascular accident (0.9% vs 0.9%), valvular heart disease (0.9% vs 0.9%), transient ischemic attack (0.4% vs 0.9%), atrial flutter (0.9% vs 0.9%), venous thromboembolic event (1.3% vs 0.4%), and left ventricular dysfunction (0.9% vs 0.4%).
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 significantly reduced in the acalabrutinib versus the ibrutinib group



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

Figure 5. Treatment with acalabrutinib reduced overall 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 1L 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. Barr PM *et al. Blood Adv* 2022;6:3440–50.
2. Byrd JC *et al. J Clin Oncol* 2021;39:3441–52.

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