The mutational landscape in chronic myelomonocytic leukemia and its impact on allogeneic hematopoietic cell transplantation outcomes: a Center for Blood and Marrow Transplantation Research (CIBMTR) analysis

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Contents

Supplementary Table 1. Baseline Characteristics

Patient Characteristics	Total
Number of patients	313
Number of centers	78
Median age (range), years	64 (28-77)
Age at HCT, no. (%)	
< 50	33 (11)
50-59	75 (24)
60-69	165 (53)
≥ 70	40 (13)
Sex	
Male	215 (69)
Female	98 (31)
Karnofsky score	
< 90	128 (41)
≥ 90	178 (57)
Not reported	7 (2)
HCT-CI	
0	55 (18)
1-2	67 (21)
≥ 3	134 (43)
NA / Before 2007	57 (18)
Disease-Specific Characteristics	
CMML status: WHO criteria at transplant	
CMML-0 (<2% blasts in PB and <5% blasts in BM)	166 (53)
CMML-1 (2–4% blasts in PB and/or 5–9% blasts in BM)	62 (20)
CMML-2 (5–19% blasts in PB, 10–19% blasts in BM)	27 (9)
Not reported	58 (19)
Subtype at HCT	
WBC < 13×10^9 /L (MD-CMML)	237 (76)
WBC ≥ 13×10^9 /L (MP-CMML)	74 (24)
Not reported	2 (<1)
Therapy at HCT	
HMA	190 (61)
Chemo	10 (3)
HMA + chemo	27 (9)
Not reported	86 (27)
Peripheral blasts at HCT	
0-5%	258 (82)
> 5%	15 (5)
Not reported	40 (13)

Patient Characteristics	Total
Marrow blasts at HCT	
0-5%	222 (71)
>5%	61 (19)
Not reported	30 (10)
Spleen status at HCT	
Normal	186 (59)
Splenomegaly	84 (27)
Splenectomy	4 (1)
Not reported	39 (12)
CPSS prior to transplant	
Low	91 (29)
Intermediate-1	77 (25)
Intermediate-2	96 (31)
High	14 (4)
Not reported	35 (11)
Transplant-Related	
Time from diagnosis to transplant (months)	9 (<1-112)
Donor type	
Matched related	20 (6)
Matched unrelated	238 (76)
Mismatched unrelated[+]	52 (17)
Not reported	3 (<1)
Donor-recipient sex match	
M-M	157 (50)
M-F	65 (21)
F-M	58 (19)
F-F	33 (11)
Donor-recipient CMV serostatus	
+/+	66 (21)
+/-	43 (14)
-/+	97 (31)
-/-	103 (33)
Not reported	4 (1)
Graft source	
Bone marrow	46 (15)
Peripheral blood	267 (85)

Patient Characteristics	Total
GVHD prophylaxis	
Tacrolimus-based	253 (81)
Cyclosporine-based	46 (15)
Other	12 (4)
Not reported	2 (<1)
Conditioning intensity	
MAC	135 (43)
RIC	170 (54)
Not reported	8 (3)
Conditioning regimen	
MAC	
Bu/Cy	50 (16)
Flu/Bu	60 (19)
TBI/Cy	13 (4)
Other	12 (4)
RIC	
TBI/Flu	15 (5)
Flu/Bu	73 (23)
Flu/Mel	64 (20)
Other	18 (6)
Not reported	8 (3)
ATG/alemtuzumab	
No	188 (60)
Yes	110 (35)
Not reported	15 (5)
Year of transplant	
2001-2011	108 (35)
2012-2014	84 (27)
2015-2017	121 (39)
Median follow-up of survivors (range), months	47 (3-192)

Unless otherwise noted, data are n (%).

ATG, antithymocyte globulin; BM, bone marrow; Bu, busulfan; CI, comorbidity index; CIBMTR, Center for International Blood and Marrow Transplant; CMML, chronic myelomonocytic leukemia; CMV, cytomegalovirus; CPSS, Chronic myelomonocytic leukemia-specific prognostic scoring system; Cy, cyclophosphamide; F, female; Flu, fludarabine; GVHD, graft-versus-host disease; HCT, allogeneic hematopoietic cell transplantation; M, male; MAC, myeloablative; NA, not applicable; PB, peripheral blood; RIC, reduced-intensity; TBI, total body irradiation; WBC, white blood cell, HMA, hypomethylating agent; WHO, World Health Organization;

Supplementary Table 2. Genes Included in the 135-Gene Panel

ABL1	CDKN1B	GATA1	MPL	RB1	WHSC1
ARID1A	CDKN2A	GATA2	MYC	RFC4	WHSC1L1
ASXL1	CDKN2B	GNA13	MYD88	RPS15	WT1
ATM	CDKN2C	GNAS	NFKB2	RUNX1	XPO1
B2M	CEBPA	HCK	NOTCH1	SETBP1	ZEB1
BCL2	CHD2	HRAS	NOTCH2	SF3B1	ZRSR2
BCL6	CRBN	ID3	NPM1	SMC1A	
BCOR	CREBBP	IDH1	NRAS	SMC3	
BCORL1	CSF3R	IDH2	NTRK1	SOCS1	
BIRC3	CUX1	IGLL5	PAX5	SOCS6	
BRAF	CXCR4	IKZF1	PDCD1	SPI1	
BTK	DDx3x	IL6	PDGFRA	SRSF2	
CALR	DIS3	IL7R	PHF6	STAG2	
CARD11	DNMT3A	IRF4	PIGA	STAT3	
CBL	E2F1	JAK1	PIK3CA	STAT5A	
CBLB	EGFR	JAK2	PIK3CD	STAT5B	
CCND1	EP300	JAK3	PIK3CG	STAT6	
CCND3	ETV6	KDM6A	PIK3R5	SUZ12	
CD38	EZH2	KIT	PLCG2	TCF3	
CD3E	FAM46C	KRAS	POT1	TET2	
CD3G	FBXW7	LCK	PRDM1	TNFAIP3	
CD79A	FGFR3	LMO2	PTEN	TP53	
CD79B	FH	MAPK1	PTK2B	TP63	
CDK4	FLT3	MEF2B	PTPN11	U2AF1	
CDK7	FOXO1	MGA	RAD21	UBR5	

Supplementary Table 3. Mutational Profile

Characteristic	N (%)
Number of mutations[a]	
0	23 (7)
1	37 (12)
2	50 (16)
3	64 (20)
4	67 (21)
5	33 (11)
6	25 (8)
7	6 (2)
8	5 (2)
9	2 (<1)
10	1 (<1)
ASXL1 mutations	
No	119 (38)
Yes	194 (62)
ATM mutations	
No	310 (99)
Yes	3 (<1)
BCOR mutations	
No	305 (97)
Yes	8 (3)
BRAF mutations	
No	304 (97)
Yes	9 (3)
CALR mutations	
No	310 (99)
Yes	3 (<1)
CBL mutations	
No	271 (87)
Yes	42 (13)
CDKN1B mutations	
No	312
Yes	1 (<1)
CEBPA mutations	
No	306 (98)
Yes	7 (2)
CSF3R mutations	
No	305 (97)
Yes	8 (3)

Characteristic	N (%)
CUX1 mutations	
No	297 (95)
Yes	16 (5)
DNMT3A mutations	
No	281 (90)
Yes	32 (10)
EZH2 mutations	
No	292 (93)
Yes	21 (7)
FLT3 mutations	
No	307 (98)
Yes	6 (2)
GATA2 mutations	
No	303 (97)
Yes	10 (3)
IDH1 mutations	
No	312
Yes	1 (<1)
IDH2 mutations	
No	290 (93)
Yes	23 (7)
JAK2 mutations	
No	294 (94)
Yes	19 (6)
KIT mutations	
No	306 (98)
Yes	7 (2)
KRAS mutations	
No	270 (86)
Yes	43 (14)
MPL mutations	
No	312
Yes	1 (<1)
NPM1 mutations	
No	305 (97)
Yes	8 (3)
NRAS mutations	
No	252 (81)
Yes	61 (19)

Characteristic	N (%)
PHF6 mutations	
No	305 (97)
Yes	8 (3)
PTPN11 mutations	
No	296 (95)
Yes	17 (5)
RUNX1 mutations	
No	262 (84)
Yes	51 (16)
SETBP1 mutations	
No	270 (86)
Yes	43 (14)
SF3B1 mutations	
No	303 (97)
Yes	10 (3)
SRSF2 mutations	
No	216 (69)
Yes	97 (31)
STAG2 mutations	
No	299 (96)
Yes	14 (4)
TET2 mutations	
No	204 (65)
Yes	109 (35)
TP53 mutations	
No	303 (97)
Yes	10 (3)
U2AF1 mutations	
No	296 (95)
Yes	17 (5)
WT1 mutations	
No	307 (98)
Yes	6 (2)
ZRSR2 mutations	
No	302 (96)
Yes	11 (4)

[a] 23 patients had no identifiable somatic mutations.

Supplementary Table 4a. Mutational Profile by subtype (CMML-MD vs CMML-MP) at HCT

Characteristic	CMML-MD	CMML-MP	P Value
Number of mutations			**0.005**
0	23 (10)	0	
1	35 (15)	2 (3)	
2	36 (15)	13 (18)	
3	47 (20)	17 (23)	
4	46 (19)	20 (27)	
5	24 (10)	9 (12)	
6	16 (7)	9 (12)	
7	6 (3)	0	
8	3 (1)	2 (3)	
9	1 (<1)	1 (1)	
10	0	1 (1)	
ASXL1 mutation			**<0.001**
No	104 (44)	13 (18)	
Yes	133 (56)	61 (82)	
ATM mutation			0.70
No	235 (99)	73 (99)	
Yes	2 (<1)	1 (1)	
BCOR mutation			0.45
No	230 (97)	73 (99)	
Yes	7 (3)	1 (1)	
BRAF mutation			0.91
No	230 (97)	72 (97)	
Yes	7 (3)	2 (3)	
CALR mutation			0.08
No	236	72 (97)	
Yes	1 (<1)	2 (3)	
CBL mutation			0.24
No	208 (88)	61 (82)	
Yes	29 (12)	13 (18)	
CDKN1B mutation			0.58
No	236	74	
Yes	1 (<1)	0	
CEBPA mutation			0.55
No	231 (97)	73 (99)	
Yes	6 (3)	1 (1)	
CSF3R mutation			0.08
No	233 (98)	70 (95)	
Yes	4 (2)	4 (5)	

Characteristic	CMML-MD	CMML-MP	P Value
CUX1 mutation			0.05
No	228 (96)	67 (91)	
Yes	9 (4)	7 (9)	
DNMT3A mutation			0.87
No	213 (90)	66 (89)	
Yes	24 (10)	8 (11)	
EZH2 mutation			**0.001**
No	227 (96)	63 (85)	
Yes	10 (4)	11 (15)	
FLT3 mutation			0.13
No	234 (99)	71 (96)	
Yes	3 (1)	3 (4)	
GATA2 mutation			0.22
No	231 (97)	70 (95)	
Yes	6 (3)	4 (5)	
IDH1 mutation			0.07
No	237	73 (99)	
Yes	0	1 (1)	
IDH2 mutation			0.21
No	217 (92)	71 (96)	
Yes	20 (8)	3 (4)	
JAK2 mutation			0.12
No	226 (95)	67 (91)	
Yes	11 (5)	7 (9)	
KIT mutation			**0.003**
No	235 (99)	69 (93)	
Yes	2 (<1)	5 (7)	
KRAS mutation			0.24
No	202 (85)	67 (91)	
Yes	35 (15)	7 (9)	
MPL mutation			0.58
No	236	74	
Yes	1 (<1)	0	
NPM1 mutation			0.11
No	229 (97)	74	
Yes	8 (3)	0	
NRAS mutation			0.07
No	196 (83)	54 (73)	
Yes	41 (17)	20 (27)	

Characteristic	CMML-MD	CMML-MP	P Value
PHF6 mutation			0.94
No	231 (97)	72 (97)	
Yes	6 (3)	2 (3)	
PTPN11 mutation			0.23
No	222 (94)	72 (97)	
Yes	15 (6)	2 (3)	
RUNX1 mutation			0.96
No	198 (84)	62 (84)	
Yes	39 (16)	12 (16)	
SETBP1 mutation			0.29
No	207 (87)	61 (82)	
Yes	30 (13)	13 (18)	
SF3B1 mutation			0.30
No	228 (96)	73 (99)	
Yes	9 (4)	1 (1)	
SRSF2 mutation			**0.003**
No	175 (74)	41 (55)	
Yes	62 (26)	33 (45)	
STAG2 mutation			0.39
No	225 (95)	72 (97)	
Yes	12 (5)	2 (3)	
TET2 mutation			0.07
No	162 (68)	42 (57)	
Yes	75 (32)	32 (43)	
TP53 mutation			0.30
No	228 (96)	73 (99)	
Yes	9 (4)	1 (1)	
U2AF1 mutation			0.02
No	220 (93)	74	
Yes	17 (7)	0	
WT1 mutation			0.13
No	234 (99)	71 (96)	
Yes	3 (1)	3 (4)	
ZRSR2 mutation			0.66
No	228 (96)	72 (97)	
Yes	9 (4)	2 (3)	

Due to subtype not reported, 2 patients were excluded.

CMML-MD, chronic myelomonocytic leukemia myelodysplastic type; CMML-MP, chronic myelomonocytic leukemia myeloproliferative type; HCT, hematopoietic cell transplantation

Supplementary Table 4b: Mutational Profile by WHO criteria at HCT

Characteristic	CMML-0	CMML-1	CMML-2	P Value
Number of mutations				0.23
0	17 (10)	2 (3)	1 (4)	
1	24 (14)	5 (8)	2 (7)	
2	25 (15)	10 (16)	4 (15)	
3	33 (20)	14 (23)	5 (19)	
4	39 (23)	11 (18)	6 (22)	
5	13 (8)	9 (15)	4 (15)	
6	9 (5)	9 (15)	2 (7)	
7	3 (2)	1 (2)	1 (4)	
8	2 (1)	1 (2)	1 (4)	
9	1 (<1)	0	0	
10	0	0	1 (4)	
ASXL1 mutation				**0.04**
No	73 (44)	16 (26)	10 (37)	
Yes	93 (56)	46 (74)	17 (63)	
ATM mutation				0.36
No	165 (99)	61 (98)	26 (96)	
Yes	1 (<1)	1 (2)	1 (4)	
BCOR mutation				**0.04**
No	163 (98)	60 (97)	24 (89)	
Yes	3 (2)	2 (3)	3 (11)	
BRAF mutation				**0.04**
No	163 (98)	59 (95)	24 (89)	
Yes	3 (2)	3 (5)	3 (11)	
CALR mutation				0.17
No	165 (99)	62	26 (96)	
Yes	1 (<1)	0	1 (4)	
CBL mutation				0.19
No	141 (85)	56 (90)	26 (96)	
Yes	25 (15)	6 (10)	1 (4)	
CDKN1B mutation				0.21
No	166	61 (98)	27	
Yes	0	1 (2)	0	
CEBPA mutation				**0.03**
No	165 (99)	61 (98)	25 (93)	
Yes	1 (<1)	1 (2)	2 (7)	
CSF3R mutation				**0.005**
No	163 (98)	62	24 (89)	
Yes	3 (2)	0	3 (11)	

Characteristic	CMML-0	CMML-1	CMML-2	P Value
CUX1 mutation				0.19
No	157 (95)	56 (90)	27	
Yes	9 (5)	6 (10)	0	
DNMT3A mutation				0.37
No	150 (90)	54 (87)	22 (81)	
Yes	16 (10)	8 (13)	5 (19)	
EZH2 mutation				0.27
No	158 (95)	57 (92)	27	
Yes	8 (5)	5 (8)	0	
FLT3 mutation				**0.006**
No	164 (99)	61 (98)	24 (89)	
Yes	2 (1)	1 (2)	3 (11)	
GATA2 mutation				**0.006**
No	165 (99)	57 (92)	25 (93)	
Yes	1 (<1)	5 (8)	2 (7)	
IDH1 mutation				**0.01**
No	166	62	26 (96)	
Yes	0	0	1 (4)	
IDH2 mutation				**0.02**
No	155 (93)	58 (94)	21 (78)	
Yes	11 (7)	4 (6)	6 (22)	
JAK2 mutation				0.19
No	157 (95)	56 (90)	27	
Yes	9 (5)	6 (10)	0	
KIT mutation				0.44
No	163 (98)	59 (95)	26 (96)	
Yes	3 (2)	3 (5)	1 (4)	
KRAS mutation				0.13
No	139 (84)	58 (94)	22 (81)	
Yes	27 (16)	4 (6)	5 (19)	
MPL mutation				0.76
No	165 (99)	62	27	
Yes	1 (<1)	0	0	
NPM1 mutation				0.11
No	162 (98)	62	25 (93)	
Yes	4 (2)	0	2 (7)	
NRAS mutation				**0.001**
No	142 (86)	49 (79)	15 (56)	
Yes	24 (14)	13 (21)	12 (44)	

Characteristic	CMML-0	CMML-1	CMML-2	P Value
PHF6 mutation				0.65
No	161 (97)	60 (97)	27	
Yes	5 (3)	2 (3)	0	
PTPN11 mutation				0.32
No	159 (96)	58 (94)	24 (89)	
Yes	7 (4)	4 (6)	3 (11)	
RUNX1 mutation				0.22
No	137 (83)	48 (77)	25 (93)	
Yes	29 (17)	14 (23)	2 (7)	
SETBP1 mutation				0.22
No	148 (89)	50 (81)	24 (89)	
Yes	18 (11)	12 (19)	3 (11)	
SF3B1 mutation				0.46
No	158 (95)	60 (97)	27	
Yes	8 (5)	2 (3)	0	
SRSF2 mutation				0.24
No	121 (73)	38 (61)	19 (70)	
Yes	45 (27)	24 (39)	8 (30)	
STAG2 mutation				**<0.001**
No	164 (99)	58 (94)	22 (81)	
Yes	2 (1)	4 (6)	5 (19)	
TET2 mutation				**0.02**
No	101 (61)	47 (76)	22 (81)	
Yes	65 (39)	15 (24)	5 (19)	
TP53 mutation				0.63
No	162 (98)	59 (95)	26 (96)	
Yes	4 (2)	-3 (5)	1 (4)	
U2AF1 mutation				0.34
No	158 (95)	56 (90)	26 (96)	
Yes	8 (5)	6 (10)	1 (4)	
WT1 mutation				0.10
No	164 (99)	61 (98)	25 (93)	
Yes	2 (1)	1 (2)	2 (7)	
ZRSR2 mutation				0.47
No	160 (96)	61 (98)	27	
Yes	6 (4)	1 (2)	0	

Due to CMML WHO criteria status not reported, 58 patients were excluded.

CMML, chronic myelomonocytic leukemia; HCT, hematopoietic cell transplantation; WHO, World Health Organization

Supplementary Table 5. Outcomes for the entire cohort

Outcomes	N	Prob (95% CI)
Overall survival	313	
100-day		83.4 (79.1-87.3)%
1-year		53.7 (48.1-59.3)%
2-year		43.8 (38.1-49.6)%
3-year		39 (33.2-44.9)%
4-year		32.7 (26.8-38.9)%
Relapse	308	
100-day		10.7 (7.5-14.4)%
1-year		35.7 (30.4-41.2)%
2-year		40.3 (34.8-45.9)%
3-year		41.6 (36-47.3)%
4-year		42.8 (37.1-48.6)%
Treatment-related mortality	308	
100-day		13.3 (9.7-17.3)%
1-year		25.2 (20.5-30.2)%
2-year		27.9 (23-33.1)%
3-year		28.8 (23.8-34.1)%
4-year		30.6 (25.3-36.2)%
Disease-free survival	308	
100-day		76 (71-80.6)%
1-year		39.1 (33.7-44.6)%
2-year		31.8 (26.6-37.3)%
3-year		29.6 (24.4-35.1)%
4-year		26.6 (21.3-32.1)%

Supplementary Table 6a. Multivariate Analysis: Overall Survival (Mutation Profile)

Variable	HR	95%CI Lower Limit	95%CI Upper Limit	P Value	Adjusted P Values Using False Discovery Rate
ASXL1 mutation	0.91	0.67	1.23	0.5465	0.8618
NRAS mutation	1.20	0.84	1.72	0.3064	0.8618
RUNX1 mutation	1.00	0.67	1.50	0.9826	0.9826
SETBP1 mutation	0.88	0.58	1.33	0.5374	0.8618
BCOR mutation	1.23	0.53	2.86	0.6236	0.8618
BRAF mutation	1.56	0.63	3.90	0.3382	0.8618
CBL mutation	1.07	0.70	1.63	0.7572	0.8784
CEBPA mutation	1.08	0.40	2.94	0.8822	0.9475
CSF3R mutation	1.34	0.58	3.10	0.4988	0.8618
CUX1 mutation	0.81	0.39	1.65	0.5525	0.8618
DNMT3A mutation	1.70	1.11	2.60	**0.0147**	**0.2132**
EZH2 mutation	0.71	0.38	1.32	0.2791	0.8618
FLT3 mutation	2.01	0.79	5.09	0.1424	0.7753
GATA2 mutation	1.69	0.81	3.50	0.1604	0.7753
IDH2 mutation	1.10	0.65	1.87	0.7132	0.8618
JAK2 mutation	1.37	0.74	2.52	0.3136	0.8618
KIT mutation	0.68	0.24	1.89	0.4572	0.8618
KRAS mutation	0.88	0.57	1.34	0.5393	0.8618
NPM1 mutation	0.92	0.34	2.53	0.8758	0.9475
PHF6 mutation	1.46	0.59	3.61	0.4192	0.8618
PTPN11 mutation	0.61	0.31	1.19	0.1468	0.7753
SF3B1 mutation	0.58	0.21	1.56	0.2787	0.8618
SRSF2 mutation	1.06	0.78	1.44	0.6965	0.8618
STAG2 mutation	1.15	0.62	2.16	0.6556	0.8618
TET2 mutation	1.09	0.80	1.48	0.6003	0.8618
TP53 mutation	2.72	1.37	5.39	**0.0042**	**0.1218**
U2AF1 mutation	1.57	0.89	2.76	0.1177	0.7753
WT1 mutation	0.98	0.35	2.73	0.9661	0.9826
ZRSR2 mutation	1.21	0.56	2.58	0.6305	0.8618

Supplementary Table 6b. Multivariate Analysis: Disease-Free Survival (Mutation Profile)

Variable	HR	95%CI Lower Limit	95%CI Upper Limit	P value	Adjusted P Values using False Discovery Rate
ASXL1 mutation	0.88	0.66	1.16	0.3572	0.7886
NRAS mutation	1.28	0.92	1.77	0.1393	0.7886
RUNX1 mutation	0.96	0.67	1.39	0.8395	0.9863
SETBP1 mutation	0.90	0.61	1.32	0.5735	0.9863
BCOR mutation	0.96	0.42	2.18	0.9184	0.9863
BRAF mutation	1.50	0.70	3.23	0.2999	0.7886
CBL mutation	0.95	0.65	1.41	0.8094	0.9863
CEBPA mutation	1.09	0.45	2.66	0.8428	0.9863
CSF3R mutation	0.90	0.40	2.04	0.7930	0.9863
CUX1 mutation	1.02	0.55	1.87	0.9625	0.9863
DNMT3A mutation	1.66	1.11	2.49	**0.0138**	**0.2001**
EZH2 mutation	0.74	0.43	1.28	0.2814	0.7886
FLT3 mutation	1.50	0.61	3.67	0.3807	0.7886
GATA2 mutation	1.52	0.71	3.26	0.2776	0.7886
IDH2 mutation	1.12	0.68	1.86	0.6553	0.9863
JAK2 mutation	1.79	1.06	3.03	**0.0293**	**0.2832**
KIT mutation	0.78	0.28	2.13	0.6219	0.9863
KRAS mutation	0.96	0.65	1.42	0.8451	0.9863
NPM1 mutation	0.64	0.23	1.72	0.3711	0.7886
PHF6 mutation	0.99	0.41	2.43	0.9863	0.9863
PTPN11 mutation	0.67	0.35	1.27	0.2158	0.7886
SF3B1 mutation	0.85	0.40	1.81	0.6649	0.9863
SRSF2 mutation	1.18	0.89	1.57	0.2429	0.7886
STAG2 mutation	0.98	0.53	1.80	0.9345	0.9863
TET2 mutation	1.15	0.87	1.53	0.3224	0.7886
TP53 mutation	2.94	1.50	5.79	**0.0018**	**0.0522**
U2AF1 mutation	1.39	0.80	2.40	0.2395	0.7886
WT1 mutation	0.96	0.35	2.62	0.9398	0.9863
ZRSR2 mutation	1.24	0.61	2.52	0.5506	0.9863

Supplementary Table 6c: Relapse (Mutation Profile)

Variable	HR	95%CI Lower Limit	95%CI Upper Limit	P value	Adjusted P Values Using False Discovery Rate
ASXL1 mutation	0.80	0.55	1.15	0.2307	0.9466
NRAS mutation	1.15	0.74	1.78	0.5372	0.9630
RUNX1 mutation	0.90	0.55	1.46	0.6625	0.9630
SETBP1 mutation	0.82	0.48	1.39	0.4570	0.9466
BCOR mutation	1.14	0.42	3.14	0.7983	0.9630
BRAF mutation	1.03	0.32	3.28	0.9630	0.9630
CBL mutation	0.94	0.56	1.58	0.8156	0.9630
CEBPA mutation	1.13	0.36	3.55	0.8398	0.9630
CSF3R mutation	0.27	0.04	1.97	0.1982	0.9466
CUX1 mutation	0.90	0.40	2.06	0.8038	0.9630
DNMT3A mutation	1.50	0.86	2.59	0.1514	0.8781
EZH2 mutation	0.73	0.35	1.52	0.4014	0.9466
FLT3 mutation	1.48	0.47	4.72	0.5048	0.9630
GATA2 mutation	2.08	0.84	5.14	0.1137	0.8781
IDH2 mutation	1.34	0.73	2.46	0.3533	0.9466
JAK2 mutation	1.72	0.86	3.45	0.1282	0.8781
KIT mutation	0.36	0.05	2.59	0.3084	0.9466
KRAS mutation	0.63	0.35	1.13	0.1229	0.8781
NPM1 mutation	0.58	0.14	2.35	0.4436	0.9466
PHF6 mutation	0.93	0.29	2.94	0.8947	0.9630
PTPN11 mutation	1.02	0.49	2.12	0.9496	0.9630
SF3B1 mutation	1.03	0.42	2.54	0.9504	0.9630
SRSF2 mutation	1.07	0.73	1.57	0.7201	0.9630
STAG2 mutation	0.65	0.24	1.76	0.3928	0.9466
TET2 mutation	1.09	0.75	1.59	0.6398	0.9630
TP53 mutation	2.94	1.18	7.28	**0.0201**	**0.5829**
U2AF1 mutation	1.14	0.53	2.47	0.7311	0.9630
WT1 mutation	0.43	0.06	3.11	0.4028	0.9466
ZRSR2 mutation	0.79	0.25	2.49	0.6874	0.9630

Supplementary Table 6d. MVA: Treatment-Related Mortality (Mutation Profile)

Variable	HR	95%CI Lower Limit	95%CI Upper Limit	P Value	Adjusted P Values Using False Discovery Rate
ASXL1 mutation	0.74	0.46	1.18	0.2084	0.9005
NRAS mutation	1.18	0.70	1.98	0.5389	0.9005
RUNX1 mutation	0.83	0.47	1.46	0.5091	0.9005
SETBP1 mutation	0.85	0.48	1.50	0.5693	0.9005
BCOR mutation	0.52	0.12	2.19	0.3723	0.9005
BRAF mutation	1.96	0.70	5.51	0.2027	0.9005
CBL mutation	0.80	0.44	1.46	0.4635	0.9005
CEBPA mutation	0.68	0.16	2.89	0.6035	0.9005
CSF3R mutation	1.26	0.49	3.24	0.6375	0.9005
CUX1 mutation	0.92	0.36	2.32	0.8552	0.9505
DNMT3A mutation	1.89	1.03	3.44	**0.0388**	**0.5626**
EZH2 mutation	0.70	0.30	1.61	0.3979	0.9005
FLT3 mutation	1.30	0.31	5.44	0.7212	0.9365
GATA2 mutation	0.82	0.20	3.35	0.7809	0.9365
IDH2 mutation	0.74	0.30	1.85	0.5198	0.9005
JAK2 mutation	1.47	0.65	3.32	0.3491	0.9005
KIT mutation	1.07	0.32	3.50	0.9177	0.9505
KRAS mutation	1.30	0.76	2.22	0.3470	0.9005
NPM1 mutation	0.72	0.18	2.96	0.6521	0.9005
PHF6 mutation	0.79	0.19	3.31	0.7450	0.9365
PTPN11 mutation	0.21	0.05	0.86	**0.0300**	**0.5626**
SF3B1 mutation	0.61	0.15	2.49	0.4881	0.9005
SRSF2 mutation	1.01	0.63	1.62	0.9723	0.9723
STAG2 mutation	0.901	0.39	2.08	0.8073	0.9365
TET2 mutation	0.976	0.62	1.54	0.9169	0.9505
TP53 mutation	2.612	0.94	7.24	0.0649	0.6274
U2AF1 mutation	1.617	0.73	3.56	0.2328	0.9005
WT1 mutation	1.680	0.52	5.47	0.3894	0.9005
ZRSR2 mutation	1.884	0.76	4.67	0.1714	0.9005

Supplementary Table 7. Multivariate Analysis: Pre-Transplant CPSS and CPSS-Mol

	CPSS (AIC= 2023.29)					CPSS-Mol (AIC= 2023.58)				
			95% CI					95% CI		
Variable	N	HR	Lower Limit	Upper Limit	P Value	N	HR	Lower Limit	Upper Limit	P Value
Overall survival										
CPSS or CPSS-Mol										
Low	91	1.00			0.0067	39	1.00			0.0148
Intermediate-1	77	1.13	0.75	1.70	0.5512	52	1.07	0.60	1.90	0.8296
Intermediate-2	96	1.46	1.00	2.13	0.0494	118	1.27	0.76	2.10	0.3600
High	14	3.22	1.69	6.15	0.0004	78	2.00	1.20	3.34	0.0079
Not reported	35	1.29	0.78	2.15	0.3270	26	1.34	0.69	2.60	0.3830
Transplant donor type										
Matched related	20	1.00			0.0034	20	1.00			0.0047
Matched unrelated	238	0.92	0.50	1.68	0.7799	238	0.91	0.49	1.67	0.7517
Mismatched unrelated	52	1.74	0.89	3.39	0.1047	52	1.69	0.86	3.33	0.1284
Not reported	3	2.26	0.60	8.48	0.2262	3	2.13	0.57	7.97	0.2598
HCT-CI										
0	55	1.00			0.0049	55	1.00			0.0124
1-2	67	1.71	1.02	2.86	0.0406	67	1.57	0.94	2.61	0.0843
≥ 3	134	2.05	1.29	3.25	0.0024	134	1.99	1.26	3.14	0.0032
NA / before 2007	57	2.35	1.44	3.85	0.0007	57	2.09	1.28	3.43	0.0034
Contrast										
Intermediate-1 vs intermediate-2		0.77	0.53	1.14	0.1903		0.84	0.54	1.31	0.4439
Intermediate-1 vs high		0.35	0.18	0.67	0.0016		0.53	0.34	0.84	0.0065
Intermediate-2 vs high		0.45	0.24	0.85	0.0137		0.63	0.45	0.90	0.0102
1-2 vs ≥ 3		0.84	0.57	1.24	0.3674		0.79	0.53	1.17	0.2343
Matched unrelated vs mismatched unrelated		0.53	0.37	0.76	0.0005		0.54	0.37	0.77	0.0007

Variable	CPSS (AIC= 2023.29)					CPSS-Mol (AIC= 2023.58)				
			95% CI					95% CI		
	N	HR	Lower Limit	Upper Limit	P Value	N	HR	Lower Limit	Upper Limit	P Value
Disease-free survival										
CPSS or CPSS-Mol										
Low	89	1.00			0.0762	38	1.00			0.1546
Intermediate-1	77	1.11	0.76	1.62	0.5803	51	1.16	0.68	1.97	0.5939
Intermediate-2	95	1.36	0.96	1.92	0.0850	118	1.43	0.90	2.26	0.1292
High	13	2.24	1.20	4.19	0.0115	76	1.73	1.07	2.80	0.0243
Not reported	35	1.42	0.88	2.27	0.1471	26	1.44	0.78	2.67	0.2448
Number of mutations [a]		1.09	1.01	1.17	0.0220		NA	NA	NA	NA
Contrast										
Intermediate-1 vs intermediate-2		0.82	0.58	1.17	0.2689		0.81	0.54	1.21	0.3026
Intermediate-1 vs high		0.50	0.27	0.93	0.0290		0.67	0.44	1.02	0.0604
Intermediate-2 vs high		0.61	0.32	1.12	0.1080		0.82	0.59	1.14	0.2424
Relapse										
CPSS prior to transplant										
Low	89	1.00			0.1582	38	1.00			0.7237
Intermediate-1	77	1.08	0.68	1.74	0.7390	51	1.59	0.82	3.10	0.1722
Intermediate-2	95	1.07	0.69	1.69	0.7549	118	1.45	0.79	2.67	0.2307
High	13	2.73	1.25	5.99	0.0120	76	1.49	0.78	2.86	0.2309
Not reported	35	1.05	0.54	2.01	0.8909	26	1.33	0.57	3.10	0.5159
Year of HCT [b]										
2008-2011	104	1.00			0.0236	NA	NA	NA	NA	NA
2012-2014	84	1.52	0.99	2.35	0.0561	NA	NA	NA	NA	NA
2015-2017	121	0.86	0.55	1.35	0.5119	NA	NA	NA	NA	NA
Contrast										
Intermediate-1 vs intermediate-2		1.01	0.63	1.62	0.9722		1.10	0.68	1.76	0.7084
Intermediate-1 vs high		0.40	0.18	0.88	0.0220		1.07	0.63	1.81	0.8067
Intermediate-2 vs high		0.39	0.18	0.86	0.0196		0.98	0.62	1.53	0.9143
2012-2014 vs 2015-2017		1.77	1.15	2.71	0.0089		NA	NA	NA	NA

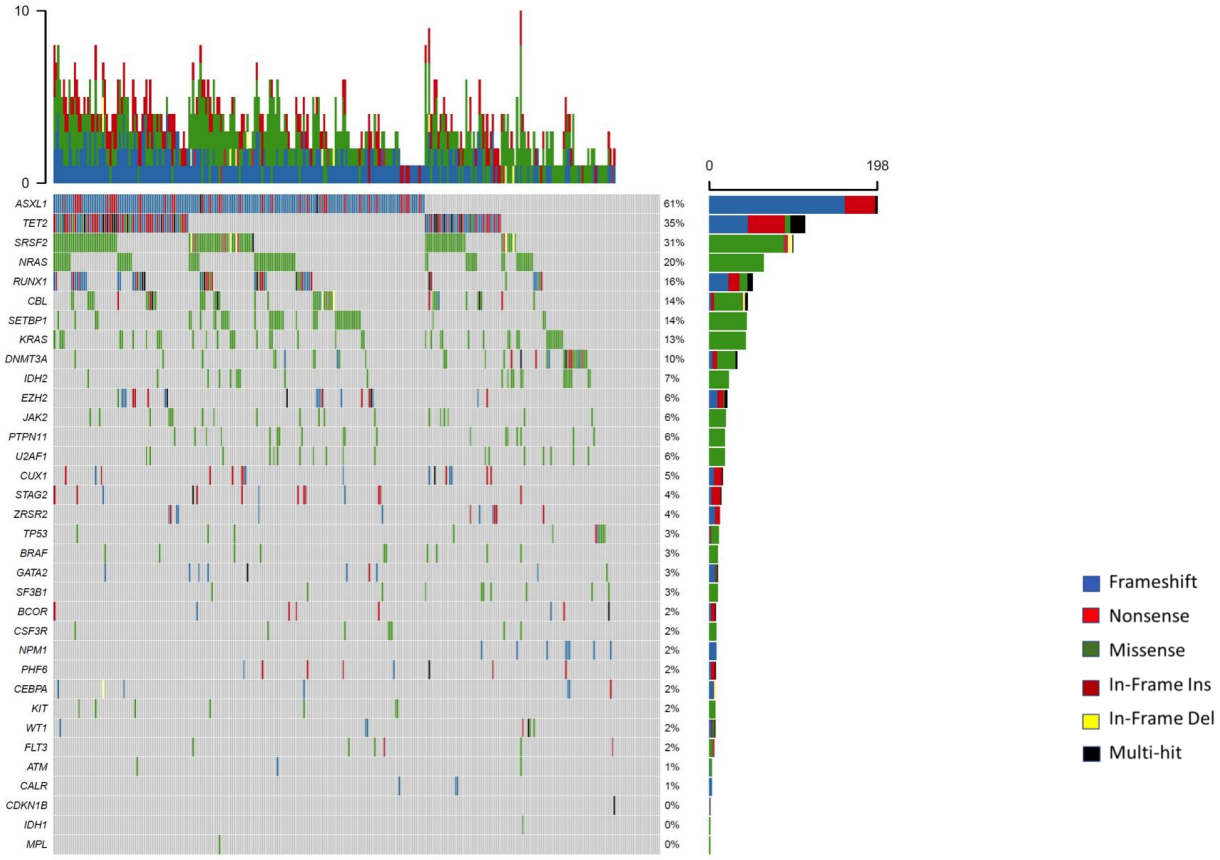
Variable	CPSS (AIC= 2023.29) N	HR	95% CI Lower Limit	95% CI Upper Limit	P Value	CPSS-Mol (AIC= 2023.58) N	HR	95% CI Lower Limit	95% CI Upper Limit	P Value
Treatment-related mortality										
CPSS prior to transplant										
Low	89	1.00			0.1141	38	1.00			0.1111
Intermediate-1	77	1.27	0.69	2.34	0.4495	51	0.50	0.19	1.31	0.1575
Intermediate-2	95	1.93	1.11	3.37	0.0205	118	1.12	0.54	2.31	0.7693
High	13	2.02	0.68	5.96	0.2038	76	1.53	0.72	3.27	0.2725
Not reported	35	2.01	0.99	4.07	0.0543	26	1.30	0.52	3.27	0.5727
Number of mutations		1.17	1.06	1.31	0.0031		1.13	1.02	1.27	0.0267
Contrast										
Intermediate-1 vs intermediate-2		0.66	0.39	1.11	0.1167		0.44	0.20	1.00	0.0500
Intermediate-1 vs high		0.63	0.22	1.82	0.3924		0.32	0.14	0.74	0.0078
Intermediate-2 vs high		0.63	0.22	1.82	0.3924		0.32	0.14	0.74	0.0078

[a] Number of mutations was not significant in the CPSS-Mol model for disease-free survival.

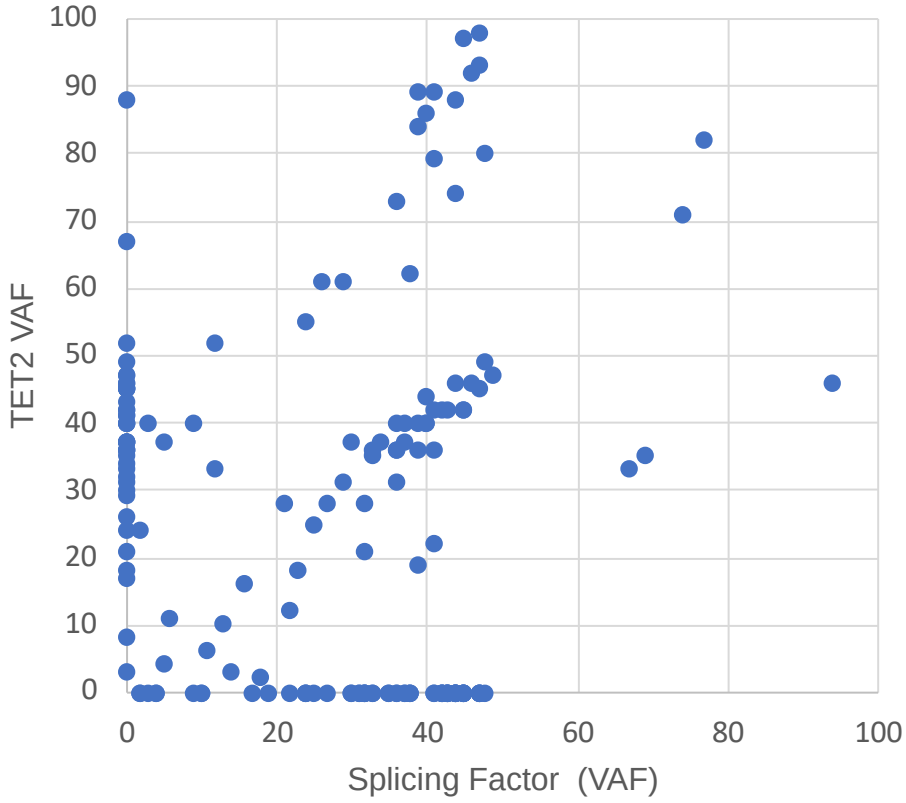
[b] Year of transplant was not significant in the CPSS-Mol model for relapse.

Abbreviations: CMML, chronic myelomonocytic leukemia; CPSS, CMML-specific prognostic scoring system; CPSS-Mol, Molecular CMML-specific scoring system; HCT, hematopoietic cell transplantation; HCT-CI; Hematopoietic Cell Transplantation Comorbidity Index; NA, not applicable.

Supplementary Figure 1. Oncoplot for the entire cohort



Supplementary Figure 2 – TET2 and splicing factor mutations



Mutation Analysis

Mutation analysis was performed centrally at City of Hope. Next-generation sequencing (NGS) libraries were prepared from genomic DNA (40 ng) using the SureSelect target enrichment system (Agilent Technologies Inc.) after transposase-based fragmentation and adapter ligation. The adapter-ligated library was amplified by polymerase chain reaction, and quality control was performed for sizing and concentration. Target regions were captured using a customized SureSelect library (Agilent Technologies) for all coding exons plus 10 flanking bases of 131 genes (Supplementary Table 2). After hybridization of 750 ng of adapter-ligated library with biotin-labeled probes that are specific to target regions, the dual-index tag was added during post-capture polymerase chain reaction amplification. The amplified captured libraries were quality-controlled using a high sensitivity DNA Bioanalyzer kit

(Agilent Technologies Inc.) then pooled and sequenced using HiSeq 150 bp paired-end sequencing. Alignment of sequence reads to the human genome (GRCh37/hg19), variant calling and annotation were performed independently using two software applications – CLC Biomedical Workbench (CLC Bio, Aarhus, Denmark) and NextGENe (SoftGenetics, State Collage, PA, USA). Annotated variants were processed using previously published criteria.(24, 25) Synonymous variants, variants located >2 bp outside protein-coding regions, polymorphisms present in >1% in population databases including ExAC, gnomAD, Exome Variant Server and the 1000 Genomes Project, and variants with <30x coverage were filtered. The remaining variants were evaluated using tumor-specific databases (COSMIC, cBioPortal), information retrieved from literature, sequence conservation, and in silico prediction algorithms, including SIFT, Polyphen-2, and FATHMM, for clinical significance.