Outcomes of Patients Treated with Venetoclax-Based Combination Therapy in Acute Myeloid Leukemia and High-Grade Myeloid Neoplasms; Real World Data from A Single Center Cohort

Bilal Ashraf, MD, Haekyung Jeon-Slaughter, PhD, Hang Nguyen, MS, Fieke Hoff, MD, PhD, Jude Khatib, MD, Hetalkumari Patel, PharmD, Madhuri Vusirikala, MD, Robert H. Collins, MD, Olga Weinberg, MD Stephen Chung, MD, Yazan F. Madanat, MD

UT Southwestern Medical Center, Department of Internal Medicine, Division of Hematology-Oncology

UT Southwestern Medical Center

Background

The outcomes of older patients with acute myeloid leukemia (AML) ineligible for intensive chemotherapy remain poor. The addition of venetoclax (ven) to HMAs or low dose cytarabine has become the standard of care based on the VIALE-A and VIALE-C trials. VIALE-A excluded patients with prior HMA therapy, and both trials excluded patients with relapsed or refractory AML (RR-AML). We investigated the outcomes of patients treated with ven-based therapy in both newly diagnosed and R/R settings.

Methods

Population:
Patient diagnosed with AML between 2/1/2018 and 2/1/2022 who completed at least once cycle of ven-based therapy at our center were extracted from the medical record.

Data Collection:
Clinical and cytogenetic data were collected via chart review. Next generation sequencing data evaluating a panel of genes commonly mutated in AML was extracted. Response to treatment was assessed using the International Working Group (IWG) criteria.

Data Interpretation
Variables were compared using Fisher's exact test, t-test, and chi-square test where applicable. Overall survival (OS) was calculated from ven initiation and estimated using Kaplan-Meier survival analysis. The relationship between factors associated with response and survival were assessed via multivariable cox-regression.

Results

Table 1. Descriptive Demographics (n=69)

Category		Results	
Age	Years	Median (range)	71.0 (27.9, 87.6)
Gender	Female	Female, n (%)	35 (50.7)
Status	Alive	Alive, n (%)	25 (36.2)
Duration of follow up	Months	Median months to death/last follow up (range)	7.0 (0.4, 42.3)

Table 2. Venetoclax Use Descriptive Statistics (n=69)

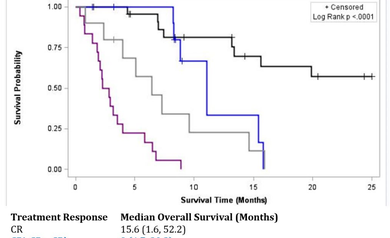
Category		
Venetoclax Use		
Newly Diagnosed	N (%)	41 (59.4)
Relapsed/Refractory	N (%)	28 (40.6)
AML ELN Risk		
Favorable	N (%)	5 (7.3)
Intermediate	N (%)	11 (15.9)
High	N (%)	53 (76.8)
Prior AML Therapy		
Yes	N (%)	26 (37.7)
No	N (%)	43 (62.3)
Number of Lines of Prior Therapy	Median (Range)	2 (1, 5)
Prior HMA Therapy		
Yes	N (%)	28 (40.6)
No	N (%)	40 (58.0)
N/A	N (%)	1 (1.5)
Number of Cycles of HMA	Median (Range)	3.5 (1, 30)
Best Response		
CR, CRi, CRh, CRp	N (%)	39 (56.5)
Overall Response	N (%) (All except for PD and NR)	51 (73.9)
PD or NR	N (%)	18 (26.1)
Other (MLFS, PR)	N (%)	10 (14.5)
N/A	N (%)	2 (2.9)
Number of Cycles to Best Response	Median (Range)	1 (1, 6)

Table 3. Venetoclax Response Rates vs Prior HMA Use, Disease Status, Cytogenetic Risk, and Genomic Anomalies (n=69)

Category			Complete Remission (CR, CRi, CRh, CRp)		P-Value
			Yes (n=39)	No (n=30)	
Prior HMA Use	Yes	N (%)	15 (38.5)	13 (43.3)	0.4547 #
Disease Status					0.4535 #
	Newly Diagnosed	N (%)	25 (64.1)	16 (53.4)	
	R/R	N (%)	14 (35.9)	14 (46.6)	
Cytogenetic Risk					0.0003 #
	Favorable	N (%)	1 (2.5)	0 (0)	
	Intermediate	N (%)	26 (66.7)	7 (23.3)	
	High	N (%)	12 (30.8)	20 (66.7)	
	NA	N (%)	0 (0)	3 (10.0)	
Total Genetic Abnormalities	Mean ± SD		2.7 ± 1.8	2.5 ± 1.7	0.5166 +
TET2 Abnormality	Yes	N (%)	8 (20.5)	7 (23.3)	0.7783 *
IDH 1/2 Abnormality	Yes	N (%)	16 (41.3)	3 (10.0)	0.0042 *
FLT3-ITD Abnormality	Yes	N (%)	7 (18.0)	0 (0)	0.0161 #
NPM1 Abnormality	Yes	N (%)	8 (20.5)	1 (3.3)	0.0672 #
DNMT3A Abnormality	Yes	N (%)	10 (25.6)	4 (13.3)	0.2076 *
NRAS Abnormality	Yes	N (%)	4 (10.3)	3 (10.0)	1.0000 #
RUNX1 Abnormality	Yes	N (%)	10 (25.6)	5 (16.7)	0.3703 *
TP53	Yes	N (%)	5 (12.8)	6 (20.0)	0.5140 *

Notes: #: Fisher's exact test; *: Chi-square test; +: t-test

Figure 1. Survival Analysis for Response at 2 Months



Treatment Response	Median Overall Survival (Months)
CR	15.6 (1.6, 52.2)
CRi, CRp, CRh	9 (4.7, 20.2)
NR, PD	4.2 (0.6, 22.8)
PR, MLFS	8.8 (4.2, 24.3)

Figure 2. Survival Analysis for Disease Class

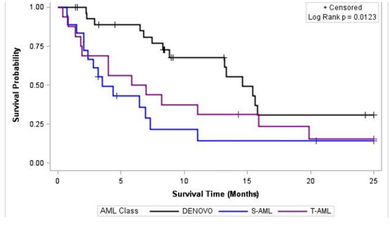
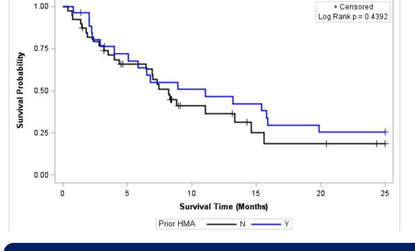


Figure 3. Survival Analysis for Prior HMA Therapy



Discussion

This study of real-world outcomes with ven-based therapy in AML assessed factors associated with and predictive of treatment response and OS. In this cohort, patients with denovo AML had improved OS compared with t-AML/sAML. The only factor predictive of improved outcomes in our cohort was having an IDH1/2 mutation. There was no additional association between mortality and any of the other identified genetic abnormalities, likely given the small size of this cohort. OS was particularly poor in patients with R/R AML. We also found no relationship between prior HMA therapy and OS. More studies are needed to further delineate the role of venetoclax based combinations in the relapsed/refractory settings.