

Background

- Chronic myelomonocytic leukemia (CMML) is characterized by marked clinical heterogeneity.
- Generally associated with poor outcomes, median overall survival (mOS) is 3 years.
- Multiple prognostic models consider cardinal clinical, cytogenetic and molecular features critical in estimating individual risk and outlining treatment.
- Identification and longitudinal assessment of features of interest become important to predict which patients tend to have a more indolent course compared to those who will progress

Methods

- Retrospective cohort of patients with CMML treated at Moffitt between 1995-2020
- Patients were stratified into 2 cohorts: those remaining in observation for >3 years versus those who required treatment <3 years after presentation.
- Treatment-naïve patients lost to f/u within 3 years were excluded

Results

- Out of 729 patients 68.3% were male (498) and 88.5% were Caucasian (645).
- Median age at diagnosis was 71 (17-95).
- A total of 123 patients (17%) did not require treatment within 3 years of diagnosis.
- mOS was 70mo among those who did not require early treatment compared to 25mo for those who did (p<.005).
- Clinically, higher platelet count at baseline was associated with longer time to treatment (p=0.022).
- Elevated WBC (proliferative CMML), lymphocytes, monocytes and marrow blasts were associated with earlier initiation of treatment (p<.005).
- Patients not needing immediate treatment had lower risk disease by IPSS, R-IPSS and all CMML risk models.
- JAK2, SF3B1, and IDH2 mutations were associated with more indolent course obviating the need for intervention within 3 years (p<.005).
- NRAS portended a more aggressive course (p=0.004).
- Patients harboring ASXL1 showed a trend towards early progression (p=0.067)

Conclusions

- A small subset of CMML patients (17%) have a more indolent disease course. Clinical and molecular features at diagnosis can be assessed to identify them.
- Next, we aim to identify changes in clinical and molecular features from baseline immediately anteceding the need for treatment to establish whether they predict evolution of disease

Tables & Figures

Table 1. Baseline Characteristics According to Disease Phenotype

Variable	Indolent-CMML n= 123 (17%)	Non-Indolent-CMML n= 606 (83%)	p-value
Age at Diagnosis, median (range)	69 (19-86)	67 (19-94)	p=0.579
Gender, n (%)			p=0.667
Male	82 (66.7%)	416 (68.6%)	
Female	41 (33.3%)	190 (31.4%)	
Race			p=0.628
Caucasian	113 (91.9%)	532 (88.5%)	
Black	4 (3.3%)	28 (4.7%)	
Hispanic	3 (2.4%)	30 (5.0%)	
Others	3 (2.4%)	11 (1.9%)	
WHO Category, n (%)			p<0.001
CMML-1	121 (100%)	501 (82.9%)	
CMML-2	0 (0.0%)	103 (17.1%)	
Lab values, mean			
WBC x10 ⁹ /L	14.7	24.8	p<0.001
ANC x10 ⁹ /L	7.8	13.2	p<0.001
ALC x10 ⁹ /L	1.8	1.9	p=0.004
Monocytes x10 ⁹ /L	2.8	4.6	p<0.001
Immature myeloid %	4.5	15.1	p=0.308
Blasts %	1.1	1.5	p=0.565
Hb d/dl	11.9	10.7	p=0.008
Platelets x10 ⁹ /L	174	139	p=0.022
Iron mcg/dL	85	104	p=0.032
Elevated LDH			p=0.001
Yes	40 (37.7%)	301 (56.1%)	
No	66 (62.3%)	236 (43.9%)	
Elevated Ferritin >1000			p<0.001
Yes	12 (12.5%)	156 (32.8%)	
No	84 (87.5%)	319 (67.2%)	
Blasts in PB			p<0.001
Yes	17 (14.8%)	200 (34.1%)	
No	98 (85.2%)	386 (65.9%)	
Number of cytopenias			P<0.001
None	44 (37.0%)	143 (23.9%)	
1 line	65 (54.6%)	285 (47.6%)	
Bicytopenia	9 (7.6%)	159 (26.5%)	
Pancytopenia	1 (0.8%)	12 (2.0%)	
Blast % in marrow biopsy	17 (14.8%)	200 (34.1%)	p=0.009
Cellularity % in marrow biopsy	17 (14.8%)	200 (34.1%)	p<0.001
Transfusion dependence (RBC)			p<0.001
Yes	14 (11.5%)	234 (38.7%)	
No	108 (88.5%)	370 (61.3%)	
Transfusion dependence (Platelets)			p<0.001
Yes	10 (8.2%)	127 (21.0%)	
No	112 (91.8%)	477 (79.0%)	
Splenomegaly			p=0.752
Yes	30 (24.6%)	442 (74.0%)	
No	92 (75.4%)	155 (26.0%)	
CPSS karyotype Risk			p<0.001
Good	106 (86.9%)	415 (70.6%)	
Intermediate	12 (9.8%)	76 (12.9%)	
Poor	4 (3.3%)	97 (16.5%)	
IPSS karyotype category			p<0.001
Good	108 (88.5%)	425 (72.3%)	
Intermediate	14 (11.5%)	101 (17.2%)	
Poor	0 (0.0%)	62 (10.5%)	
IPSS-R			p<0.001
Very Low	49 (43.0%)	109 (18.7%)	
Low	51 (44.7%)	208 (35.7%)	
Intermediate	12 (10.5%)	134 (23.0%)	
High	2 (1.8%)	89 (15.3%)	
Very High	0 (0.0%)	42 (7.2%)	
Mayo Molecular Model			p<0.001
Low Risk	29 (26.1%)	61 (10.5%)	
Intermediate Risk	53 (47.7%)	187 (32.1%)	
High Risk	29 (26.1%)	335 (57.5%)	
CPSS-Mol			p<0.001
Low	58 (49.6%)	113 (19.3%)	
Intermediate-1	44 (37.6%)	209 (35.8%)	
Intermediate-2	14 (12.0%)	210 (36.0%)	
High	1 (0.8%)	52 (8.9%)	
GFM			p<0.001
Low Risk	49 (57.0%)	150 (34.1%)	
Intermediate Risk	32 (37.2%)	168 (38.2%)	
High Risk	5 (5.8%)	122 (27.7%)	
AML transformation rate	20 (16.3%)	176 (29.0%)	p=0.004
OS months, median (95% CI)	70.3 (53.8-86.8)	25.3 (22.6–28.1)	p<0.001

Tables & Figures

Table 2. Mutations of Interest in Indolent and Non-Indolent CMML Phenotypes

Mutation, n (%)	Indolent-CMML n= 123 (17%)	Non-Indolent-CMML n= 606 (83%)	p-value
SF3B1	12 (19.7)	18 (5.8)	p<0.001
JAK2	16 (20.0)	36 (8.8)	p=0.003
NRAS	2 (3.3)	55 (17.6)	p=0.004
IDH2	5 (8.2)	9 (2.9)	p=0.044
ASXL1	20 (31.7)	145 (44.2)	p=0.067
PHF6	4 (6.7)	8 (2.5)	p=0.097
EZH2	3 (4.8)	37 (11.4)	p=0.112
TP53	0 (0.0)	12 (3.7)	p=0.121
RUNX1	7 (11.1)	62 (19.1)	p=0.128
DNMT3A	2 (3.3)	24 (7.6)	p=0.229
MPL	2 (3.2)	4 (1.2)	p=0.244
ZRSR2	2 (3.3)	22 (7.1)	p=0.272
IDH1	0 (0.0)	5 (1.6)	p=0.322
U2AF1	3 (4.9)	25 (8.0)	p=0.401

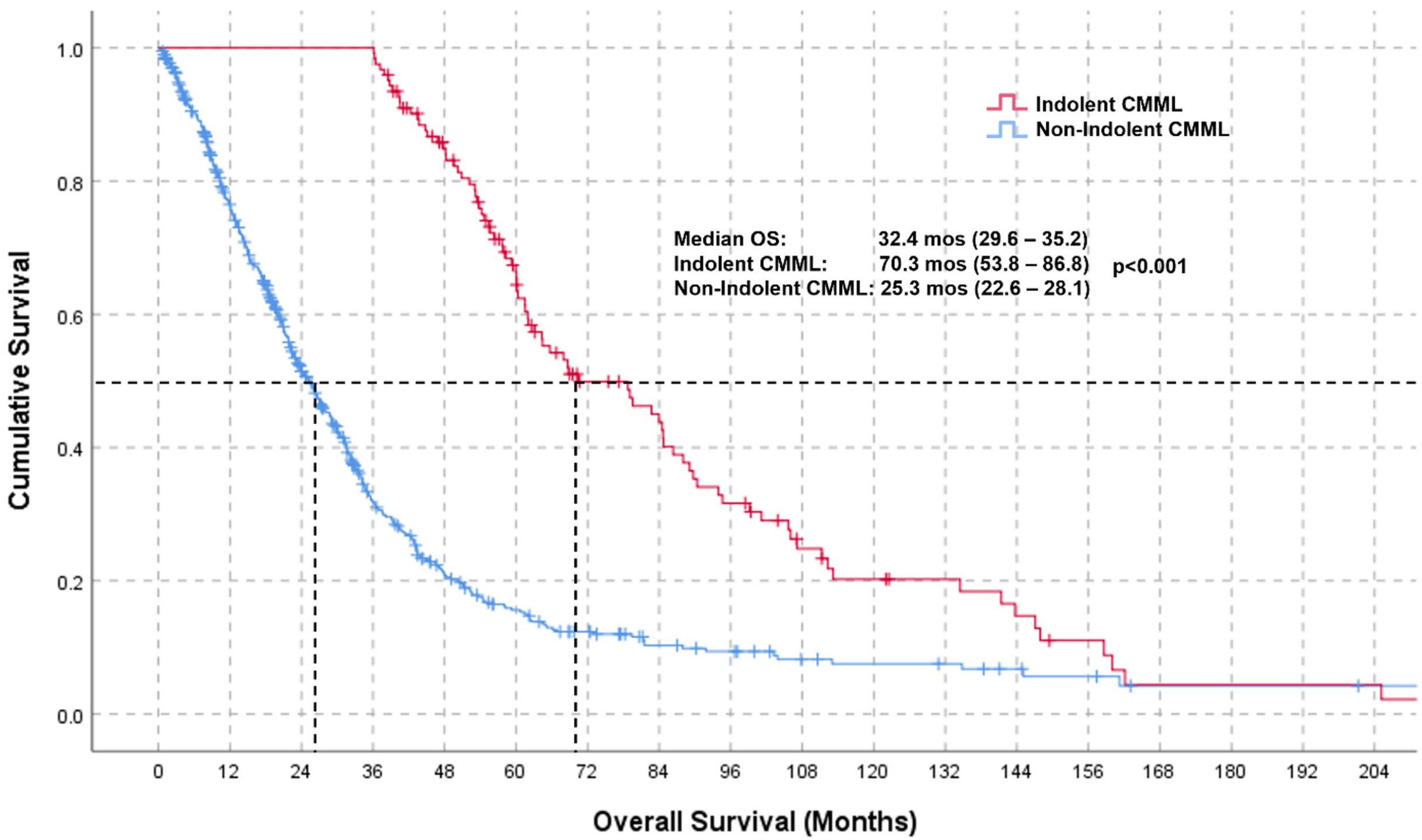


Figure 1. Estimated Overall Survival Based on Disease Phenotype (Indolent vs. Non-Indolent CMML)

References

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