Post-transplant outcomes of AML with cytogenetic evolution

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Background

■ Cytogenetic abnormalities at diagnosis is a crucial prognostic marker in patients with acute myeloid leukemia.
■ Cytogenetic evolution (CE) is defined by additional cytogenetic aberrations and its incidence is around 30-40%.
■ CE is not well defined in AML while it heralds a unfavorable prognosis in CML and ALL.
■ Patients with AML develop CE at relapse either before or after allogeneic stem cell transplant (AlloSCT) may have worse outcomes..

Objective

■ We evaluated a prognostic role of pre-transplant CE in patients with AML who underwent AlloSCT in CR2.

Patients and Methods

Study Population

Included 62 patients in second remission after first relapsed AML who underwent AlloSCT between 2005 and 2018 at University of Minnesota. 24 patients had CE events at the time of first relapse.

Definition

Cytogenetic evolution is defined by any additional cytogenetic abnormalities detected by conventional G-banding at the first relapse. Cytogenetic risk classification is performed by European Leukemia Network (ELN) 2017 risk stratification.

Statistical Analyses

The distributions of demographic/clinical characteristics were summarized using counts and frequencies (for categorical variables) or means and standard deviations (for continuous ones). Survival curves were estimated using the Kaplan-Meier product-limit method and compared by log-rank test. Multivariate Cox regression was used to analyze the effects of cytogenetic evolution on the post-transplant survival.

Results

Patients Characteristics

Baseline patient characteristics were similar for age at diagnosis, sex, secondary AML, and ELN cytogenetic risk at diagnosis. However, average WBC count at diagnosis was higher without CE (mean 56.5 x10^9/L) compared with CE (mean 32.3 x10^9/L).

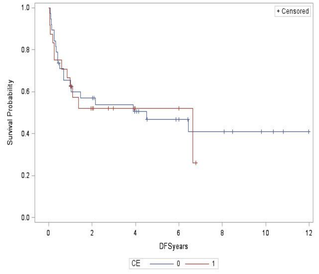
Disease characteristics

Variables	No CE (n=38)	CE (n=24)	P value
ELN risk at diagnosis			0.935
Favorable	14 (37%)	10 (42%)	
Intermediate	19 (50%)	11 (46%)	
Poor	5 (13.3%)	3 (12%)	
Core binding factor AML			0.374
No	30 (79%)	16 (67%)	
Yes	8 (21%)	8 (33%)	
FLT3 mutation			**0.039**
N-Miss	17 (45%)	10 (42%)	
Negative	11 (29%)	13 (54%)	
Positive	10 (26%)	1 (4%)	
Induction chemotherapy			0.304
Standard 7+3	30 (79.0%)	22 (92%)	
Reinduction	7 (18%)	1 (4%)	
Others	1 (3%)	1 (4%)	
Consolidation chemotherapy			0.758
HiDAC	24 (62%)	15 (63%)	
Others	7 (19%)	6 (25%)	
None	7 (19%)	3 (12%)	
CR1 duration			**0.059**
Mean (Range)	476 days (57-3865)	860 days (90-4755)	
< 1 year	22 (58%)	8 (33%)	
> 1 year	16 (42%)	16 (67%)	
Cytogenetic risk at relapse			0.320
Favorable	13 (34%)	21 (88%)	
Intermediate	21 (55%)	11 (46%)	
Poor	4 (11%)	6 (26%)	
Disease status at transplant			0.961
MRD negative CR2	12 (32%)	7 (29%)	
MRD positive CR2	1 (3%)	1 (4%)	
Morphologic CR2	23 (60%)	14 (58%)	
Cytogenetic relapse	2 (5%)	2 (8%)	

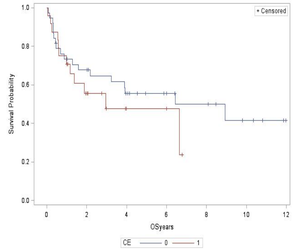
Transplant related characteristics

Variables	No CE (n=38)	CE (n=24)	p-value
Mean HCT CI score (range)	2.2 (0-11)	2.0 (0-7)	0.67
Karnofsky PS score	89.5 (60-100)	90.4 (80-100)	0.774
Donor source			0.291
Related	17 (44%)	6 (25%)	
Unrelated	1 (3%)	0 (0%)	
Cord blood	19 (50%)	17 (71%)	
Haploidentical	1 (3%)	1 (4%)	
Conditioning intensity			0.606
Non-myeloablative	22 (58%)	12 (50%)	
Myeloablative	16 (42%)	12 (50%)	
GVHD prophylaxis			0.812
CSA/MMF	25 (66%)	14 (58%)	
MTX/CSA	6 (16%)	4 (17%)	
Others	7 (18%)	6 (25%)	
Post-transplant relapse			0.260
No	24 (63%)	19 (79%)	
Yes	14 (37%)	5 (21%)	

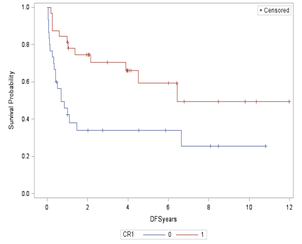
DFS
The DFS at 5-year was estimated 47% in patients without CE and 52% in patients with CE (p-value = 0.786).



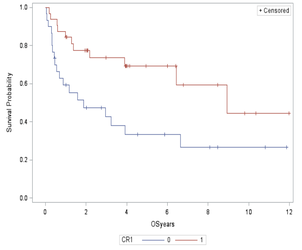
OS
The OS at 5-year was estimated 55% in patients without CE and 48% in patients with CE (p-value = 0.378).



DFS
The DFS at 5-year was estimated 60% in patients with CR1 duration > 1 year in comparison with 34% in patients with CR1 duration < 1 year (p= 0.006).



OS
The OS at 5-year was estimated 69% in patients with CR1 duration > 1 year in comparison with 33% in patients with CR1 duration < 1 year (p= 0.011).



Discussion

■ Cytogenetic evolution in patients with AML was not uncommon and occurred in 40% of patients who underwent AlloSCT in CR2.

■ Pre-transplant cytogenetic evolution at relapse was not prognostic for transplant outcomes in patients who achieved CR2 and proceeded with AlloSCT.

■ The duration of CR1 (<1 year VS > 1 year) was significant to predict post-transplant survival outcomes.

■ The outcomes of patients transplanted from cord blood seemed comparable to patients transplanted from other sources.

Disclosures: There are no relevant conflicts of interest to disclose.