Outcomes Are Similar Following Allogeneic Hematopoietic Stem Cell Transplant for Newly Diagnosed Patients who Received Venetoclax + Azacitidine Versus Intensive Chemotherapy

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1. Background/Hypothesis

- Hematopoietic stem cell transplant (HSCT) remains one of the only curative therapies for acute myeloid leukemia (AML) in adult patients.
- Venetoclax-based regimens are now FDA-approved for treatment of AML in older patients or in those unfit to tolerate intensive chemotherapy (IC).
- Outcomes for newly diagnosed patients who receive venetoclax-based therapies and proceed to a potentially curative HSCT have largely been unreported.
- In the current study we compared outcomes of patients who received HSCT following either IC or venetoclax + azacitidine (ven/aza) at the University of Colorado Hospital. We hypothesized that post-transplant outcomes would be similar between the two groups, with respect to relapse-free survival (RFS) and overall survival (OS) in particular.

2. Methods

- Patients 18 years or older who received HSCT in first remission (CR1) of AML between 2010-2020 were included in the analysis.
- IC arm was defined as patients an induction cycle containing cytarabine and an anthracycline alone or in combination with other targeted agents (e.g., FLT3 inhibitor) and who subsequently went to HSCT in CR1.
- Ven/aza arm was defined as patients receiving ven/aza as first-line therapy followed by HSCT.
- Patients were excluded if they received a combination of both IC and ven/aza prior to HSCT and if they went to HSCT in anything other than CR1.
- Demographic and clinical information for all included patients was extracted from the electronic medical record.
- Statistical Analysis: ***

3. Demographic and Disease Characteristics

- One hundred sixty-nine (169) patients met inclusion criteria, 140 having received IC + HSCT and 29 having received ven/aza + HSCT.

Table 1. Ven/aza patients were older compared to IC patients. * indicates p-values that are statistically significant.

	IC (n=140)	Ven/Aza (n=29)	P-value
Age at Diagnosis			
Median [Min, Max]	55.5 [18, 73]	65 [22, 73]	<0.001*
Categorical (<65y)	121 (86%)	13 (45%)	
Categorical (>=65y)	19 (14%)	16 (55%)	<0.001*
Gender			
Male	81 (58%)	11 (38%)	0.08
Female	59 (42%)	18 (62%)	
SWOG Classification			
Favorable	6 (4%)	0 (0%)	0.19
Intermediate	72 (51%)	10 (35%)	
Unfavorable	50 (36%)	16 (55%)	
Unknown	12 (9%)	3 (10%)	
ELN Risk Group			
Favorable	19 (14%)	4 (14%)	0.10
Intermediate	37 (26%)	5 (17%)	
Adverse	57 (41%)	19 (66%)	
Unknown	27 (19%)	1 (3%)	
Sorror Comorbidity Index			
0-2	93 (66%)	15 (52%)	0.24
3-4	40 (29%)	12 (41%)	
>=5	7 (5%)	2 (7%)	

4. Therapy Response and Transplant Details

Table 2. The ven/aza cohort had lower incidence of MRD clearance pre-transplant, lower proportion of patients receiving myeloablative conditioning (MAB), and higher proportion of patients receiving post-transplant venetoclax maintenance compared with the IC cohort.

	IC (n=140)	Ven/Aza (n=29)	P-value
Pre-HSCT Disease Status			<0.001*
CR with MRD	47 (34%)	19 (66%)	
CR without MRD	83 (59%)	6 (21%)	
CRi	5 (4%)	0 (0%)	
Aplasia/MLFS	3 (2%)	4 (13%)	
Other	2 (1%)	0 (0%)	
Pre-HSCT Flow MRD			0.007*
Negative	43 (31%)	16 (55%)	
Positive	24 (17%)	7 (24%)	
Not Done	73 (52%)	6 (21%)	
Conditioning Regimen			
MAB	99 (71%)	9 (31%)	<0.001*
non-MAB	27 (19%)	8 (28%)	
RIC	14 (10%)	12 (41%)	
Transplant Type			
Cord	90 (64%)	20 (69%)	0.31
Haplo	1 (1%)	1 (3%)	
Matched Related Donor	41 (29%)	8 (28%)	
Matched Unrelated Donor	8 (6%)	0 (0%)	
Post-HSCT Maintenance?			
None	109 (78%)	14 (48%)	<0.001*
Venetoclax	4 (2%)	15 (52%)	
FLT3 Inhibitor	15 (11%)	0 (0%)	
Hedgehog Inhibitor	12 (9%)	0 (0%)	

5. Post-transplant outcomes for IC and ven/aza cohorts were identical.

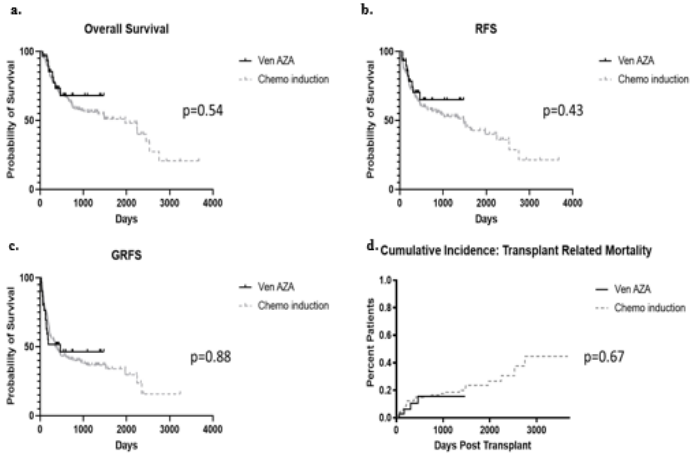

Figure 1. Survival post-transplant was identical for IC and ven/aza patients receiving HSCT. Overall survival (a), relapse-free survival (b), GVHD-free relapse-free survival (c), and cumulative incidence of TRM (d) were not significantly different between patients receiving IC (dashed grey line) versus ven/aza (solid black line) as pre-transplant therapy.

6. MRD persistence by flow predicts worse OS.

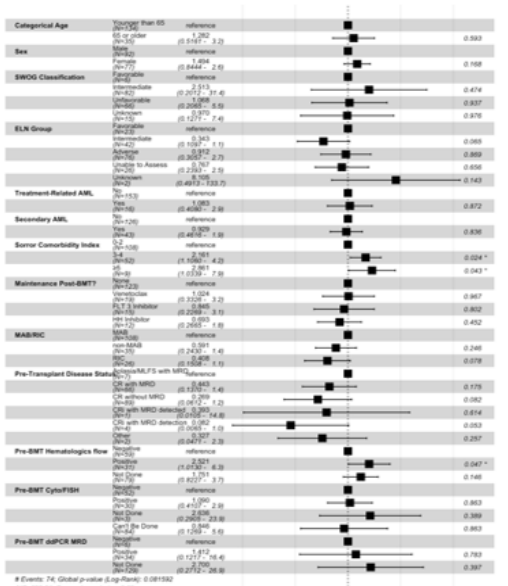

Figure 2. Pre-HSCT flow cytometry MRD predicted poorer overall survival post-HSCT. Multivariate analysis of variables in the entire cohort identified flow cytometry MRD positivity pre-HSCT as a risk factor for poorer survival (p-value 0.047).

7. Conclusions

- Despite older age, higher incidence of MRD pre-HSCT, and fewer patients receiving myeloablative conditioning, post-HSCT outcomes for ven/aza patients were identical to those for patients receiving intensive induction chemotherapy.
- Flow cytometry pre-HSCT MRD was a key prognostic factor for post-HSCT outcomes.
- Ven/aza is a viable option for remission induction in AML.

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