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POSTER ABSTRACTS

642.CHRONIC LYMPHOCYTIC LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Clinical Outcomes with Venetoclax-Based Treatment Regimens in Patients with Chronic Lymphocytic Leukemia (CLL)

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INTRODUCTION
We aim to identify factors that impact outcomes of venetoclax for patients with CLL treated in routine practice at a tertiary center. We report on the use of venetoclax in the most frequently encountered disease scenarios: first-line, relapsed/Bruton tyrosine kinase inhibitor (BTKi)-naïve, and relapsed/BTKi-exposed.
METHODS
We identified patients who received venetoclax therapy for CLL (between 4/2012-4/2023) from the Mayo Clinic CLL Database. Undetectable measurable residual disease (uMRD) was defined as <1 CLL cell per 10,000 leukocytes using 8-color flow cytometry on peripheral blood (PB) or bone marrow (BM). Overall survival (OS) was defined as the time from venetoclax start until date of death or last known to be alive. Treatment-free survival (TFS) after venetoclax was defined as the time from venetoclax start until the earliest of date of next treatment, or death. Kaplan-Meier was used to display OS and TFS. Multivariable Cox proportional hazards regression models were used to estimate associations of factors with time-to-event outcomes.
RESULTS
A total of 155 patients received venetoclax: firstline therapy (in combination with obinutuzumab, n=55) and relapsed CLL (n=100; 17 had relapsed/BTKi-naïve CLL, and 83 had previously received BTKi [55 with progression after BTKi], relapsed/BTKi-exposed). The median follow-up for the cohorts of first-line therapy, relapsed/BTKi-naïve, and relapsed/BTKi-exposed was 12.9 months, 37.0 months, and 27.6 months, respectively. Baseline characteristics at the time of venetoclax initiation for all patients are shown in *Table 1*. The median TFS for the overall cohort was 39.0 months. The median OS was 54.6 months.
Among patients treated with venetoclax as first-line therapy (n=55), the 2-year TFS (*Figure 1*) and 2-year OS rates were both 91%. MRD testing was performed in 28 patients and was uMRD in 23 (82%) patients (only PB assessed, n=7; only BM assessed, n=2; PB and BM assessed, n=14). Detectable MRD was identified in 3 patients, and 2 patients had discordant results (PB uMRD and BM detectable disease).
Among patients treated with venetoclax in the relapsed/BTKi-naïve setting (n=17), the 2-year TFS rate was 73% (*Figure 1*) and the 2-year OS rate was 100%. MRD testing was performed in 7 patients and was uMRD in all 7 (100%) (only PB assessed, n=3; only BM assessed, n=2; PB and BM assessed, n=2). The median time to first uMRD result was 14.1 months.
Among relapsed/BTKi-exposed venetoclax-treated patients (n=83), the median TFS was 26.9 months (*Figure 1*), and the median OS was 39.4 months.In this subgroup, the median TFS for patients with (n=55) and without (n=28) prior disease

progression on prior BTKi were 22.3 and 42.3 months, respectively. Median TFS with venetoclax monotherapy (n=30) was 24.0 months, venetoclax in combination with rituximab (n=37) was 26.9 months, and venetoclax in combination with obinutuzumab (n=16) was 39.0 months. BTKi-exposed patients that were chemotherapy-naïve (n=27) and chemotherapy-exposed (n=56) had median TFS of 29.1 and 24.0 months, respectively. MRD testing was performed in 28 patients and was uMRD in 16 (57%) patients (only PB assessed, n=9; only BM assessed, n=2; PB and BM assessed, n=5). Detectable MRD was identified in 11 patients, and 1 had discordant results (PB uMRD and BM detectable disease). The median time to first uMRD result was 11.5 months.

TP53 disruption, unmutated *IGHV* genes, older age, complex karyotype (CK; defined as more than 3 chromosomal aberrations on CpG stimulated karyotype), and disease progression on prior BTKi were associated with shorter TFS in the overall cohort on univariate analysis. *TP53* disruption, older age, CK, and disease progression on prior BTKi were associated with shorter OS in the overall cohort on univariate analysis. Multivariable analysis was performed by including only those patients where all variables significant in univariable analysis were available (OS model n=65, TFS model n=53). In these models, only CK was significantly associated with shorter TFS (HR 8.5; 95%CI 2.5-29.1; P<0.001) and shorter OS (HR 4.1; 95%CI 1.2-14; P=0.03).

CONCLUSIONS

Patients with BTKi-exposed CLL, particularly those with prior disease progression on BTKi, had worse outcomes. Our study identified CK as one of the most important baseline predictors of adverse TFS and OS in the overall cohort of patients, supporting karyotype assessment for prognostication prior to venetoclax treatment.

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Table 1: Baseline characteristics at the time of venetoclax start

Parameter		Number (%) or Median [range]			
		All patients	Firstline	Relapsed/ BTKi-naïve	Relapsed/BTKi-exposed
N		**155**	**55**	**17**	**83**
Age, years		66 [41-93]	65 [41-84]	67 [51-83]	68 [43-93]
Males		108 (70)	36 (66)	12 (71)	60 (72)
Prior lines of therapy		1 [0-11]	0	1 [1-6]	3 [1-11]
Combination with anti-CD20mAb	Rituximab	45 (29)	0 (0)	8 (47)	37 (45)
	Obinutuzumab	80 (52)	55 (100)	9 (53)	16 (19)
	Monotherapy	30 (19)	0 (0)	0 (0)	30 (36)
Rai stage, n=148	0	20 (14)	2 (4)	2 (13)	16 (20)
	I-II	62 (42)	30 (58)	5 (31)	27 (34)
	III-IV	66 (45)	20 (39)	9 (56)	37 (46)
Absolute Lymphocyte Count (x 10^9/L)*, n=150		22.4 [0-539]	80.7 [0-539]	16.2 [4-108]	13.0 [0.3-533]
IGHV mutation status*, n=129	Unmutated	93 (72)	20 (39)	8 (57)	8 (13)
FISH*, n=134	None detected	20 (15)	11 (21)	4 (27)	5 (8)
	Other	5 (4)	0 (0)	0 (0)	5 (8)
	13q-	34 (25)	16 (30)	4 (27)	14 (21)
	Trisomy 12	23 (17)	11 (21)	2 (13)	10 (15)
	11q-	28 (21)	13 (25)	4 (27)	11 (17)
	17p-	24 (18)	2 (4)	1 (7)	21 (32)
Complex karyotype*, n=69	Complex (≥3 abnormalities)	27 (39)	3 (12)	3 (38)	21 (58)
TP53 Disruption (either del17p or *TP53* mutation)*, n=136	Present (Abnormal)	32 (24)	2 (4)	2 (13)	28 (41)

*not available for all patients

Figure 1: Treatment-free survival from the start of venetoclax for patients grouped by disease scenario

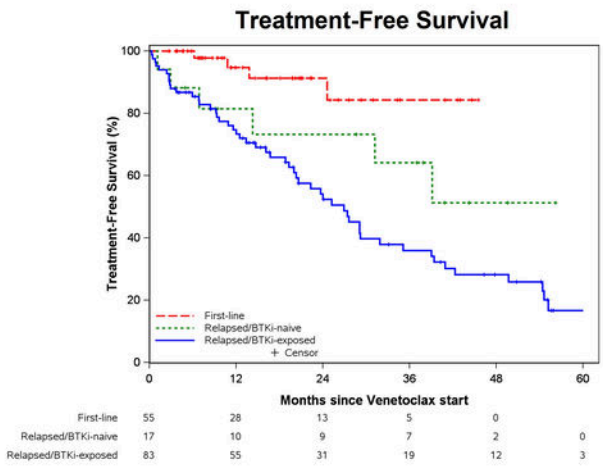

Figure 1

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