SOHO ANNUAL MEETING 2024

Outcomes of Azacitidine-Venetoclax therapy in upfront and relapsed/refractory setting in Acute Myeloid Leukemia: Real world experience from India

Shouriyo Ghosh[1], MBBS, MD, DM, Sharthak Ghosh[2], Btech, Sutapa Chatterjee[3], Msc, Arijit Nag[1], MBBS, MRCP, DM, Debranjani Chattopadhyay[1], MBBS, MD, DM, Dibakar Podder[1], MBBS, MD, DM, Jeevan Kumar[1], MBBS, MD, DNB, Rizwan Javed[1], MBBS, MD, Asish Rath[4], MBBS, MD, DM, Deepak Mishra[4], MBBS, MD, Sushant Vinarkar[4], MBBS, MD, Mayur Parihar[4], MBBS, MD, Reena Nair[1], MBBS, MD

1 - Clinical Haematology and Cellular Therapies, Tata Medical Center, Kolkata, India, 2 – Dell Technologies Inc., 3 – Clinical Trials Unit, Tata Medical Center, India, 4 – Department of Laboratory Haematology, Tata Medical Center, India

TATA MEDICAL CENTER

CONTEXT

- The VIALE-A trial led to approval of Azacitidine-Venetoclax (Aza-Ven) combination in the treatment of acute myeloid leukemia (AML) patients, ineligible for intensive chemotherapy (IC)
- Although not approved, there is emerging data of this combination in the relapsed/refractory (R/R) setting

AIMS AND OBJECTIVES

- To analyze outcomes of Aza-Ven treatment in frontline and R/R settings in AML
  - Outcome measures: Overall response (ORR) including Complete remission (CR) Partial response (PR), and Morphological leukemia free state (MLFS) – as per ELN 2022 criteria
  - Duration of response (DOR)
  - Event free and Overall survival (EFS and OS)
  - Predictors of response

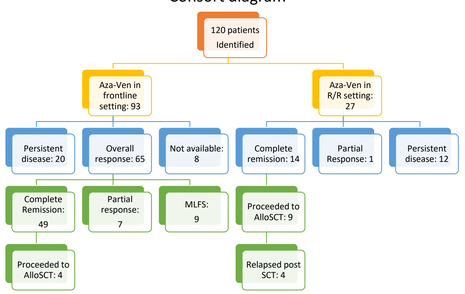
METHODS

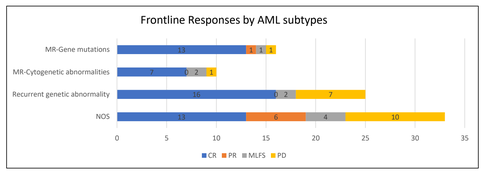
- Retrospective chart review
- **Duration of study:** January 2019 and October 2023
- **Settings:**
  - Frontline: AML patients, unfit for IC or with active infections at diagnosis
  - Relapsed/refractory (R/R): Patients failing 1-2 lines of IC or patients relapsing after treatment
- **Dosing:**
  - Venetoclax: 100 mg/day x 14-28 days per cycle with potent azoles – Voriconazole/Posaconazole
  - Azacitidine: 75 mg/m^2/day x 7 days per cycle
- Patients with at-least 1 month follow-up were included
- OS was calculated from diagnosis to death from any cause
- EFS was calculated from CR to relapse/death
- DOR was calculated in patients achieving CR, PR or MLFS
- Categorical variables were compared using Chi-square and Fisher exact tests
- Kaplan-Meier survival method and log rank test were used to estimate and compare survival

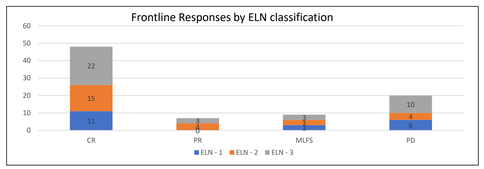
RESULTS

- Total patients: 120
- Median duration of follow-up of the entire cohort was 499 days (30-1879 days)
- Median duration of Venetoclax use: 14 days (7-28)
- Median number of cycles required to achieve response:
  - Frontline: 3 (1-6) R/R: 3 (1-3)
- Prior diagnoses before AML:
  - MDS: 4; MDS/MPN: 2; Therapy related: 2
- Allogeneic transplant after achieving remission:
  - Frontline: 4/93 (4.3%)
  - R/R: 9/27 (33.3%)
- Incidence of febrile neutropenia decreased with subsequent cycles
  - Cycle 1: 68/93 (73.2%) Cycle 2: 45/81 (55.6%)
  - Cycle 3: 28/69 (40.6%) Cycle 4: 17/62 (27.4%)

Consort diagram

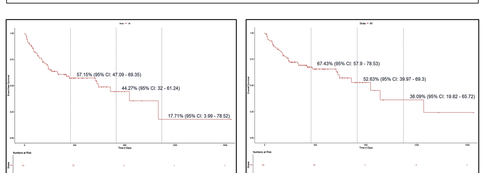




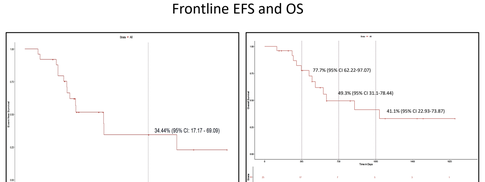


Baseline Characteristics		Aza-Ven (frontline)	Aza-Ven (R/R)
Total patients		93	27
Median Age, (range)		60 years, (19-78)	42 years, (23-59)
Sex	Male	52 (55.9%)	19 (70.4%)
	Female	41 (44.1%)	8 (29.6%)
ECOG performance status	0	3 (3.2%)	3 (11.1%)
	1	43 (46.2%)	20 (74.1%)
	2	27 (29%)	3 (11.1%)
	3	14 (15.1%)	1 (3.7%)
	4	6 (6.5%)	-
Prior lines of induction failure		-	1 line - 21/27 (81.4%) 2 lines - 5/27 (18.5%)
AML subtypes	Recurrent genetic abnormality	26 (28%)	8 (29.6%)
	Myelodysplasia Related Cytogenetic abnormalities	10 (10.8%)	2 (7.4%)
	Myelodysplasia related gene mutations	23 (24.7%)	5 (18.5%)
	NOS	33 (35.4%)	11 (40.7%)
	Therapy related AML	1 (1.1%)	1 (3.7%)
Extramedullary infiltration		3	3
Karyotype	Normal	50 (56.8%)	16 (59.3%)
	Favourable	14 (15.9%)	2 (7.4%)
	Adverse risk	24 (27.3%)	9 (33.3%)
	Not available	5 (5%)	-
NGS data available		47 (51.1%)	21 (77%)
Adverse risk mutations		23 (24.7%)	8 (29.6%)
ELN 2022 risk stratification	Favourable	21 (23.3%)	3 (11.1%)
	Intermediate	30 (33.3%)	10 (37%)
	Adverse	39 (43.3%)	14 (51.9%)
	Not available	3 (3.2%)	-

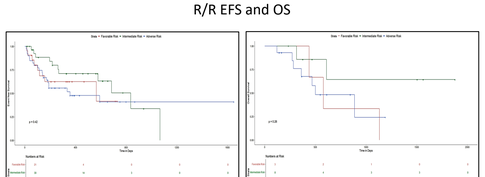
Outcomes			Aza-Ven (frontline)	Aza-Ven (R/R)
Total patients			93	27
Response	Overall Response		65 (69.8%)	15 (55.5%)
	CR		49 (52.6%)	14 (51.9%)
	PR		7 (7.5%)	1 (3.7%)
	MLFS		9 (9.6%)	-
	PD		20 (21.5%)	12 (44.4%)
	Not available		8 (9%)	-
Median Duration of response			322 days (range 30-1067)	154 days (range 83-516 days)
Median Event Free survival	1 year		57.15% (CI 47.09-69.35)	34.4% (CI 17.16-69.1)
	2 years		44.27% (CI 32-61.24)	-
	3 years		17.71% (CI 3.99-78.52)	-
Median Overall Survival	1 year		67.43% (CI 57.9-78.53)	77% (CI 62.22-97.07)
	Entire cohort		836 days (CI 577-NA)	233 days (CI 125-NA)
Deaths			35/93 (37.6%)	12/27 (44.4%)
Overall Response Frontline: N=65 R/R: (percentage within subgroup)	AML subtypes	Recurrent genetic abnormality	18/26 (69%)	4/8 (50%)
		MR-cytogenetic changes	9/10 (90%)	1/2 (50%)
		MR- genetic mutations	15/23 (65%)	3/5 (60%)
		Therapy related	0/1 (0)	1/1 (100%)
		NOS	23/33 (69%)	6/11 (54.4%)
	ELN	Favourable	14/21 (66%)	1/3 (33.3%)
		Intermediate	22/30 (73%)	6/10 (60%)
		Adverse	28/39 (71%)	8/14 (57.1%)
	Karyotype	Favourable	9/14 (64.2%)	0/3 (0)
		Normal	38/50 (56.7%)	11/16 (68.7%)
		Adverse	15/24 (62.5%)	4/9 (44%)
	Adverse risk mutations present		21/23 (91.3%)	5/8 (62.5%)



Frontline EFS and OS



R/R EFS and OS



Outcomes stratified by ELN risk

CONCLUSIONS

- Aza-Ven offers good CR rates in frontline and R/R settings
- Efficacy is maintained in adverse risk cohorts of AML –
  - Patients failing 1-2 lines of IC
  - Adverse risk genetic mutations and cytogenetic abnormalities
- A lower cumulative dose of Venetoclax (14 days)
  - Is efficacious and provides similar CR rates as described in the VIALE-A trial
  - Decreases the toxicity associated with treatment (FN rates)
- Response assessment is preferable after 3 cycles of treatment
- A predictive model for optimal dose and duration of treatment can be the objective of future studies

REFERENCES

- DiNardo CD, Jonas BA, Pullarkat V, Thirman MJ, et al. Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia. N Engl J Med. 2020 Aug 13;383(7):617-629. doi: 10.1056/NEJMoa2012971. PMID: 32786187.
- Döhner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022 Sep 22;140(12):1345-1377. doi: 10.1182/blood.2022016867. PMID: 35797463.

ACKNOWLEDGEMENTS

- To all the data managers of Tata Medical Center, Kolkata
- The clinical and laboratory hematology departments at Tata Medical Center
- To Mr. Sharthak Ghosh for the detailed statistical analysis

CONTACT INFORMATION

Dr. Shouriyo Ghosh
Associate Consultant, Clinical Haematology and Cellular Therapies
Tata Medical Center, Kolkata, West Bengal, India
Email ID: shouriyo.ghosh@tmckolkata.com

AML-454