Clinical Outcomes Beyond Progression on Ibrutinib in Patients with Chronic Lymphocytic Leukemia

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CLL-506

Background

- Disease progression and toxicity are the most common reasons for ibrutinib discontinuation.[1,2]
- Patients who stop ibrutinib due to disease progression have worse progression-free and overall survival compared to patients discontinuing ibrutinib due to toxicity.
  - PFS[1] ~9-10 vs. ~15-16 months
  - OS[3] 16 vs. 33 months

A better understanding of expected outcomes in patients with true disease progression on ibrutinib is necessary to establish a benchmark for evaluating future studies.

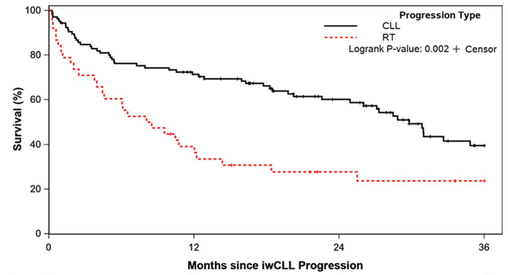
Methods

- Date of progression according to 2018 iwCLL guidelines was ascertained for patients with CLL treated with ibrutinib at a Mayo Clinic Cancer Canter site.
- Treatment-free survival was analyzed as the duration from the start of treatment immediately after ibrutinib failure to the start of the subsequent line therapy or death, whichever occurred earlier.
- Overall survival was analyzed as the time from date of progression while on ibrutinib and from subsequent therapy start date until date of death or last known to be alive.
- Overall and treatment-free survival were analyzed using the Kaplan-Meier method (with comparisons by characteristics analyzed by the log rank test) and Cox proportional hazards model.

Patient and Disease Characteristics

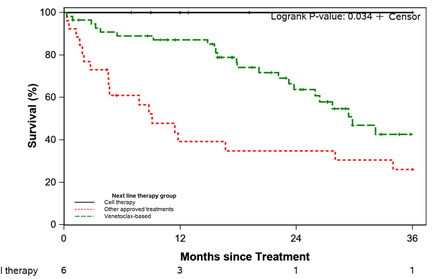
Parameter		Number (%) or Median [range]	
		At Ibrutinib Start	At Progression on Ibrutinib
Age, years		65 [40-91]	68 [43-92]
Males		106 (74%)	
Frontline therapy		23 (16%)	
Rai stage	0	24 (17%)	31 (22%)
	I-II	52 (37%)	40 (28%)
	III-IV	66 (46%)	72 (50%)
	Missing	2	1
Absolute Lymphocyte Count (x 10^9/L)		24.3 [0.3-357.2]	7.6 [0.1-244.3]
	Missing	10	7
IGHV mutation status	Unmutated	100 (90%)	
	Missing	33	
FISH	None detected	18 (14%)	15 (13%)
	Other	2 (2%)	3 (3%)
	13q-	18 (14%)	20 (18%)
	Trisomy 12	13 (10%)	13 (11%)
	11q-	22 (18%)	15 (13%)
	17p-	53 (42%)	48 (42%)
	Missing	18	30
TP53 Disruption (either del17p or *TP53* mutation)	Abnormal	57 (45%)	57 (50%)
	Missing	18	29

Post-Progression Overall Survival

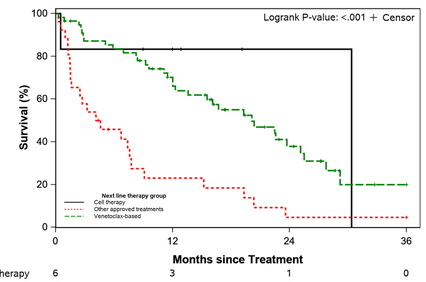


- Median overall survival for the entire cohort after progression on ibrutinib was 25.5 months; 29.8 months for patients with CLL disease progression and 8.3 months following Richter transformation.

Post-Progression Overall and Treatment-free Survival by Subsequent Therapy

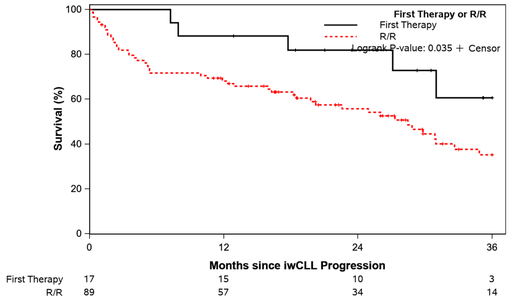


- Median overall survival was longer among patients treated with CAR T (not reached) or venetoclax-based regimens (29.8 months) compared to other approved treatments, such as chemoimmunotherapy, PI3K inhibitors (9.1 months).

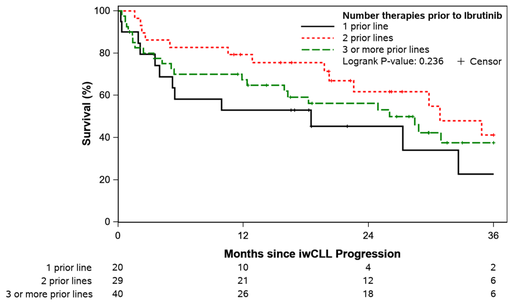


- Median treatment-free survival with CAR T (30.4 months) and venetoclax-based regimens (20.1 months) were significantly longer than with other approved treatments (4.4 months).

Post-Progression Overall Survival by Line of Therapy

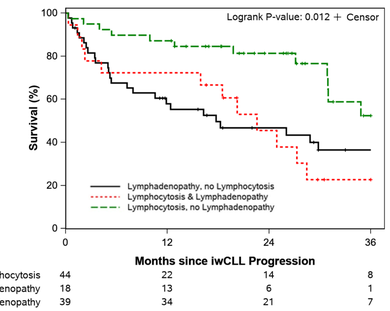


- Median overall survival was longer amongst patients who experienced CLL disease progression on ibrutinib as frontline therapy (not reached) compared to those treated with ibrutinib in the relapsed/refractory setting (28.5 months).



- Median overall survival after CLL disease progression was similar amongst patients treated in the relapsed/refractory setting, whether ibrutinib was used after 1, 2, or 3+ prior lines of therapy.

Post-Progression Overall Survival by Progression Pattern



- Median overall survival of patients with CLL disease progression on ibrutinib was longest among patients with lymphocytosis without lymphadenopathy (46.7 months compared to 17.7 months [lymphadenopathy alone] and 22.6 [lymphadenopathy and lymphocytosis])

Discussion

- These findings suggest an unmet need for this growing patient population while supporting the current practice of next-line venetoclax-based treatment and participation in clinical trials.
- The impact of pattern of progression and associated resistance mechanisms requires further study.
- The current study is limited by its retrospective nature and the primarily relapsed/refractory treatment setting.

References

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