PF611

Real-World Outcomes in Patients With CLL Treated With First-Line Ibrutinib or Acalabrutinib and Undergoing Dose Reductions: A Chart Review Study

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OBJECTIVE

To characterize demographics and baseline characteristics and evaluate real-world progression-free survival (PFS) and duration of treatment (DOT) in patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) undergoing dose reduction (DR) with ibrutinib or acalabrutinib

CONCLUSIONS

This real-world study demonstrates that patients with CLL/SLL treated with first-line (1L) ibrutinib and undergoing DR had similar DOT and a longer time to progression compared with patients treated with 1L acalabrutinib undergoing DR

These results indicate that DRs during ibrutinib treatment potentially lead to favorable PFS outcomes compared with DRs during acalabrutinib treatment, thus offering a valuable strategy for managing adverse events while maintaining treatment efficacy

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INTRODUCTION

- Bruton tyrosine kinase inhibitors (BTKis), including ibrutinib and acalabrutinib, are standard first-line (1L) therapy for patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)[1,2]
- Adverse events (AEs) occurring during 1L treatment with ibrutinib and acalabrutinib in CLL/SLL often lead to treatment discontinuation[3,4]
- Real-world data suggest that ibrutinib dose reductions (DRs) can mitigate AEs without compromising treatment efficacy, potentially reducing discontinuation rates[5]

METHODS

Data Source

- In this retrospective US chart review, data were abstracted from historical medical records by 142 participating physicians from academic and community practices across various US regions
- Eligible physicians were hematologists-oncologists who had >2 years of experience managing treatment of patients with CLL/SLL and had treated ≥5 patients with CLL/SLL in the past 12 months (including ≥2 patients treated with a BTKi)
- Data were abstracted using a secure, web-based, electronic data collection form (eDCF) to collect anonymized patient data

Study Population

- Adult patients aged ≥18 years with a clinician-confirmed diagnosis of CLL/SLL were included if they received 1L treatment with ibrutinib or acalabrutinib for CLL/SLL during the case selection window (October 1, 2017, through October 31, 2023)
- Patients were required to have started therapy at the standard dose of 420 mg/day for ibrutinib or 200 mg/day for acalabrutinib and to have ≥12 months of potential follow-up since the start of 1L therapy (with the exception of death)
  - Soft quotas were implemented to achieve reasonable cell sizes across analysis subgroups defined by the AE status (ie, DR due to AEs of interest and DR due to other causes)
- Patients were excluded if they had participated in clinical trials of CLL treatment, had evidence of another cancer before the diagnosis of CLL, had missing data on dates of CLL/SLL diagnosis or BTKi therapy initiation, or had a history of Richter syndrome before BTKi therapy initiation

Outcomes and Statistical Analyses

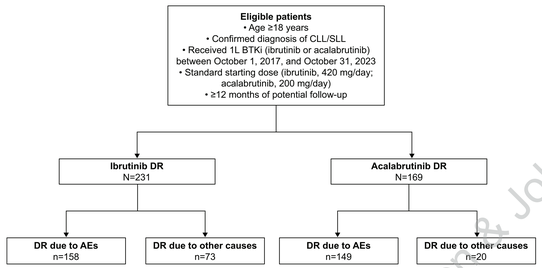
- Duration of treatment (DOT) was defined as the time from the start of 1L treatment (index date) until discontinuation or death and was assessed in patients with DR due to AEs
- Progression-free survival (PFS) was defined as the time from the start of 1L treatment until documented disease progression or death and was assessed in cohorts comprising all patients with DR and those with DR due to AEs
  - Patients with unknown date of progression were excluded from the analysis
- DOT and PFS were estimated using the Kaplan-Meier (K-M) method; patients without events were censored at last follow-up
- Hazard ratios (HRs) and 95% CIs were calculated using multivariable Cox regression analysis, adjusting for baseline characteristics, including demographics (eg, age and sex), insurance status, region, academic setting, index year, clinical characteristics (eg, number of AEs, Rai stage, Eastern Cooperative Oncology Group score, months from CLL diagnosis to index date), biomarkers where available, comorbidities and regimen type (monotherapy or combination)
- Restricted mean survival time (RMST) was estimated to address potential violation of the proportional hazards assumption

RESULTS

Study Sample and Baseline Characteristics

- The current analysis included 231 patients who underwent DR with 1L ibrutinib and 169 patients who underwent DR with 1L acalabrutinib
  - DRs were due to AEs in 158 and 149 patients treated with ibrutinib and acalabrutinib, respectively

Patient Sample and Cohorts for Analysis[a]



[a]According to prespecified soft sampling quotas.

Baseline Characteristics Across Cohorts

Baseline characteristics	Ibrutinib DR		Acalabrutinib DR	
	Due to AE n=158	Due to other causes n=73	Due to AE n=149	Due other causes n=20
Median age at index date (range), years	65.2 (22.8–87.1)	65.5 (41.2–80.4)	64.3 (21.5–93.5)	65.7 (30.3–76.8)
Male, n (%)	95 (60.1)	40 (54.8)	93 (62.4)	9 (45.0)
Median follow-up (range), months	28.5 (12.0–80.1)	32.7 (12.5–65.9)	22.6 (9.9–76.8)	29.7 (15.2–62.0)
High-risk features, n (%)				
del(17p)	30 (19.0)	7 (9.6)	40 (26.9)	5 (25.0)
TP53 mutation	16 (10.1)	7 (9.6)	24 (16.1)	7 (35.0)
del(11q)	16 (10.1)	7 (9.6)	15 (10.1)	2 (10.0)
Median CCI score (range)	1 (0–5)	1 (0–4)	1 (0–5)	1 (0–5)
Comorbidities, n (%)[a]				
Hypertension	63 (39.9)	22 (30.1)	61 (40.9)	4 (20.0)
Thyroid disease	28 (17.7)	18 (24.7)	9 (6.0)	2 (10.0)
Depression	25 (15.8)	8 (11.0)	18 (12.1)	2 (10.0)
History of tobacco use/ smoking	22 (13.9)	16 (21.9)	16 (10.7)	3 (15.0)
Diabetes without end-organ damage	21 (13.3)	17 (23.3)	31 (20.8)	4 (20.0)
Peptic ulcer disease	17 (10.8)	0	6 (4.0)	0
Chronic obstructive pulmonary disease	8 (5.1)	0	11 (7.4)	2 (10.0)
Myocardial infarction	6 (3.8)	3 (4.1)	10 (6.7)	1 (5.0)
Atrial fibrillation/other arrhythmia	5 (3.2)	2 (2.7)	7 (4.7)	0
Congestive heart failure	4 (2.5)	0	14 (9.4)	0
Dementia	4 (2.5)	8 (11.0)	6 (4.0)	4 (20.0)
Peripheral vascular disease	3 (1.9)	1 (1.4)	8 (5.4)	2 (10.0)

CCI, Charlson Comorbidity Index.
[a]Comorbidities present at or within 12 months of the index date in ≥3% of patients in the overall ibrutinib or acalabrutinib cohorts are reported.

Duration of Treatment

- Overall, the median follow-up duration since 1L treatment initiation was 30.5 months for patients with ibrutinib DR and 23.5 months for those with acalabrutinib DR
  - Median follow-up durations were 28.5 and 22.6 months, respectively, for the subset of patients with DR due to AEs
- The median time to first DR was 6.8 months with ibrutinib and 5.1 months with acalabrutinib
  - Median time to first DR was 5.1 and 4.7 months, respectively, in the subset of patients with DR due to AEs
- In patients with DR due to AEs, K-M estimates showed no statistically significant difference in DOT between ibrutinib and acalabrutinib (adjusted HR, 0.78; 95% CI, 0.50–1.22; *P*=0.272)
- In the RMST analysis, mean DOT among patients with DR due to AEs was 28.4 months with ibrutinib and 28.5 months with acalabrutinib (*P*=0.945)

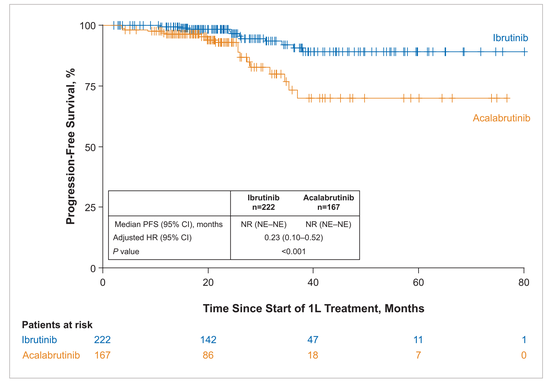
K-M Estimates of DOT Were Similar With Ibrutinib Versus Acalabrutinib Among Patients With DR Due to AEs

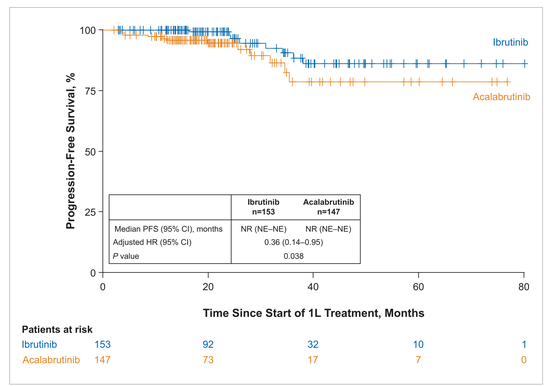
NE, not estimable; NR, not reached.

Progression-Free Survival

- Among all patients with DR, K-M estimates of PFS showed a statistically significant reduction in the risk of progression or death with ibrutinib versus acalabrutinib (adjusted HR, 0.23; 95% CI, 0.10–0.52; *P*<0.001)
  - Median PFS was not reached with either ibrutinib or acalabrutinib, with 36-month PFS rates of 92.2% for ibrutinib and 73.5% for acalabrutinib
- Likewise, K-M estimates of PFS showed a statistically significant reduction in the risk of progression or death with ibrutinib versus acalabrutinib among patients with DR due to AEs (adjusted HR, 0.36; 95% CI, 0.14–0.95; *P*=0.038)
  - Median PFS was not reached with either ibrutinib or acalabrutinib, with 36-month PFS rates of 90.7% and 78.7%, respectively
- In the RMST analysis, mean PFS among all patients with DR was 36.0 months for ibrutinib versus 33.9 months for acalabrutinib (*P*=0.006)
  - Mean PFS among patients with DR due to AEs was 34.6 months for ibrutinib versus 33.4 months for acalabrutinib (*P*=0.073)

K-M Estimates of PFS Were Significantly Better With Ibrutinib Versus Acalabrutinib Among (A) All Patients With DR and (B) Patients With DR Due to AEs





Limitations

- This study included a convenience sample of physicians who were willing to participate, which may limit the generalizability of the findings to all patients with CLL/SLL
- Information captured in the eDCF was limited to data available in the patients' medical records and may not include information on healthcare received outside of the physician's care setting
- Although data validation mechanisms were incorporated into the eDCF to reduce the risk of data entry errors, data may be subject to entry errors or reporting inaccuracies

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