Supplemental Table 1. Full list of 54 myeloid neoplasm-relevant genes studied in targeted NGS sequencing.

Gene name	Target region (exon)	Gene name	Target region (exon)
ABL	4-6	***JAK3***	13
ASXL1	12	***KDM6A***	full
ATRX	8-10 and 17-31	***KIT***	2, 8-11, 13+17
BCOR	full	***KRAS***	2+3
BCORL1	full	***MLL***	5-8
BRAF	15	***MPL***	10
CALR	9	***MYD88***	3-5
CBL	8+9	***NOTCH1***	26-28, 34
CBLB	9, 10	***NPM1***	12
CBLC	9, 10	***NRAS***	2+3
CDKN2A	full	***PDGFRA***	12, 14, 18
CEBPA	full	***PHF6***	full
CSF3R	14-17	***PTEN***	5+7
CUX1	full	***PTPN11***	3+13
DNMT3A	full	***RAD21***	full
ETV6	full	***RUNX1***	full
EZH2	full	***SETBP1***	4 (partial)
FBXW7	9+10+11	***SF3B1***	13-16
FLT3	14+15+20	***SMC1A***	2, 11, 16+17
GATA1	2	***SMC3***	10, 13, 19, 23, 25+28
GATA2	2-6	***SRSF2***	1
GNAS	8+9	***STAG2***	full
HRAS	2+3	***TET2***	3-11
IDH1	4	***TP53***	2-11
IDH2	4	***U2AF1***	2+6
IKZF1	full	***WT1***	7+9
JAK2	12+14	***ZRSR2***	full

Supplemental Table 2. Univariate analysis (Cox regression) of the impact of different immune cell fractions on the overall survival in the 316 MDS patients

Cell composition (%)	Hazard ratio	95% confidence interval		*P* value
		Lower	Higher	
Mast cells resting	1.075	0.987	1.17	0.099
Macrophages M2	1.071	1.015	1.13	0.012
T cells CD4 memory resting	1.064	0.996	1.137	0.065
T cells CD4 naive	1.058	0.991	1.13	0.092
B cells memory	1.057	0.98	1.139	0.151
Eosinophils	1.048	1.012	1.086	0.009
Plasma cells	1.039	0.999	1.08	0.055
B cells naive	1.027	0.986	1.07	0.199
Neutrophils	1.021	0.999	1.045	0.065
NK cells resting	1.011	0.983	1.04	0.451
Mast cells activated	1.009	0.985	1.034	0.467
T cells gamma delta	1.004	0.719	1.402	0.982
Dendritic cells activated	0.999	0.93	1.073	0.982
Monocytes	0.997	0.983	1.012	0.700
T cells CD4 memory activated	0.997	0.936	1.061	0.919
T cells CD8	0.993	0.972	1.015	0.538
Macrophages M1	0.983	0.579	1.668	0.948
T cells regulatory (Tregs)	0.976	0.886	1.076	0.630
Macrophages M0	0.962	0.946	0.978	<0.001
T cells follicular helper	0.868	0.739	1.02	0.086
Dendritic cells resting	0.828	0.432	1.588	0.570
NK cells activated	0.767	0.224	2.631	0.674

P values of <0.05 are statistically significant.

Supplemental Table 3. Cox regression of the impact of immune-cell scores on the overall survival of 316 MDS patients

Variable (reference: score 0*)	HR	Lower 95% CI	Upper 95% CI	*P* value
Score 1	1.161	0.692	1.945	0.572
Score 2	1.964	1.201	3.213	0.007
Score 3	4.062	2.168	7.609	<0.001
Variable (reference: score 1)	**HR**	**Lower 95% CI**	**Upper 95% CI**	***P* value**
Score 2	1.707	1.145	2.543	0.009
Score 3	3.578	2.046	6.259	<0.001
Variable (reference: score 2)	**HR**	**Lower 95% CI**	**Upper 95% CI**	***P* value**
Score 3	2.082	1.220	3.555	0.007

P values of <0.05 are statistically significant.

*Patients got one point if they had each one of the following: lower M0, higher M2, or higher eosinophils. The immune-cell score (from 0 to 3) of a patient was the sum of points he/she got from each of the three cell populations

Abbreviations: HR, Hazard ratios; CI, confidence interval.

Supplemental Table 4. Comparison of cytogenetic changes among 307 MDS patients in different risk groups based on the immune-cell scoring system

Variables	Total (n=307)	Low-risk (n=174)	Intermediate-risk (n=111)	High-risk (n=22)	*P* value
Normal karyotype	171 (55.7)	101 (58.0)	61 (55.0)	9 (40.9)	0.307
Any abnormality	136 (44.3)	73 (42.0)	50 (45.0)	13 (59.1)	
Loss Y*	11 (3.6)	9 (5.2)	1 (0.9)	1 (4.5)	0.162
Del 20q*	14 (4.6)	8 (4.6)	6 (5.4)	0 (0)	0.540
Trisomy 8*	24 (7.8)	16 (9.2)	5 (4.5)	3 (13.6)	0.204
Del 5q*	2 (0.7)	1 (0.6)	1 (0.9)	0 (0)	0.875
Poor risk karyotype[†]	45 (14.7)	17 (9.8)	23 (20.7)	5 (22.7)	0.021
Monosomy 7*	9 (2.9)	3 (1.7)	4 (3.6)	2 (9.1)	0.135
Complex karyotype	36 (11.7)	15 (8.6)	18 (16.2)	3 (13.6)	0.145
Other abnormalities	40 (13.0)	21 (12.1)	15 (13.5)	4 (18.2)	0.712

*As the sole abnormality.

[†]Good: normal karyotype, isolated -Y, del(5q) or del(20q); Poor: complex (≧ 3 abnormalities) or chromosome 7 anomalies; Intermediate: other abnormalities.

Supplemental Table 5. Comparison of genetic alterations among 302 patients in different risk groups based on the immune-cell scoring system

Genes	Total (n=302)	Low-risk (n=174)	Intermediate-risk (n=106)	High-risk (n=22)	*P* value
ASXL1	68 (22.5)	36 (20.7)	27 (25.5)	5 (22.7)	0.649
BCOR	13 (4.3)	7 (4.0)	4 (3.8)	2 (9.1)	0.514
CALR	1 (0.3)	1 (0.6)	0	0	0.691
CBL	6 (2.0)	2 (1.1)	3 (2.8)	1 (4.5)	0.416
CEBPA	10 (3.3)	7 (4.0)	2 (1.9)	1 (4.5)	0.591
CUX1	2 (0.7)	2 (1.1)	0	0	0.477
DNMT3A	26 (8.6)	14 (8.0)	9 (8.5)	3 (13.6)	0.677
ETV6	5 (1.7)	3 (1.7)	2 (1.9)	0	0.815
EZH2	23 (7.6)	12 (6.9)	10 (9.4)	1 (4.5)	0.631
***FLT3*-ITD**	1 (0.3)	1 (0.6)	0	0	0.691
GATA2	4 (1.3)	4 (2.3)	0	0	0.225
GNAS	2 (0.7)	1 (0.6)	1 (0.9)	0	0.863
IDH1	3 (1.0)	0	3 (2.8)	0	0.061
IDH2	12 (4.0)	5 (2.9)	7 (6.6)	0	0.184
IKZF1	1 (0.3)	0	1 (0.9)	0	0.396
JAK2	2 (0.7)	0	2 (1.9)	0	0.155
KIT	4 (1.3)	1 (0.6)	3 (2.8)	0	0.237
KRAS	6 (2.0)	5 (2.9)	1 (0.9)	0	0.419
MLL	5 (1.7)	2 (1.1)	3 (2.8)	0	0.462
MPL	2 (0.7)	2 (1.1)	0	0	0.477
NOTCH1	1 (0.3)	1 (0.6)	0	0	0.691
NPM1	12 (4.0)	3 (1.7)	6 (5.7)	3 (13.6)	0.014
NRAS	16 (5.3)	5 (2.9)	10 (9.4)	1 (4.5)	0.059
PHF6	6 (2.0)	3 (1.7)	2 (1.9)	1 (4.5)	0.668
PTPN11	1 (0.3)	1 (0.6)	0	0	0.691
RAD21	3 (1.0)	1 (0.6)	1 (0.9)	1 (4.5)	0.209
RUNX1	52 (17.2)	27 (15.5)	21 (19.8)	4 (18.2)	0.648
SETBP1	8 (2.6)	6 (3.4)	2 (1.9)	0	0.530
SF3B1	42 (13.9)	32 (18.4)	10 (9.4)	0	0.016
SMC1A	2 (0.7)	2 (1.1)	0	0	0.477
SRSF2	30 (9.9)	16 (9.2)	12 (11.3)	2 (9.1)	0.839
STAG1	2 (0.7)	1 (0.6)	1 (0.9)	0	0.863
STAG2	30 (9.9)	15 (8.6)	13 (12.3)	2 (9.1)	0.608
TET2	44 (14.6)	28 (16.1)	12 (11.3)	4 (18.2)	0.483
TP53	39 (12.9)	17 (9.8)	15 (14.2)	7 (31.8)	0.013
U2AF1	23 (7.6)	14 (8.0)	8 (7.5)	1 (4.5)	0.843
WT1	2 (0.7)	0	1 (0.9)	1 (4.5)	0.042
ZRSR2	20 (6.6)	12 (6.9)	7 (6.6)	1 (4.5)	0.916

Data are presented as median [range] or n (%).

P values of <0.05 are statistically significant.

Supplemental Table 6. Univariate analysis (Cox regression) of the impact of different variables on the overall survival of 316 MDS patients

Variable	HR	Lower 95% CI	Upper 95% CI	*P* value
Age*	1.024	1.012	1.036	<0.001
IPSS-R[†, ‡]	1.873	1.600	2.193	<0.001
ICSS[§]	1.430	1.232	1.660	<0.001
Gene alteration[¶]				
ASXL1	1.445	0.979	2.132	0.064
BCOR	0.421	0.134	1.323	0.138
CALR	0.049	<0.001	978.7	0.551
CBL	2.183	0.805	5.923	0.125
CEBPA	1.803	0.792	4.102	0.160
CUX1	0.049	<0.001	1054	0.554
DNMT3A	1.327	0.762	2.310	0.318
ETV6	1.160	0.368	3.652	0.800
EZH2	2.539	1.470	4.386	<0.001
***FLT3*-ITD**	2.937	0.408	21.13	0.285
GATA2	0.048	<0.001	50.14	0.392
GNAS	0.523	0.064	4.252	0.544
IDH1	0.049	<0.001	626.2	0.532
IDH2	0.838	0.342	2.052	0.700
IKZF1	1.825	0.254	13.09	0.550
JAK2	19.23	4.568	80.94	<0.001
KIT	1.434	0.354	5.803	0.614
KRAS	1.137	0.361	3.578	0.826
MLL	1.274	0.405	4.012	0.679
MPL	0.038	<0.001	18.52	0.300
NOTCH1	0.049	<0.001	376413	0.710
NPM1	1.716	0.799	3.684	0.166
NRAS	1.453	0.761	2.773	0.258
PHF6	1.566	0.578	4.245	0.378
PTPN11	1.611	0.225	11.55	0.635
RAD21	3.418	0.837	13.96	0.087
RUNX1	1.695	1.124	2.554	0.012
SETBP1	1.580	0.696	3.587	0.274
SF3B1	0.293	0.143	0.599	0.001
SMC1A	1.574	0.219	11.32	0.652
SRSF2	1.424	0.875	2.319	0.155
STAG1	0.755	0.105	5.410	0.780
STAG2	1.767	1.085	2.876	0.022
TET2	1.406	0.896	2.208	0.139
TP53	5.812	3.812	8.861	<0.001
U2AF1	0.848	0.445	1.617	0.617

WT1	0.049	<0.001	107.4	0.442
ZRSR2	1.486	0.801	2.757	0.210

Abbreviations: HR, Hazard ratios; CI, confidence interval.

P values of <0.05 are statistically significant.

*Age, as a continuous variable analysis.

[†]IPSS-R risk groups: Very good, good, intermediate, poor, very poor

[‡]307 patients had cytogenetic data at diagnosis

[§]immune-cell scoring system: low, intermediate, high

[¶]302 patients had gene mutation data at diagnosis

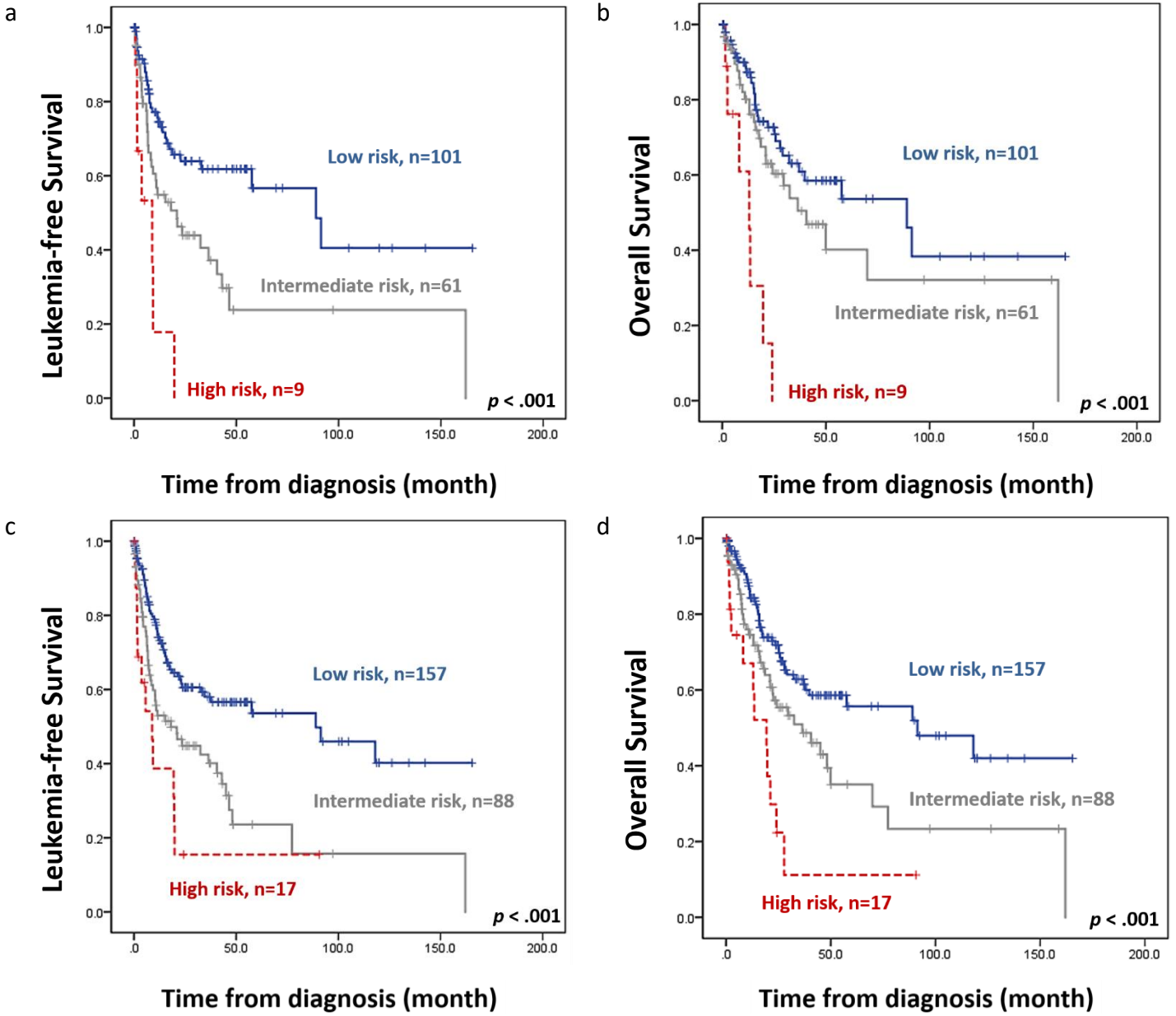
Supplemental Table 7. Relevant genes that are differentially expressed in nuclear factor kappa B signaling (NF-κB) signaling, oxidative stress response and the core enriched HSC/leukemic stem cells (CE-HSC/LSC) signatures.

NF-κB signaling	*ATF3*	*CXCL8*	*IGFBP3*	*PTGER4*
	ATP2B1	*DNAJB4*	*IL1B*	*SERPINE1*
	BHLHE40	*DUSP2*	*IL23A*	*TGIF1*
	BIRC3	*DUSP5*	*JAG1*	*THBS1*
	CCL4	*EGR1*	*JUN*	*TNF*
	CCL5	*EGR2*	*MAFF*	*TNFAIP3*
	CD69	*EGR3*	*MSC*	*TNFSF9*
	CD83	*FOSB*	*NFKBIA*	*TSC22D1*
	CXCL2	*GPR183*	*NR4A1*	*ZBTB10*
	CXCL3	*IER5*	*PDE4B*	*ZFP36*

Oxidative stress response	*BCL2*	*CDKN1A*	*HMOX1*	*NQO1*
	C1QA	*CDKN1C*	*HSPA1B*	*TNF*
	C1S	*CYCS*	*JUN*	*TRAF1*
	C2	*DDIT3*	*MAP3K9*	
	C5	*EGR1*	*NFKBIE*	

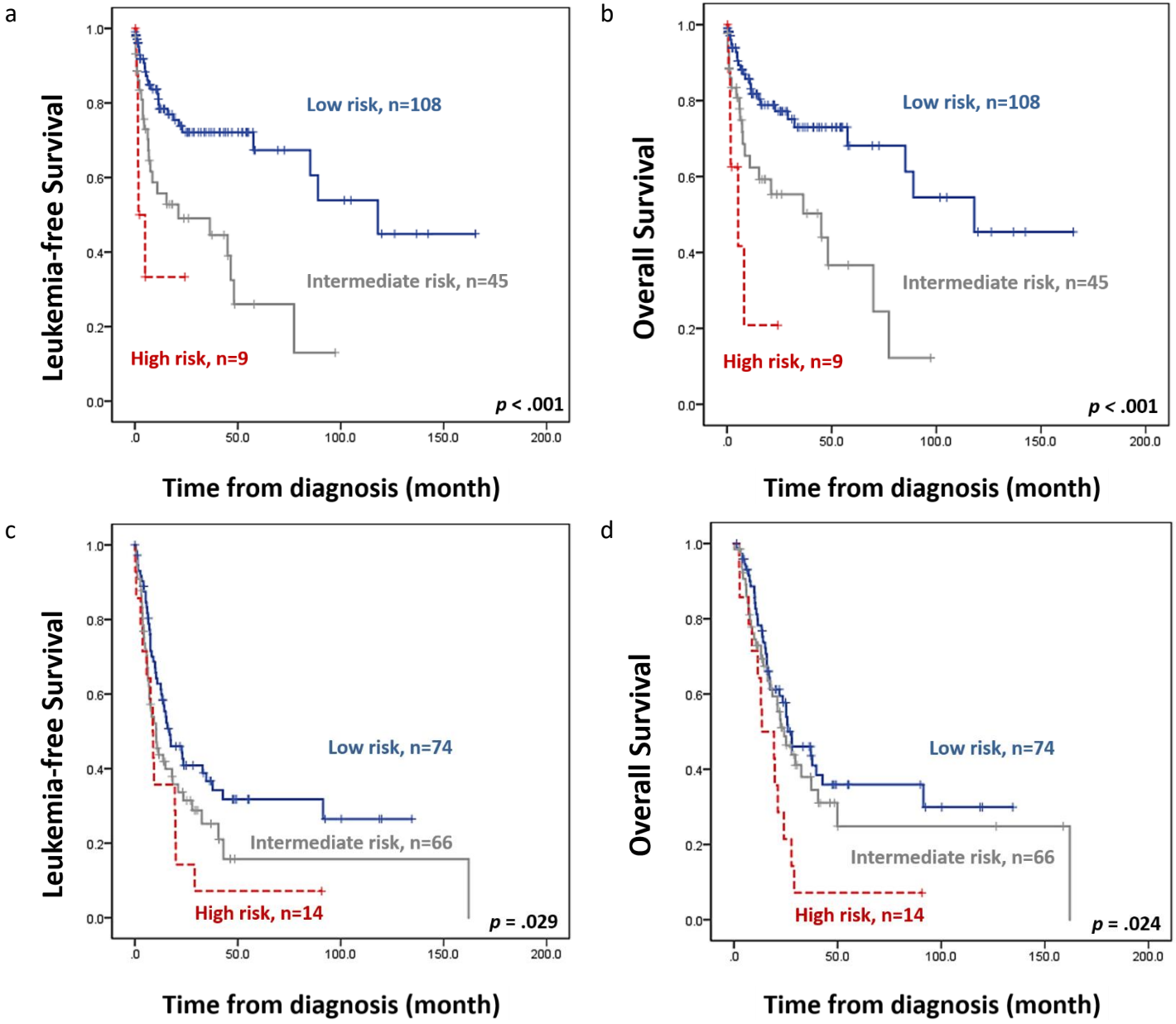
CE-HSC/LSC	*ABCB1*	*GCNT2*	*MSI2*	*RUNX2*
	BAALC	*GNL1*	*MSMO1*	*SEL1L3*
	BCL11A	*HOPX*	*MYO5C*	*SLC17A9*
	BTBD11	*HOXB2*	*NPR3*	*SLC25A36*
	CALN1	*HOXB3*	*PNP*	*SMARCA2*
	CD109	*INPP4B*	*PPP1R16B*	*SOCS2*
	CFH	*INSIG1*	*PRKCH*	*TCEAL9*
	COL5A1	*IPO11*	*PROM1*	*TCF12*
	CRHBP	*JUN*	*PTK2*	*TFPI*
	DST	*KBTBD8*	*RBPMS*	*ZBTB4*
	DUSP6	*KMT2A*	*RIMKLB*	*ZDHHC21*
	ELK3	*LPP*	*RLIM*	*ZNF165*
	FLT3	*MEIS1*	*RNF125*	
	FOXO1	*MLLT3*	*RSL1D1*	

Supplemental Figure 1. Kaplan-Meier survival curves stratified by immune-cell scoring system (ICSS) in patients with normal karyotype and those without poor-risk karyotypes Outcome of the 307 patients who had cytogenetic data at diagnosis. (a) LFS and (b) OS of patients with normal karyotype; and (c) LFS and (d) OS of patients without poor-risk karyotypes. ICSS could well risk-stratify patients in either group irrespective of karyotypes.



Supplemental Figure 2. Kaplan-Meier survival curves stratified by ICSS in patients treated with different modalities.

(a) LFS and (b) OS of 162 patients who received supportive care; and (c) LFS and (d) OS of patients who received active treatment. ICSS could well risk-stratify patients in either group.



Supplemental Figure 3. Kaplan-Meier survival curves of patients receiving hypomethylation agents (HMA) and hematopoietic stem cell transplant (HSCT).

(a) LFS and (b) OS of 115 patients who received HMA. The detrimental effect of higher immune-cell scores was alleviated in these patients. (c) LFS and (d) OS of 47 patients who underwent HSCT. The difference in survival was diminished between patients with variable immune-cell scores.