Real-World Characteristics and Outcomes of Patients With Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Treated With Long-Term Ibrutinib: Results From the Prospective, Observational informCLL Registry

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OBJECTIVE

To present the real-world characteristics and outcomes of previously untreated patients with CLL who received long-term (≥3 years) 1L treatment with ibrutinib while enrolled in the informCLL Registry

CONCLUSIONS

Baseline characteristics did not influence maintenance on long-term ibrutinib therapy, suggesting that patients with CLL with a broad range of baseline characteristics can benefit from long-term therapy with 1L ibrutinib

Analyses from the informCLL Registry show sustained time-to-next-treatment and OS benefits in patients treated with ≥3 years of ibrutinib

Consistent with the recent findings from RESONATE-2,[1] patients in this real-world registry who had dose modifications were able to receive long-term therapy with 1L ibrutinib with low occurrence of treatment discontinuation due to AEs

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INTRODUCTION

- Recent analyses from the phase 3 RESONATE-2 study of patients with previously untreated chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) showed that more than half of patients treated with ibrutinib continued to benefit from long-term ibrutinib therapy for ≥5 years regardless of baseline characteristics and had sustained efficacy benefits[1]
  - Ibrutinib, a once-daily oral Bruton tyrosine kinase inhibitor, is the only targeted therapy to demonstrate significant overall survival (OS) benefit in randomized phase 3 studies of first-line (1L) treatment of CLL/SLL[2,3]
  - Limited data are available on patient characteristics associated with long-term ibrutinib treatment in the real-world setting
- The informCLL Registry is a large, US-based, prospective, observational registry of patients who initiated treatment for CLL/SLL after the US Food and Drug Administration (FDA) approval of ibrutinib in 2013 and represents an opportunity to explore real-world outcomes in patients primarily treated in community-based practices

METHODS

PCYC-1134 Study Design

- Patients diagnosed with CLL/SLL who initiated FDA-approved treatment (within ±45 days of enrollment) were enrolled between October 2015 and June 2019
- The following outcomes were assessed:
  - Baseline demographics and characteristics
  - Time to next treatment
  - OS
  - Baseline factors associated with receiving long-term ibrutinib
  - Safety (in patients treated with 1L ibrutinib for ≥3 years)
  - Patient-reported outcomes
    - Health-related quality of life was assessed by the Functional Assessment of Cancer Therapy–General (FACT-G) questionnaire[4]
    - Questionnaires were completed by all patients at baseline, at 3 and 6 months, every 6 months thereafter, and at end of study or discontinuation

RESULTS

- A total of 1459 eligible patients were enrolled in the informCLL Registry; of the 383 patients treated with 1L ibrutinib, 100 patients (26%) received ≥3 years of ibrutinib therapy, and the median treatment duration was 44 months (range, 36–61)
- At study exit, 161 patients (42%) treated with ibrutinib were still receiving the drug, including 82 patients whose treatment lasted <3 years due to study closure

Characteristic	≥3 Years n=100	<3 Years Due to Reasons Not Related to Study Closure n=201[a]	<3 Years Due to Study Closure n=82[a]	Total N=383
Median age (range), years	70 (40–90)	74 (41–89)	70 (45–87)	72 (40–90)
Age ≥65 years, n (%)	70 (70)	156 (78)	58 (71)	284 (74)
Age ≥75 years, n (%)	33 (33)	89 (44)	25 (30)	147 (38)
Male, n (%)	59 (59)	123 (61)	51 (62)	233 (61)
Median time from initial diagnosis to treatment at registry enrollment (range), months	21.9 (0.2–241)	21.3 (<0.1–471)	19.5 (0.2 –398)	21.3 (<0.1–471)
Race, n (%)				
White	90 (90)	184 (92)	72 (88)	346 (90)
Black/African American	9 (9)	14 (7)	6 (7)	29 (8)
American Indian/Alaska Native	0	2 (1)	0	2 (<1)
Unknown/not available	1 (1)	1 (<1)	4 (5)	6 (2)
ECOG performance status, n (%)				
0	45 (45)	86 (43)	48 (59)	179 (47)
1	49 (49)	100 (50)	30 (37)	179 (47)
≥2	2 (2)	13 (6)	3 (4)	20 (5)
Rai stage III/IV, n/N (%)	33/64 (52)	58/131 (44)	28/62 (45)	119/257 (46)
del(17p), n/N (%)	16/57 (28)	21/103 (20)	12/51 (24)	49/211 (23)
History of other malignancy, n (%)	25 (25)	58 (29)	17 (21)	100 (26)
Median CCI score (range)	1 (0–4)	1 (0–6)	1 (0–7)	1 (0–7)
CCI score ≥2, n (%)	22 (22)	66 (33)	20 (24)	108 (28)
Number of sites	62	102	57	132
Institution/site type (%)				
Community	59/62 (95)	93/102 (91)	51/57 (89)	122/132 (92)
Academic	3/62 (5)	9/102 (9)	6/57 (11)	10/132 (8)

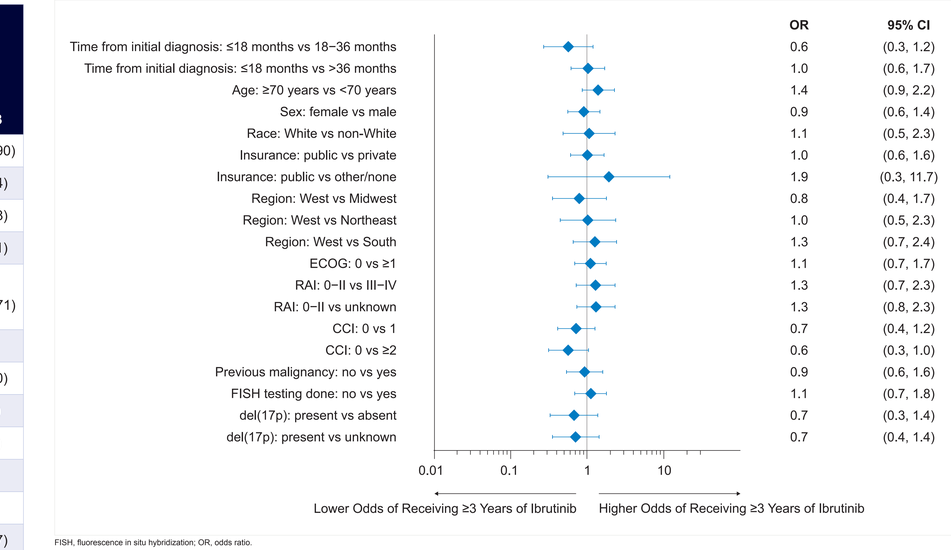
CCI, Charlson Comorbidity Index; ECOG, Eastern Cooperative Oncology Group.

[a]Because baseline characteristics were largely similar between the subgroups with <3 years of ibrutinib treatment due to study exit (n=82) and for reasons non-related to study exit (n=201), these subgroups were combined as the <3 years treatment group (n=283).

Factors Associated With Receiving Long-Term Ibrutinib Therapy

- In univariate analysis, high comorbidity burden (CCI ≥2) approached significance as a factor associated with lower odds of receiving ibrutinib for ≥3 years

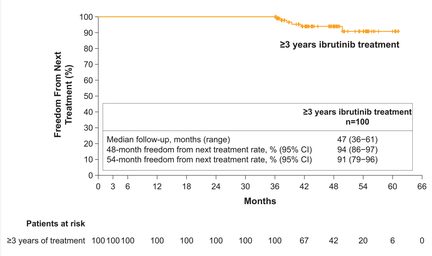
Baseline Characteristics Did Not Influence Patients Receiving Long-Term Ibrutinib Therapy



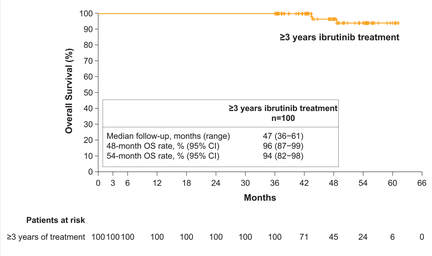
FISH, fluorescence in situ hybridization; OR, odds ratio.

Time to Next Treatment and OS

Longer Duration (≥3 Years) of Ibrutinib Therapy Was Associated With >90% of Patients Remaining Without Next-Line Therapy at 48 and 54 Months



OS Among Patients Receiving ≥3 Years of Ibrutinib Therapy Was ≥94% at 48 and 54 Months



Safety

Longer Duration (≥3 Years) of Ibrutinib Use Was Associated With Infrequent Discontinuation Due to AEs

Patients With AEs, n (%)	≥3 Years Ibrutinib Treatment n=100
Any AE	55 (55)
Serious AE	32 (32)
Reported in >3 patients	
Pneumonia	5 (5)
Atrial fibrillation	4 (4)
AE leading to discontinuation	7 (7)
Confusional state	1 (1)
Increased hepatic enzyme	1 (1)
Mucosal inflammation	1 (1)
Myalgia	1 (1)
Palmar-plantar erythrodysesthesia	1 (1)
Richter syndrome	1 (1)
AE leading to dose modification	19 (19)
AE resolved	50 (91)

AE, adverse event.

- 19 patients (19%) had to modify the ibrutinib dose because of an AE; 14 patients continued until study closure, and 5 patients discontinued
  - 3 of 19 patients with dose modifications due to AEs were subsequently re-escalated to the 420 mg dose
  - Median time to first dose modification was 8 months (range, 0.2–41)
  - Median treatment duration after first dose modification was 38 months (range, 6–56)

Patient-Reported Outcomes

- Clinically meaningful differences in FACT-G scores were not observed between the ≥3 year and <3 year ibrutinib treatment groups over time

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