

Azacitidine and Venetoclax Combination for Upfront Treatment of Higher-Risk Myelodysplastic Syndromes

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Background

- Azacitidine (aza) remains the backbone of treating higher-risk MDS patients (pts), with less than 20% of patients achieving complete response (CR) and median overall survival of 14–18 months.
- Ongoing studies in higher-risk MDS are assessing the role of adding venetoclax (ven) to aza in higher-risk MDS.
- We report, here, single-institution experience of aza/ven combination in the upfront treatment of higher-risk MDS, comparing it to historical aza alone.

Material & Methods

- We identified 35 pts who received aza/ven for intermediate or higher-risk MDS by R-IPSS compared to 1127 similar-risk MDS pts who historically received aza upfront therapy alone.
- The median follow-up for the aza/ven group was 15 months (mo) compared to 93 mo for aza alone.

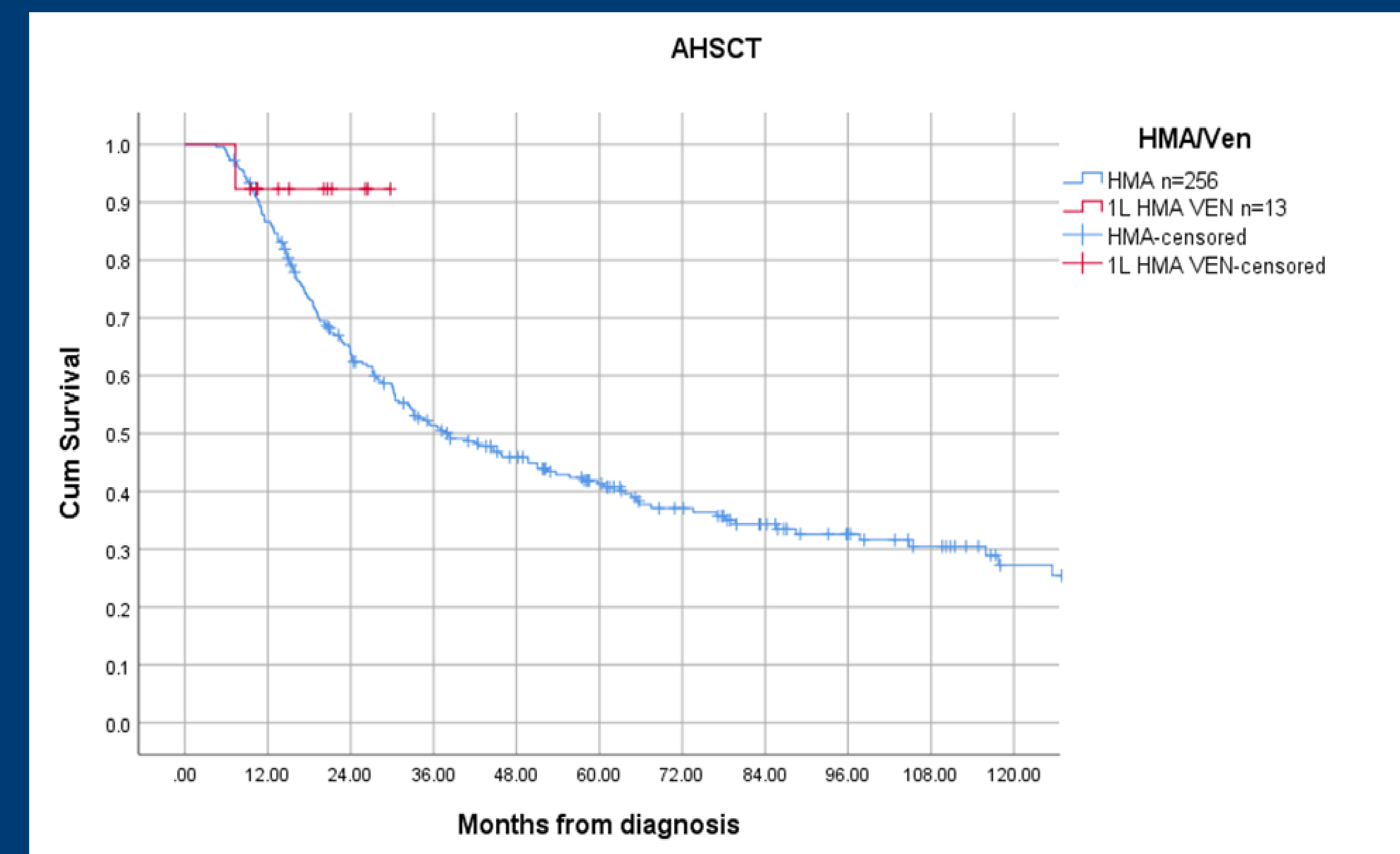
Results

- No differences were observed in baseline characteristics comparing aza/ven group to aza alone except for higher rates of *ASXL-1* and *N-RAS* somatic mutations (SM) among aza/ven treated pts. Table-1
- There was no difference in median OS among the two groups: median OS was 20 mo for both groups.
- The CR/marrow CR (mCR) rate was higher with the aza/ven combination, 71% (31%/40%), compared to 25% for aza alone (13%/12%) ($p < .005$). Among pts with *ASXL-1* SM, the CR rate was 47% compared to 9% for aza alone ($p < .005$).
- More pts treated with aza/ven proceeded to allogeneic hematopoietic stem cell transplant (AHSCT) (40% vs. 23%, $p = .04$). The median OS for pts treated with aza/ven followed by AHSCT was not reached compared to 31 mo for aza alone followed by AHSCT ($p = .17$).
- The 2-year survival rate for pts who underwent AHSCT was 90% for aza/ven compared to 51% for the aza alone group.

Table-1 Baseline characteristics comparing HMA alone versus HMA Ven first line therapy in HR-MDS

		HMA 1L	HMA/Ven 1L	P value
n		1127	35	
Age	mean	68.4	67.8	.76
Gender	Male	66%	71%	.5
Race	White	90%	97%	.66
t-MDS		24%	23%	.86
WHO 2016	MDS-SLD/MLD	18%	4%	.04
	MDS-RS	6%	4%	
	MDS-EB1	33%	9%	
	MDS-EB2	39%	78%	
R-IPSS	Intermediate	31%	17%	.22
	High	31%	37%	
	Very High	38%	46%	
Myeloblasts	Mean (%)	8	13	< .005
High	Mean (g/dl)	9	9	1.0
WBC	Mean	4	10.6	< .005
ANC	Mean	1.8	4.1	< .005
platelets	Mean	96	100	.8
Somatic Mutations (n= 546 sequenced)	SF3B1	5%	0	.3
	TET-2	16%	23%	.3
	IDH-1	3%	3%	.7
	IDH-2	5%	14%	.056
	ASXL-1	21%	46%	.002
	TP53	27%	34%	.6
	NRAS	4%	11%	.07

Figure-1 KM estimates for OS among pts who received 1L HMA/ VEN compared to HMA alone and proceeded to AHSCT



Conclusion

- Aza/ven combination is associated with higher responses overall and among *ASXL-1* SM higher risk MDS pts.
- Early data are encouraging for aza/ven as a bridge to AHSCT, with 90% 2-year OS.