Outcome Predictors and Timing Considerations for Allogeneic Stem Cell Transplantation in Chronic Myelomonocytic Leukemia

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BACKGROUND

- Chronic myelomonocytic leukemia (CMML) outcomes are poor in general with a median overall survival (mOS) of 3 years.
- Allogeneic transplant (HSCT) offers the only curative option.
- Considerations as to when to pursue HSCT, identification of relapse predictors and assessment of whether transplant-related, clinical and molecular disease features have an impact on outcomes remain crucial.

OBJECTIVE

- To characterize best timing to HSCT, best therapy to achieve CR prior to transplant, and analyze associations between molecular and transplant-related variables and relapse risk

METHODS

- Retrospective collection of clinical and molecular data of transplanted CMML patients treated at Moffitt Cancer Center between 1995–2022.
- Median duration of follow-up was 93 months.

RESULTS

- A total of 83 patients went to HSCT: 29 (35%) in BP-CMML (sAML), 38 (46%) in CMML-0/CMML-1 (Early Stage) and 16 (19%) in CMML-2.
- Median age at HSCT was 63 years (18-76).
- mOS for the transplant cohort was 62 months (95%CI 35-89 months).
- Patients who went to transplant earlier had better outcomes: mOS for ES-CMML: 202 months (95%CI NR), vs 62 months for BP-CMML (95%CI 39-84 moths) (p=0.019).
- There was no association between relapse rate and number of treatment lines prior to HSCT (p=.112) and type of donor (p=.491).

RESULTS

- There was no association between relapse rate and stem cell source (p=.768) or type of conditioning regimen (MA vs RIC/NMA) (p=.565)
- There was a trend toward better outcomes for those receiving intensive chemotherapy prior to transplant (p=.08) and with lower blast burden (mOS: 80 vs 64 months, p=.92).
- Both standard 7+3/AML-like induction and CLAG regimens were equally effective in inducing CR and superior to single-agent HMA (p<0.05).
- 28 patients (34%) experienced relapse.
- Relapse rate for those with lower blast percentage at time of HSCT was 30% (n=18) compared to 40% (p=0.458).
- Patients who developed GvHD were less likely to relapse (85.7% vs 14.3%, p=0.000).
- There was an association between DNMT3A mutations and risk of relapse (p=0.04) with a trend also favoring NRAS (p=0.08).

CONCLUSIONS

- Patients with CMML who went to transplant earlier in the disease course had better outcomes.
- There was a trend toward better outcomes for those receiving intensive chemotherapy.
- CR was more likely with CLAG and 7+3 induction.
- Relapse was less likely for those who developed GvHD and more likely to be associated with DNMT3A mutations.

REFERENCES

1. Sanz GF, Ibañez M, Mora E. Are next-generation sequencing results knocking on Heaven's door for transplantation planning in chronic myelomonocytic leukemia? Haematologica. 2020 Mar;105(3):530-533
2. Patnaik MM, Pierola AA, Vallapureddy R, et al Blast phase chronic myelomonocytic leukemia: Mayo-MDACC collaborative study of 171 cases. Leukemia. 2018 Nov;32(11):2512-2518
3. Pophali P, Matin A, Mangaonkar AA, et al. Prognostic impact and timing considerations for allogeneic hematopoietic stem cell transplantation in chronic myelomonocytic leukemia. Blood Cancer J. 2020 Nov 20;10(11):121

TABLES & FIGURES

Table 1. Baseline Characteristics According to Disease Stage

Variable	CP-CMML n= 54 (65%)	BP-CMML n= 29 (35%)	p-value
Age at Diagnosis, median (range)	62 (33-75)	56 (17-72)	p=0.199
Age at HSCT, median (range)	63 (38-76)	55 (40-73)	p=0.241
Gender, n (%)			p=0.342
Male	39 (72.2)	18 (62.1)	
Female	15 (27.8)	11 (37.9)	
FAB Category, n (%)			p=0.765
MD-CMML	18 (34.6)	11 (37.9)	
MP-CMML	34 (65.4)	18 (62.1)	
Lab values, mean			
WBC x10^9/L	31.7	21.1	p=0.249
ANC x10^9/L	16.9	11.5	P=0.335
ALC x10^9/L	4.6	3.7	p=0.472
Monocytes x10^9/L	5.2	5.3	p=0.928
Immature myeloid %	**8.8**	**4.6**	**p=0.041**
Blasts %	**0.9**	**1.8**	**p=0.058**
Hb d/dl	10.4	10.1	p=0.540
Platelets x10^9/L	146	119	p=0.380
Iron mcg/dL	113	74	p=0.173
CPSS karyotype Risk, n (%)			p=0.284
Good	40 (75.5)	17 (60.7)	
Intermediate	4 (7.5)	5 (17.9)	
Poor	9 (17)	6 (21.4)	
CPSS Risk, n (%)			p=0.209
Lower Risk	27 (51.9)	10 (37)	
Higher Risk	25 (48.1)	17 (63)	
Transfusion dependence (RBC)			p=0.973
Yes	24 (44.4)	13 (44.8)	
No	30 (55.6)	16 (55.2)	
Transfusion dependence (Platelets)			p=0.586
Yes	12 (22.2)	8 (27.6)	
No	42 (77.8)	21 (72.4)	
Splenomegaly, n (%)			p=0.621
Yes	14 (26.4)	6 (21.4)	
BM blast % at BMT, median	2.5	3.8	p=0.171
Relapse post-alloHSCT, n (%)			p=0.207
Yes	15 (27.8)	12 (41.4)	
No Relapse	39 (72.2)	17 (58.6)	

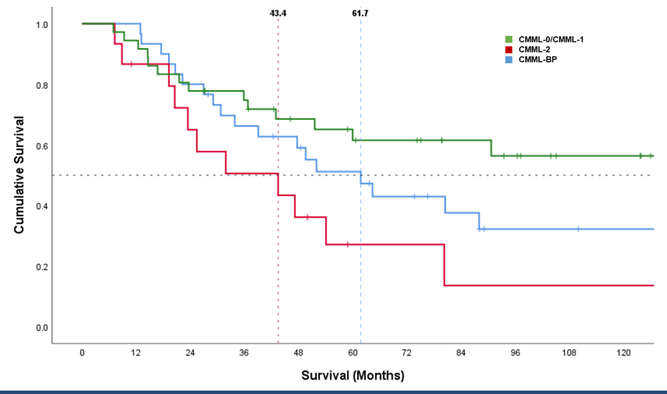


Table 2. Transplant-related Characteristics According to Disease Stage

Variable	CP-CMML n= 54 (65%)	BP-CMML n= 29 (35%)	p-value
Treatment Lines prior to BMT, n (%)			**p<0.001**
Frontline	9 (17)	0 (0)	
1	38 (71.7)	8 (27.6)	
2	3 (5.7)	13 (44.8)	
3 or more	3 (5.7)	8 (27.6)	
Best Response Prior to BMT, n (%)			**p<0.001**
No Treatment/Observation	8 (15.4)	0 (0)	
AML-like induction	2 (3.8)	9 (31)	
CLAG/CLAG-M	2 (3.8)	9 (31)	
HMA (single agent)	27 (51.9)	3 (10.3)	
HMA/venetoclax	2 (3.8)	2 (6.9)	
Lenalidomide	0 (0)	0 (0)	
Ruxolitinib	2 (3.8)	0 (0)	
HMA/Other	2 (3.8)	3 (10.3)	
MEC	1 (1.9)	1 (3.4)	
Others	6 (11.5)	2 (6.4)	
Disease Status at BMT, n (%)			**p<0.001**
CR	3 (5.8)	16 (55.2)	
CR marrow	3 (5.8)	4 (13.8)	
PR	5 (9.6)	4 (13.8)	
HI	5 (9.6)	0 (0)	
SD	33 (63.5)	3 (10.3)	
DP	3 (5.8)	2 (6.9)	
Time to BMT from Dx, median (mos)	8	9.3	p=0.446
Type of BMT conditioning, n (%)			p=0.854
Myeloablative	5 (9.4)	3 (10.7)	
RIC	48 (90.6)	25 (89.3)	
Donor Source, n (%)			p=0.576
MRD	14 (26.4)	7 (25)	
MUD	30 (56.6)	15 (53.6)	
MMUD	6 (11.3)	2 (7.1)	
Haploidentical	3 (5.7)	3 (10.7)	
Umbilical Cord	0 (0)	1 (3.6)	
Graft Source, n (%)			p=0.384
Peripheral Blood	51 (96.2)	26 (92.9)	
Bone Marrow	1 (1.9)	2 (7.1)	
Umbilical Cord	1 (1.9)	0 (0)	
aGVHD/cGVHD, n (%)			p=0.464
Yes	40 (75.5)	19 (67.9)	
No	13 (24.5)	9 (32.1)	

Figure 1. Estimated Overall Survival According to Disease Stage

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