

SUPPLEMENTAL DATA

Table S1. Univariate analysis of prognostic variables associated with overall survival in treatment-naïve chronic myelomonocytic leukemia patients (n=449).

Factor	Level	Number Total (died)	OS rate % 2:3:5 years	Median OS time (months)	Univariate p-value	Hazard Ratio (95% CI)	Overall p-value	Log-rank p-value
Age in years¹	Continuous values	499 (341)	54:39:20	26.2	0.0131	1.01(1.00,1.03)	0.0131	0.0131
	<60	90 (49)	51:42:27	24.3	0.0273	0.71(0.52,0.96)	0.0273	0.0264
	>=60	409 (292)	56:39:19	26.2		Ref		
	<70	252 (159)	53:40:24	26.2	0.0381	0.80(0.64,0.99)	0.0381	0.0373
	>=70	247 (182)	57:39:17	26.2		Ref		
	<60	90 (49)	51:42:27	24.3	0.0134	0.67(0.48,0.92)	0.0420	0.0404
	>=60, <70	162 (110)	54:39:22	26.2	0.2336	0.87(0.68,1.10)		
	>=70	247 (182)	57:39:17	26.2		Ref		
Sex group								
	F	160 (104)	60:47:23	30.5	0.1701	0.85(0.68,1.07)	0.1701	0.1695
	M	339 (237)	53:36:19	25.0		Ref		
WHO 2008								
	CMML-1	340 (222)	63:45:23	30.5	0.0003	0.66(0.53,0.83)	0.0003	0.0003
	CMML-2	159 (119)	38:28:15	18.8		Ref		
WHO 2017²								
	CMML-0	177 (107)	66:50:28	36.9	0.0552	0.77(0.59,1.00)	0.0003	0.0002

Factor	Level	Number Total (died)	OS rate % 2:3:5 years	Median OS time (months)	Univariate p-value	Hazard Ratio (95% CI)	Overall p-value	Log-rank p-value
	CMML-2	159 (119)	38:28:15	18.8	0.0323	1.33(1.02,1.72)		
	CMML-1	163 (115)	60:40:17	28.7		Ref		
FAB subtype								
	MDS-CMML	238 (138)	67:51:29	36.9	<.0001	0.53(0.42,0.65)	<.0001	<.0001
	MP-CMML	261 (203)	44:29:13	21.1		Ref		
Peripheral blood parameters								
White blood count		499 (341)	54:39:20	26.2	<.0001	1.01(1.01,1.02)	<.0001	<.0001
Absolute neutrophil count		499 (341)	54:39:20	26.2	<.0001	1.02(1.02,1.03)	<.0001	<.0001
Immature myeloid cells		499 (341)	54:39:20	26.2	<.0001	1.04(1.03,1.05)	<.0001	<.0001
Hemoglobin concentration		499 (341)	54:39:20	26.2	<.0001	0.84(0.79,0.88)	<.0001	<.0001
Platelet count		499 (341)	54:39:20	26.2	0.1116	1.00(1.00,1.00)	0.1116	0.1114
Serum lactate dehydrogenase		499 (341)	54:39:20	26.2	<.0001	1.00(1.00,1.00)	<.0001	<.0001
BM blast percentage, median (range)		499 (341)	54:39:20	26.2	0.0303	1.02(1.00,1.05)	0.0303	0.0301
MDAPS								
	High	80 (64)	29:17: 9	15.5	<.0001	3.66(2.34,5.72)	<.0001	<.0001
	INT-1	140 (86)	72:53:25	38.0	0.0433	1.55(1.01,2.38)		
	INT-2	220 (163)	47:33:17	23.0	<.0001	2.34(1.57,3.49)		
	Low	59 (28)	81:64:36	47.4		Ref		
CPSS group								

Factor	Level	Number Total (died)	OS rate % 2:3:5 years	Median OS time (months)	Univariate p-value	Hazard Ratio (95% CI)	Overall p-value	Log-rank p-value
	HIGH	45 (36)	15:12: 8	11.6	<.0001	5.27(3.40,8.17)	<.0001	<.0001
	INT-1	150 (103)	68:47:23	34.8	0.0012	1.77(1.25,2.51)		
	INT-2	204 (155)	41:25:11	19.5	<.0001	3.01(2.17,4.19)		
	Low	100 (47)	82:70:43	49.3		Ref		
CPSS cytogenetic risk group								
	High	80 (63)	24:14: 3	16.0	<.0001	2.53(1.90,3.37)	<.0001	<.0001
	Intermediate	64 (44)	56:33:18	25.1	0.1323	1.28(0.93,1.77)		
	Low	355 (234)	62:46:24	30.8		Ref		
Tang cytogenetic risk group								
	High	53 (44)	13: 5: 0	11.6	<.0001	3.85(2.75,5.39)	<.0001	<.0001
	Intermediate	91 (63)	53:32:16	24.9	0.0444	1.33(1.01,1.76)		
	Low	355 (234)	62:46:24	30.8		Ref		
Mutations								
<i>TET2</i>	Absent	82 (33)	59:49:33	29.2	0.0111	2.36(1.22,4.59)	0.0111	0.0089
	Present	60 (16)	78:75:62	83.5		Ref		
<i>ASXL1</i>	Absent	59 (16)	76:62:44	47.4	0.6358	0.84(0.41,1.73)	0.6358	0.6354
	Present	46 (15)	65:61:54	83.5		Ref		
<i>RAS</i>	Absent	266 (166)	60:42:24	29.2	0.3179	0.87(0.66,1.15)	0.3179	0.3173
	Present	107 (70)	56:42:15	26.2		Ref		
<i>TP53</i>	Absent	135 (46)	68:61:46	49.7	0.2801	0.52(0.16,1.70)	0.2801	0.2718

Factor	Level	Number Total (died)	OS rate % 2:3:5 years	Median OS time (months)	Univariate p-value	Hazard Ratio (95% CI)	Overall p-value	Log-rank p-value
	Present	7 (3)	34:NA:NA	19.5		Ref		
<i>RUNX1</i>	Absent	88 (25)	72:61:50	65.8	0.8063	0.89(0.36,2.21)	0.8063	0.8063
	Present	17 (6)	65:65:49	47.4		Ref		

1: Age <60 vs. 60-70, p=0.1296 HR (95% CI): 0.77(0.55, 1.08)

2: CMML-0 vs. CMML-2 p<0.0001 with HR (95%CI):0.58(0.45, 0.76)

Abbreviations: CMML: chronic myelomonocytic leukemia, WHO: World Health Organization; FAB: French-American-British classification; MDS: myelodysplastic; MP: myeloproliferative; CPSS: CMML-specific Prognostic Scoring System; FAB: French-American-British group; AML: acute myeloid leukemia.

Table S2A. Multivariate analysis for overall survival in treatment-naïve MP-CMML patients, WHO 2017 blast-based subgroups.

Variable	P-value	HR	95% CI for HR	
WHO 2017*				
CMML-0 vs. CMML-1	0.0102	0.626	0.437	0.895
CMML-2 vs. CMML-1	0.5140	1.116	0.803	1.551
CMML-0 vs. CMML-2	0.0011	0.561	0.396	0.793
Hemoglobin concentration	<0.0001	0.879	0.824	0.938
CPSS cytogenetic risk group*				
High vs. Low	<0.0001	2.301	1.516	3.491
Intermediate vs. Low	0.2837	1.237	0.838	1.827

*Overall p-value <0.05

Table S2A. Multivariate analysis for overall survival in treatment-naïve MDS-CMML patients, WHO 2017 blast-based subgroups.

Variable	P-value	HR	95% CI for HR	
Hemoglobin concentration	<0.0001	0.818	0.749	0.893
Age (<70 vs. ≥70)	0.0112	0.631	0.443	0.901
CPSS cytogenetic risk group*				
High vs. Low	<0.0001	2.743	1.799	4.183
Intermediate vs. Low	0.8758	0.952	0.511	1.771

*Overall p-value <0.05

Table S3A. Modified* CPSS risk groups including CMML-0 subgroup.

Risk Group	Overall Score
Low	0-1
Intermediate-1	2-3
Intermediate-2	4-5
High	6

*Modified from reference #2 in main manuscript; "WHO subtype" variable scores assigned as follows: CMML-0=0; CMML-1=1; CMML-2=2

Table S3B. Pairwise comparison between modified CPSS risk groups using Cox proportional hazards model.

Parameter	p-value	Hazard Ratio	95% Hazard Ratio Confidence Limits	
High vs. Low	<.0001	8.086	4.486	14.577
Intermediate-1 vs. Low	<.0001	1.817	1.438	2.297
Intermediate-2 vs. Low	<.0001	3.731	2.824	4.930
High vs. Intermediate-1	<.0001	4.450	2.514	7.874
Intermediate-2 vs. Intermediate-1	<.0001	2.053	1.614	2.612
High vs. Intermediate-2	0.0091	2.167	1.212	3.876

Figure S1.

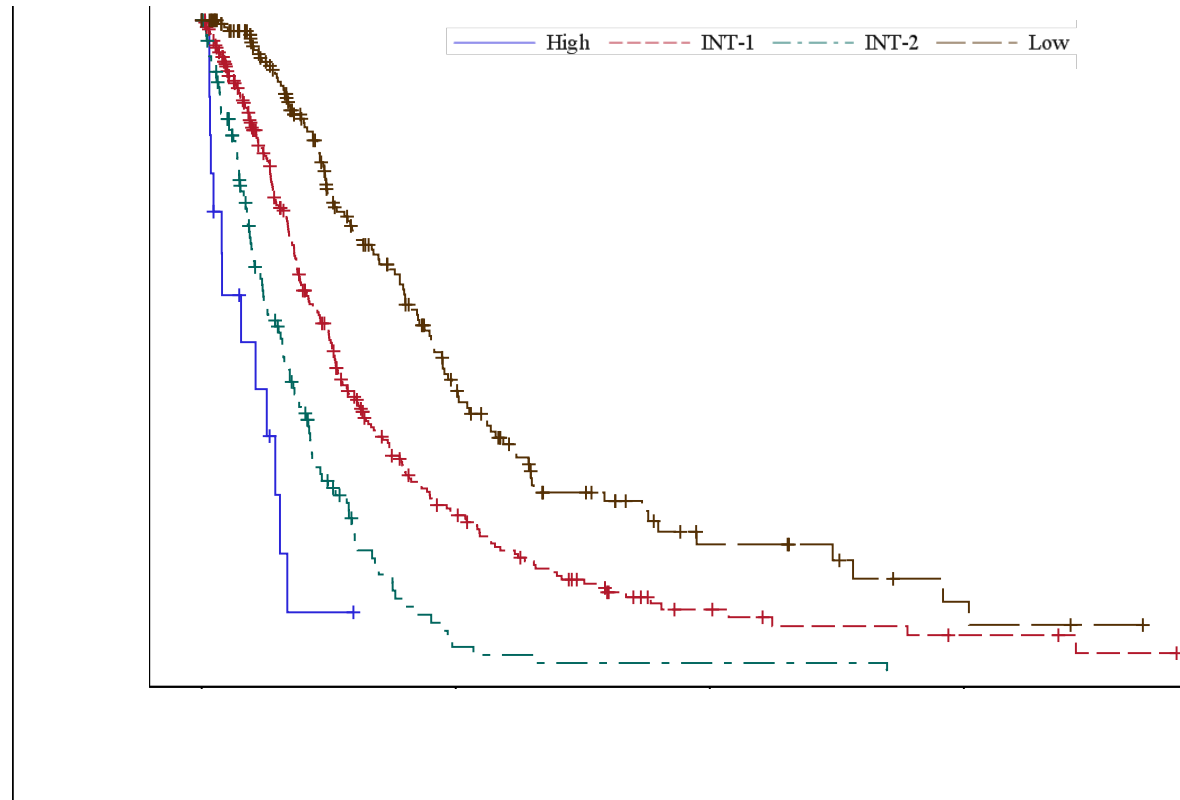


Figure S1. Kaplan-Meier plots demonstrating distinct differences in overall survival between patients stratified according to the modified CPSS scheme based on new score sums that include three-tiered blast-based CMML subgroups per WHO 2017 scheme. ($p < 0.0001$; Log-rank)