haematologica
Journal of the Ferrata Storti Foundation

The prognostic role of myeloid-related gene mutations in adult acute lymphoblastic leukemia

by Wenting Wang; Jiayuan Chen; Yan Li; Guangji Zhang; Chunlin Zhou; Qiuyun Fang; Shouyun Li; Kaiqi Liu; Dong Lin; Benfa Gong; Yuntao Liu; Chengcai Guo; Yan Hui; Ying Wang; Shaowei Qiu; Bingcheng Liu; Ying Wang; Yingchang Mi; Xiaoyuan Gong; Jianxiang Wang and Hui Wei

Received: October 13, 2025.
Accepted: March 6, 2026.

Citation: Wenting Wang; Jiayuan Chen; Yan Li; Guangji Zhang; Chunlin Zhou; Qiuyun Fang; Shouyun Li; Kaiqi Liu; Dong Lin; Benfa Gong; Yuntao Liu; Chengcai Guo; Yan Hui; Ying Wang; Shaowei Qiu; Bingcheng Liu; Ying Wang; Yingchang Mi; Xiaoyuan Gong; Jianxiang Wang and Hui Wei.
The prognostic role of myeloid-related gene mutations in adult acute lymphoblastic leukemia.
Haematologica. 2026 Mar 19. doi: 10.3324/haematol.2025.300044 [Epub ahead of print]

The prognostic role of myeloid-related gene mutations in adult acute lymphoblastic leukemia

Wenting Wang,[1,2] Jiayuan Chen,[1,2] Yan Li,[1,2] Guangji Zhang,[1,2] Chunlin Zhou,[1,2] Qiuyun Fang,[1,2] Shouyun Li,[1,2] Kaiqi Liu,[1,2] Dong Lin,[1,2] Benfa Gong,[1,2] Yuntao Liu,[1,2] Chengcai Guo,[1,2] Yan Hui,[1,2] Ying Wang,[1,2] Shaowei Qiu,[1,2] Bingcheng Liu,[1,2] Ying Wang,[1,2] Yingchang Mi,[1,2] Xiaoyuan Gong,[1,2#] Jianxiang Wang,[1,2#] Hui Wei[1,2#]

1. State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin 300020, China;

2. Tianjin Institutes of Health Science, Tianjin 301600, China.

Correspondence

Dr.Hui Wei, State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College; Nanjing Rd 288, Tianjin, 300020, China. T +86 22 23608456; Email: weihui@ihcams.ac.cn.

Dr. Jianxiang Wang, State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical

Sciences & Peking Union Medical College; Nanjing Rd 288, Tianjin, 300020, China. T +86 22 23909120; F +86 22 27301963; Email: wangjx@ihcams.ac.cn

Dr. Xiaoyuan Gong, State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College; Nanjing Rd 288, Tianjin, 300020, China. T +86 22 23909020; Email: gongxiaoyuan@ihcams.ac.cn.

Authors' contributions

HW, JW, and XG participated in concept design. WW was involved in data analysis, drafting and revising the manuscript. JC, YL, GZ, CZ, QF, SL, KL, DL, BG, and YL collected the data. CG, YH, YW, SQ, BL, YW, and YM were responsible for interpreting the results. All authors have read and approved the final manuscript.

Acknowledgements

Not applicable.

Funding

National Key Research and Development Program of China (2023YFC2508900), National Natural Science Foundation of China (82370183), CAMS Innovation Fund for Medical Sciences (2023-I2M-C&T-A-012, 2025-I2M-KJ-026), Tian Jin Natural Science Foundation (23JCZXJC00310), Haihe Laboratory of Cell Ecosystem

Innovation Fund (22HHXBSS00040), Beijing Xisike Clinical Oncology Research Foundation (Y-SYBLD2022ZD-0031)

Competing interests

The authors declare that they have no competing interests.

Data Availability Statement

The datasets from this study are available upon reasonable request from the corresponding author.

To the editor:

Acute lymphoblastic leukemia (ALL) is a highly heterogeneous hematologic malignancy with poor outcomes. The most frequent somatic mutations such as *DNMT3A*, *TET2*, *ASXL1*, *TP53,* and so on in clonal hematopoiesis are drivers of myeloid neoplasms [1-3]. However, the prognostic role of these myeloid gene mutations in ALL remains unclear. A recent study reported that myeloid mutations are frequent in adult ALL and are associated with adverse outcomes [4], but this finding has not been widely validated. We defined a set of myeloid-related genes (MyG), which include DNA methylation regulators (*TET2*, *DNMT3A*, *IDH1/2*), histone modifiers (*ASXL1*, *EZH2*), RNA splicing factors (*SF3B1*, *SRSF2*, *ZRSR2*, *U2AF1/2*), transcriptional regulators (*RUNX1*, *BCOR*, *BCORL1*, *CEBPA*, *NPM1*), and cohesion complexes (*STAG2*, *SMC3*, *SMC1A*, *RAD21*) [5-7]. We investigated the clinical characteristics and prognostic impact of MyG and *TP53* mutations in adult ALL.

With approval from the ethical committee of the Institute of Hematology and Blood Diseases Hospital and in accordance with the Helsinki Declaration, we screened 842 consecutive newly diagnosed adult ALL patients between 2016 and 2024, excluding ALAL patients, with 783 adult ALL patients included in the final analysis, including 394 Ph- B-ALL, 267 Ph+ B-ALL, and 122 T-ALL patients. The median age was 35.6 years, with 46.4% were female. Totally, 92.0% patients achieved complete remission (CR) after the first cycle of induction chemotherapy (Table 1).

We identified 964 mutations in 453 of 783 individuals, averaging 2.13 mutations per patient. *TP53* mutations occurred in 5.1% (40/783) of patients, predominantly in Ph-

B-ALL (92.5%). MyG mutations occurred in 14.2% (111/783) of cases, with distinct subtype distributions: 10.4% in Ph- B-ALL, 12.0% Ph+ B-ALL, and 31.1% in T-ALL ($P < 0.001$). Other subtype-associated mutations included *IDH1* in Ph- B-ALL, *RUNX1* in Ph+ B-ALL, and *DNMT3A/IDH2* in T-ALL. Within T-ALL, MyG mutations showed a strong correlation with ETP. MyG mutations had a median VAF of 30.2%. Analysis revealed a positive correlation between MyG VAF and blast count, but not with age, suggesting a leukemic rather than CHIP origin in this young-adult cohort.

(Figure 1, Supplementary Table 1).

Based on the status of *TP53* and MyG, ALL patients were categorized into $TP53^{mut}$, $MyG^{mut}/TP53^{wt}$, and $MyG^{wt}/TP53^{wt}$ groups. In terms of clinical characteristics (Table 1), $MyG^{mut}/TP53^{wt}$ patients were older than $MyG^{wt}/TP53^{wt}$ patients (38.7 vs. 35.1 years, $P = 0.039$), but not statistically older than $TP53^{mut}$ patients (35.7 years, $P = 0.481$). $MyG^{mut}/TP53^{wt}$ had higher PLT (93.0×10^9/L vs. 50.0×10^9/L vs. 60.0×10^9/L; $P < 0.001$) and lower LDH (368U/L vs. 495U/L vs. 619U/L; $P = 0.004$) compared with $MyG^{wt}/TP53^{wt}$ and $TP53^{mut}$ patients at diagnosis. Besides, $TP53^{mut}$ patients showed lower CR rate (72.5%) after the first induction cycle compared with $MyG^{mut}/TP53^{wt}$ (90.2%, $P = 0.024$) and $MyG^{wt}/TP53^{wt}$ (91.2%, $P = 0.003$) patients.

Survival analysis across Ph- B-ALL, Ph+ B-ALL and T-ALL patients showed T-ALL had the poorest outcomes (Supplementary Figure 1). Ph+ B-ALL had better EFS (HR 0.74, 95% CI: 0.57–0.97, $P = 0.03$), but similar OS (HR 0.91, 95% CI: 0.66–1.25, $P = 0.57$) compared with Ph- B-ALL. After censoring at transplantation, T-ALL remained poorest outcomes versus Ph- ($P < 0.01$) and Ph+ ($P < 0.01$) B-ALL. No differences

were found in EFS (P = 0.52) or OS (P = 0.42) between Ph- and Ph+ B-ALL.

Then, we explored the impact of *TP53* and MyG mutations on ALL outcomes. *TP53*^{mut} patients exhibited inferior outcomes, whereas MyG mutations had no discernible effect. Specifically, the 3-year EFS for *TP53*^{mut} patients was 36.88%, significantly lower than those of MyG^{wt}/*TP53*^{wt} (48.15%, HR 1.65, 95% CI 1.04–2.60, P = 0.03) and MyG^{mut}/*TP53*^{wt} (64.58%, HR 2.30, 95% CI 1.29–4.10, P < 0.01) patients. A similar trend toward poorer OS was also observed for *TP53*^{mut} patients versus MyG^{wt}/*TP53*^{wt} (HR 1.52, 95% CI 0.87–2.68, P = 0.14) and MyG^{mut}/*TP53*^{wt} (HR 1.82, 95% CI 0.91–3.67, P = 0.09) groups, with 3-year OS at 51.70%, 58.38%, and 64.37%, respectively. In contrast, MyG^{wt}/*TP53*^{wt} and MyG^{mut}/*TP53*^{wt} patients exhibited similar EFS (HR 0.72, 95%CI 0.48-1.07, P = 0.10) and OS (HR 0.83, 95%CI 0.53-1.33, P = 0.44) (Figure 2A, B). Age-stratified analysis (≤35 vs. >35 years) confirmed MyG mutations lacked prognostic impact in both subgroups (P > 0.05). Correspondingly, censoring at transplantation, *TP53*^{mut} patients exhibited the worst outcomes compared with MyG^{wt}/*TP53*^{wt} and MyG^{mut}/*TP53*^{wt}, and no significant differences were found in outcomes between MyG^{wt}/*TP53*^{wt} and MyG^{mut}/*TP53*^{wt} patients (Supplementary Figure 1E, F). Subsequently, we conducted a multivariate analysis of the overall cohort and demonstrated that *TP53* mutation was significantly associated with worse EFS and OS, but MyG mutation did not significantly affect EFS or OS in ALL (Supplementary Table 2).

We further analyzed the impact of MyG mutations on outcome in Ph+ B-ALL, Ph- B-ALL, and T-ALL subgroups (Figure 2). In Ph- B-ALL, *TP53*^{mut} patients had a 3-year

EFS of 38.35% inferior to MyG^{mut}/*TP53*^{wt} cases (65.17%, HR 2.33, 95 % CI 1.04–5.18, *P* = 0.04), and also tended to be lower than MyG^{wt}/*TP53*^{wt} cases (47.34%, HR 1.49, 95 % CI 0.91–2.44, *P* = 0.11). Additionally, we observed a trend toward poorer OS in *TP53*^{mut} patients (3-year OS: 54.80%) compared with MyG^{mut}/*TP53*^{wt} (68.38 %, HR 1.84, 95 % CI 0.68–4.98, *P* = 0.23) and MyG^{wt}/*TP53*^{wt} patients (60.16 %, HR 1.34, 95 % CI 0.72–2.51, *P* = 0.36). In T-ALL and Ph+ B-ALL subgroup, we did not analyzed effects of *TP53* mutations due to the low number of patients with *TP53* mutations. MyG mutation did not significantly impact EFS or OS in any subgroup. In Ph+ B-ALL, MyG^{wt}/*TP53*^{wt} and MyG^{mut}/*TP53*^{wt} patients exhibited comparable EFS and OS, with a median EFS (mEFS) of 47.37 months versus not reached (HR 0.54, 95% CI: 0.23–1.24, *P* = 0.14) and median OS (mOS) of 53.94 months versus 43.06 months (HR 0.67, 95% CI: 0.27–1.68, *P* = 0.40). In Ph- B-ALL, the 3-year EFS was 47.34% for MyG^{wt}/*TP53*^{wt} patients and 65.17% for MyG^{mut}/*TP53*^{wt} patients (HR 0.64, 95% CI: 0.33–1.26, *P* = 0.20), with 3-year OS rates of 60.16% and 68.38%, respectively (HR 0.73, 95% CI: 0.32–1.67, *P* = 0.45). In T-ALL, no significant differences were observed, with an mEFS of 18.36 months for MyG^{wt}/*TP53*^{wt} versus not reached for MyG^{mut}/*TP53*^{wt} (HR 0.75, 95% CI: 0.40–1.43, *P* = 0.39) and an mOS of 30.58 months versus not reached (HR 1.02, 95% CI: 0.48–2.14, *P* = 0.96), and stratification by ETP and *NOTCH1/FBXW7/RAS/PTEN* genetic risk yielded consistent results (P > 0.05). After censoring at transplantation (Supplementary Figure 1), in Ph- B-ALL, *TP53*^{mut} patients had significantly worse EFS than MyG^{wt}/*TP53*^{wt} (*P* = 0.02) and MyG^{mut}/*TP53*^{wt} (*P* = 0.04). For OS, *TP53*^{mut} patients showed significantly worse OS than MyG^{wt}/*TP53*^{wt} (*P*

= 0.04) and a trend toward worse OS compared to MyG^{mut}/*TP53*^{wt} (P = 0.10). However, MyG mutations did not affect outcomes in Ph+ B-ALL, Ph- B-ALL, or T-ALL (all, P > 0.05). Multivariate analysis in subgroups showed that *TP53* mutation was associated with inferior EFS but not OS in Ph- B-ALL, and no significant impact of MyG mutation on EFS or OS across the Ph+ B-ALL, Ph- B-ALL, and T-ALL subgroups (Supplementary Table 2).

This study confirms *TP53* mutation as an independent adverse prognostic factor in adult ALL [8-10]. MyG mutations were more prevalent in T-ALL/ETP, with distinct gene-subtype associations: *IDH1* mutations in Ph- B-ALL, *RUNX1* mutations in Ph+ B-ALL, and *DNMT3A/IDH2* mutations in T-ALL, but lacked independent prognostic impact.

Saygin et al. identified the adverse effect of myeloid mutation in ALL and attributed this to CHIP. In our young-adult cohort, VAF correlated with blast count but not with age, supporting a leukemic rather than age-related CHIP origin. Specifically, VAF of *DNMT3A/TET2* mutations also showed no correlation with age, further arguing against a CHIP origin. Thus, prognostic impact depends on origin. Leukemic-derived mutations are passengers diluted by dominant drivers and intensive therapy. CHIP-derived mutations may show chemoresistance. This framework reconciles our negative findings with those of Saygin et al., and is further supported by Niroula et al., who showed that CHIP does not increase lymphatic malignancy risk [11]. Additional factors may contribute to the discrepancy between studies. Our Chinese cohort received BFM-based chemotherapy, combined with TKIs for Ph+ ALL, whereas Saygin et al. studied a diverse population treated with various regimens including Hyper-CVAD and

blinatumomab. Several limitations should be acknowledged. Our cohort is young (median 35.6 years) and exclusively Chinese, limiting generalizability to older or western populations. Future studies with single-cell genomic analyses at diagnosis are needed to map mutation ontogeny and distinguish drivers from passengers, and validation in older and Western cohorts is warranted.

Rreference

1. Grossmann V, Kern W, Harbich S, et al. Prognostic relevance of RUNX1 mutations in T-cell acute lymphoblastic leukemia. Haematologica. 2011;96(12):1874-1877.
2. Fabre MA, Vassiliou GS. The lifelong natural history of clonal hematopoiesis and its links to myeloid neoplasia. Blood. 2024;143(7):573-581.
3. Genovese G, Kähler AK, Handsaker RE, et al. Clonal hematopoiesis and blood-cancer risk inferred from blood DNA sequence. N Engl J Med. 2014;371(26):2477-2487.
4. Saygin C, Zhang P, Stauber J, et al. Acute Lymphoblastic Leukemia with Myeloid Mutations Is a High-Risk Disease Associated with Clonal Hematopoiesis. Blood Cancer Discov. 2024;5(3):164-179.
5. Eckardt JN, Stasik S, Röllig C, et al. Alterations of cohesin complex genes in acute myeloid leukemia: differential co-mutations, clinical presentation and impact on outcome. Blood Cancer J. 2023;13(1):18.
6. Sportoletti P, Sorcini D, Falini B. BCOR gene alterations in hematologic diseases. Blood. 2021;138(24):2455-2468.
7. Gill H, Leung AY, Kwong YL. Molecular and Cellular Mechanisms of Myelodysplastic Syndrome: Implications on Targeted Therapy. Int J Mol Sci. 2016;17(4):440.
8. Stengel A, Schnittger S, Weissmann S, et al. TP53 mutations occur in 15.7% of ALL and are associated with MYC-rearrangement, low hypodiploidy, and a poor prognosis. Blood. 2014;124(2):251-258.
9. Dirse V, Bertasiute A, Gineikiene E, et al. A population-based single nucleotide polymorphism array analysis of genomic aberrations in younger adult acute lymphoblastic leukemia patients. Genes Chromosomes Cancer. 2015;54(5):326-333.
10. Fang Q, Gong X, Liu K, et al. The clinical characteristics and prognosis in adult Ph negative acute lymphoblastic leukemia with TP53 aberrations. Exp Hematology Oncol. 2022;11(1):22.
11. Niroula A, Sekar A, Murakami MA, et al. Distinction of lymphoid and myeloid clonal hematopoiesis. Nat Med. 2021;27(11):1921-1927.

Figures and Tables

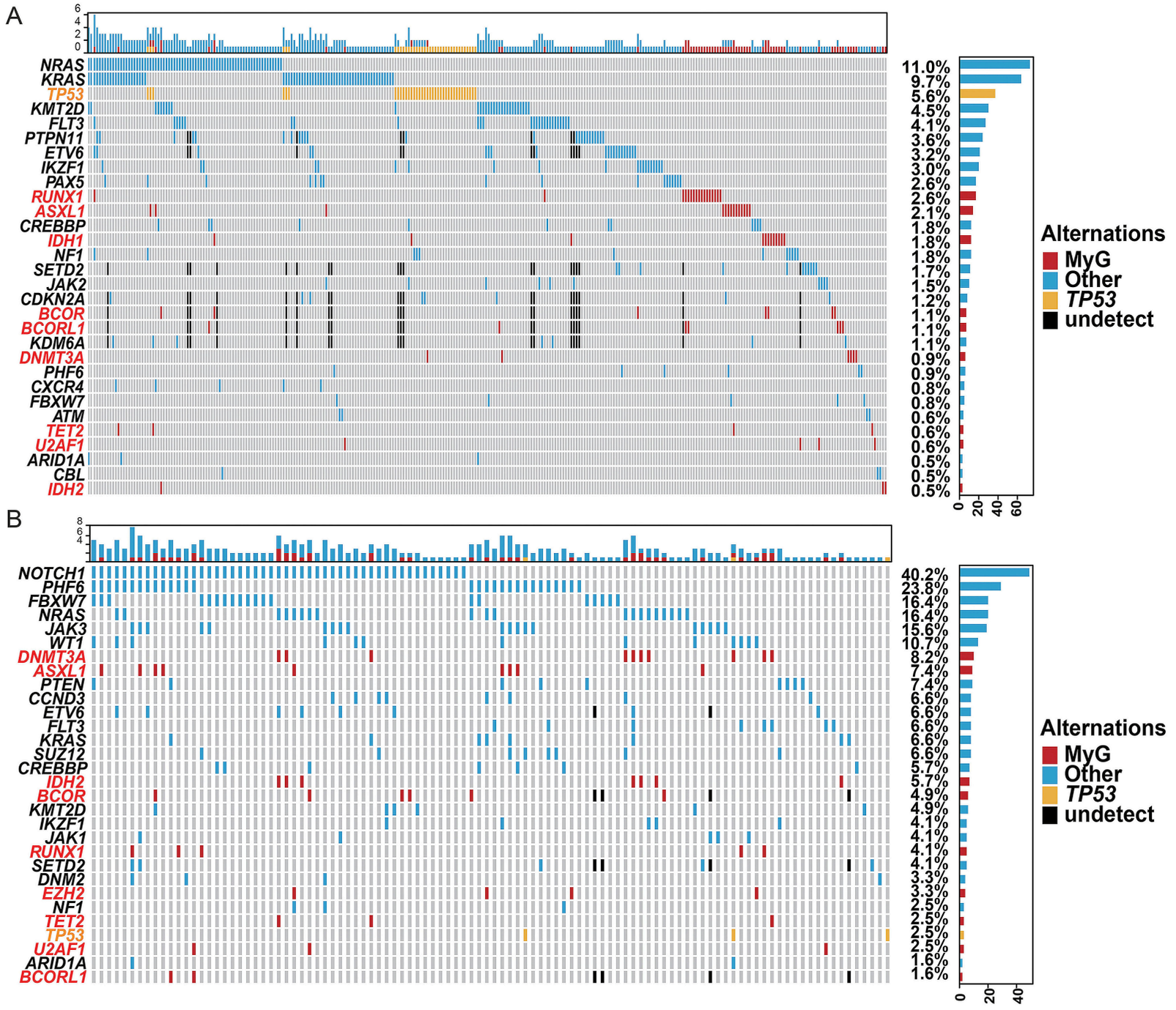
Table 1. Characteristics of patients with MyG^{mut}/*TP53*^{wt}, MyG^{wt}/*TP53*^{wt}, and *TP53*^{mut}

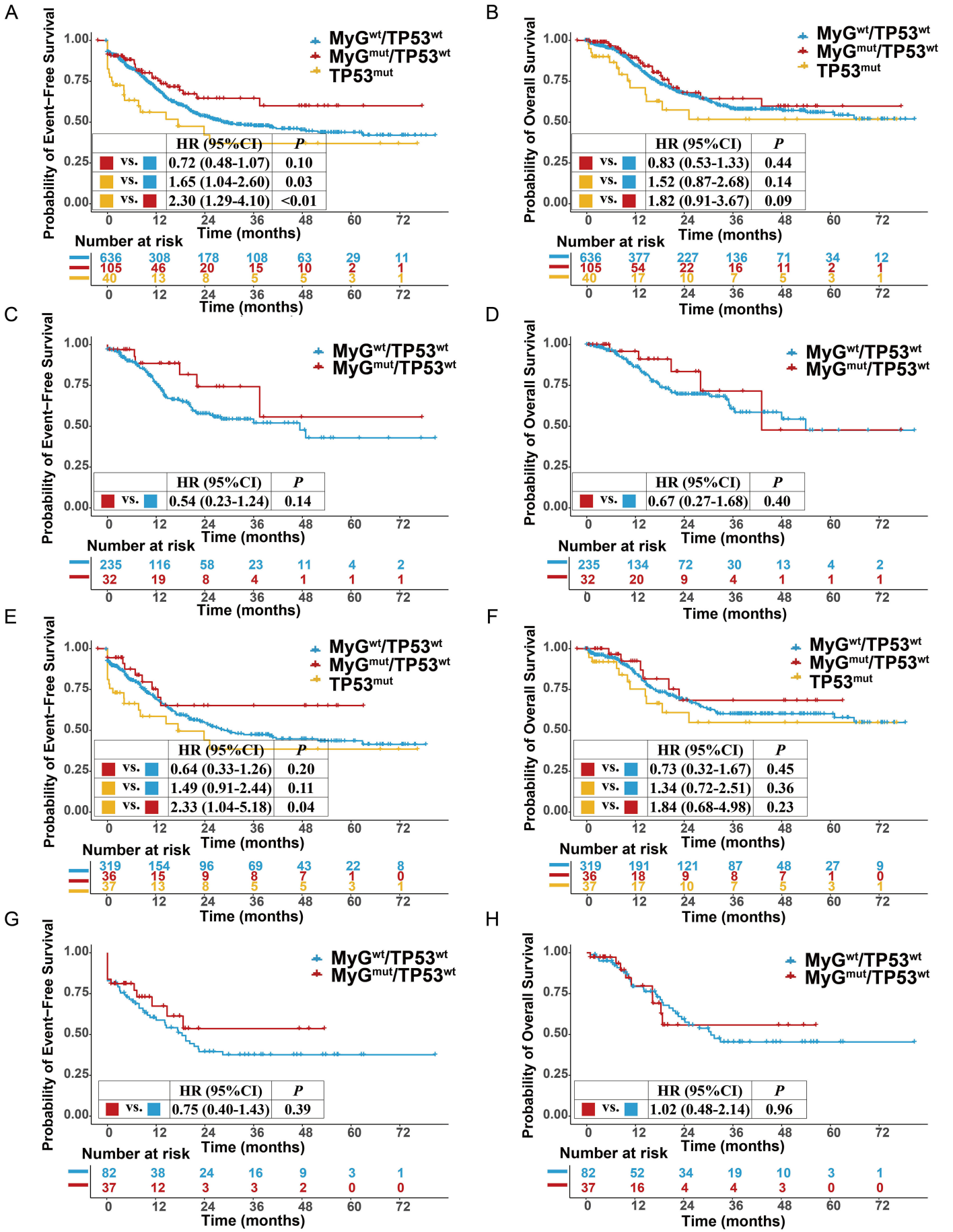
Characteristic	ALL N=783	MyG^{mut}/*TP53*^{wt} N=106	MyG^{wt}/*TP53*^{wt} N=637	*TP53*^{mut} N=40	*P1*	*P2*	*P3*	*P.overall*
Sex					0.328	0.328	0.388	0.211
Female	363 (46.4%)	56 (52.8%)	292 (45.8%)	15 (37.5%)				
Male	420 (53.6%)	50 (47.2%)	345 (54.2%)	25 (62.5%)				
Age, years	35.6	38.7	35.1	35.7	0.039	0.481	0.963	0.051
median (range)	(15, 74)	(15, 66)	(15, 74)	(15, 74)				
Laboratory, median, (IQR)								
WBC, × 10^9/L	18	14.3	19.8	5.4	0.128	0.050	0.001	0.001
	(4.7, 55.8)	(3.0, 47.6)	(5.1, 58.5)	(2.9, 16.7)				
HB, × g/L	94	96	94	86	0.577	0.504	0.504	0.524
	(71.0, 119.0)	(73.0, 120.0)	(71.0, 119.0)	(70.8, 115.0)				
PLT, × 10^9/L	55	93	50	60	<0.001	0.020	0.677	<0.001
	(28.0, 119.0)	(48.0, 150.0)	(26.0, 112.0)	(32.8, 101.0)				
LDH, × U/L	483	368	495	619	0.014	0.008	0.072	0.004
	(267, 993)	(235, 794)	(2709, 1017)	(351, 1368)				
Subtypes					<0.001	<0.001	<0.001	<0.001
Ph- B-ALL	394	37 (34.9%)	320 (50.2%)	37 (92.5%)				
Ph+ B-ALL	267	32 (30.2%)	235 (36.9%)	0 (0.0%)				
T-ALL	122	37 (34.9%)	82 (12.9%)	3 (7.5%)				
CR rate	693 (90.1%)	92 (90.2%)	572 (91.2%)	29 (72.5%)	0.879	0.024	0.003	0.002
CR1 HSCT	384 (49.0%)	47 (44.3%)	321 (50.4%)	16 (40.0%)	0.441	0.776	0.441	0.258

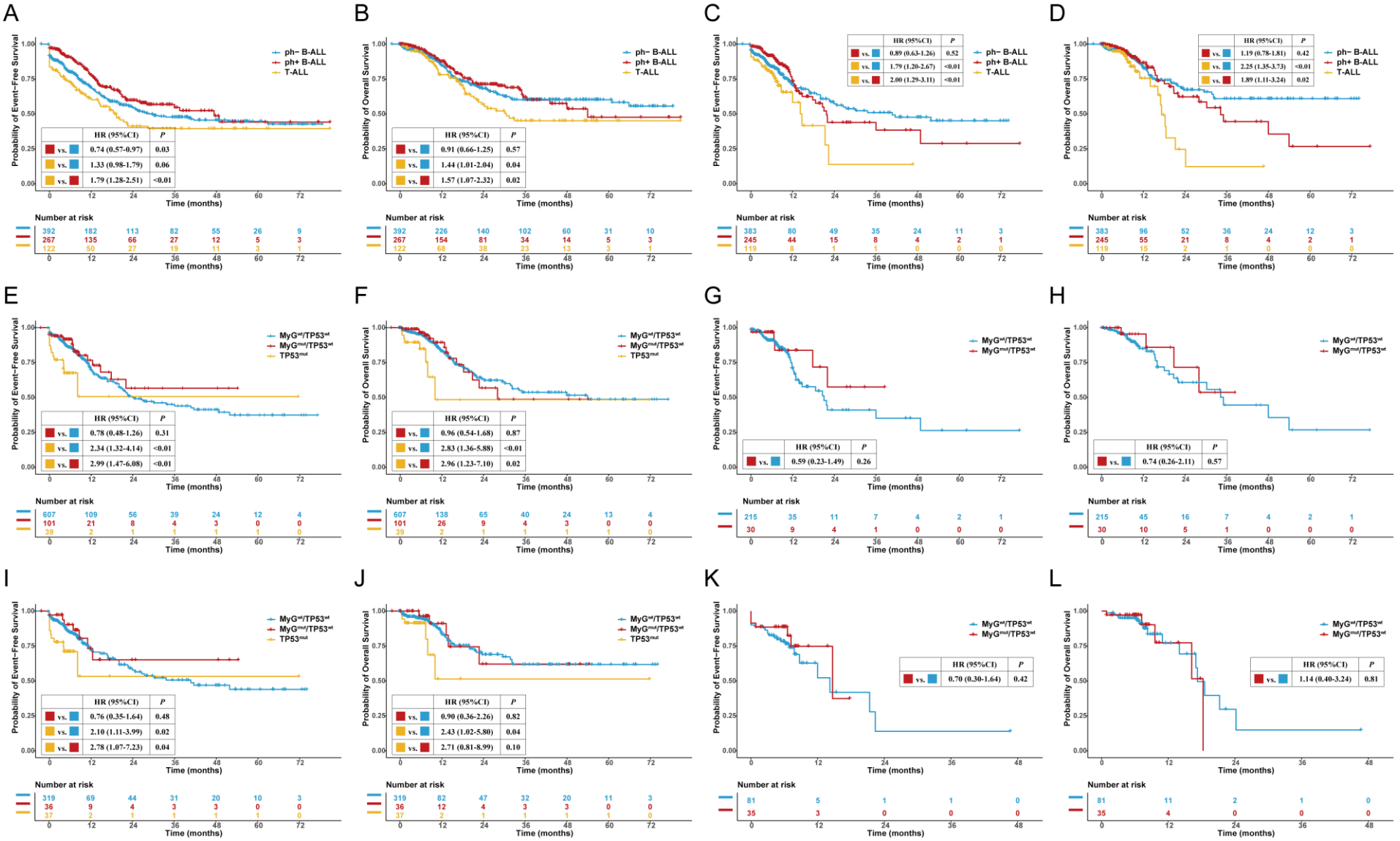
P1: MyG^{mut}/*TP53*^{wt} vs. MyG^{wt}/*TP53*^{wt}; *P2*: MyG^{mut}/*TP53*^{wt} vs. *TP53*^{mut}; *P3*: MyG^{wt}/*TP53*^{wt} vs. *TP53*^{mut}; *P.overall*: MyG^{mut}/*TP53*^{wt} vs. MyG^{wt}/*TP53*^{wt} vs. *TP53*^{mut}

Figure 1. Mutation spectrum and clinical correlations of MyG mutations in adult ALL. Oncoplots A and B show the mutation spectrum of adult B-ALL and adult T-ALL, respectively. The top 30 genes with mutation frequencies are shown in the figures. MyG are shown in red and *TP53* is shown in yellow. Plot C show associations between MyG mutations and B-ALL and T-ALL subtypes. The left panel represents the B-ALL subgroup, while the right panel represents the T-ALL subgroup. Only the color blocks with a p-value less than 0.05 are displayed. The absolute value of Log (OR) is capped at 5. Scatter plot D show the relationship between the VAF value of MyG mutation and the blast count. Scatter plot E showed the relationship between the VAF value of MyG mutation and age of corresponding patients.

Figure 2. Kaplan-Meier survival analysis based on *TP53* and MyG mutation status. Shown are EFS and OS for: the overall ALL cohort (A, B); Ph+ B-ALL (C, D); Ph- B-ALL (E, F); and T-ALL (G, H).


A
NRAS 11.0%
KRAS 9.7%
TP53 5.6%
KMT2D 4.5%
FLT3 4.1%
PTPN11 3.6%
ETV6 3.2%
IKZF1 3.0%
PAX5 2.6%
RUNX1 2.6%
ASXL1 2.1%
CREBBP 1.8%
IDH1 1.8%
NF1 1.8%
SETD2 1.7%
JAK2 1.5%
CDKN2A 1.2%
BCOR 1.1%
BCORL1 1.1%
KDM6A 1.1%
DNMT3A 0.9%
PHF6 0.9%
CXCR4 0.8%
FBXW7 0.8%
ATM 0.6%
TET2 0.6%
U2AF1 0.6%
ARID1A 0.5%
CBL 0.5%
IDH2 0.5%
Alternations
MyG
Other
TP53
undetect
B
NOTCH1 40.2%
PHF6 23.8%
FBXW7 16.4%
NRAS 16.4%
JAK3 15.6%
WT1 10.7%
DNMT3A 8.2%
ASXL1 7.4%
PTEN 7.4%
CCND3 6.6%
ETV6 6.6%
FLT3 6.6%
KRAS 6.6%
SUZ12 6.6%
CREBBP 5.7%
IDH2 5.7%
BCOR 4.9%
KMT2D 4.9%
IKZF1 4.1%
JAK1 4.1%
RUNX1 4.1%
SETD2 4.1%
DNM2 3.3%
EZH2 3.3%
NF1 2.5%
TET2 2.5%
TP53 2.5%
U2AF1 2.5%
ARID1A 1.6%
BCORL1 1.6%
Alternations
MyG
Other
TP53
undetect
C
Gene–Subtype Association Analysis
Gene
TP53
MyG
ZRSR2
U2AF2
U2AF1
TET2
STAG2
SRSF2
SMC3
SMC1A
SF3B1
RUNX1
RAD21
NPM1
IDH2
IDH1
EZH2
DNMT3A
CEBPA
BCORL1
BCOR
ASXL1
BCR::ABL
MLL
Philike
high hyperdiploidy
hypodiploidy
TCF3::PBX1
ZNF384r
MEF2Dr
ETP
TAL1/2r
MLL
HOX
Subtype
Log(OR)
5
2.5
0
−2.5
−5
Significance:
***: p < 0.001
** : p < 0.01
* : p < 0.05
D
Correlation between VAF and Blast Percentage
R = 0.4, p = 2.8e−05
y = −1.3 + 0.43 x
Mean VAF (%)
Blast (%)
E
Correlation between VAF and Age
R = −0.16, p = 0.098
y = 41 − 0.25 x
Mean VAF (%)
Age (years)


A
Probability of Event−Free Survival
MyG^wt/TP53^wt
MyG^mut/TP53^wt
TP53^mut
HR (95%CI) P
vs. 0.72 (0.48-1.07) 0.10
vs. 1.65 (1.04-2.60) 0.03
vs. 2.30 (1.29-4.10) <0.01
Number at risk
636 308 178 108 63 29 11
105 46 20 15 10 2 1
40 13 8 5 5 3 1
Time (months)
B
Probability of Overall Survival
MyG^wt/TP53^wt
MyG^mut/TP53^wt
TP53^mut
HR (95%CI) P
vs. 0.83 (0.53-1.33) 0.44
vs. 1.52 (0.87-2.68) 0.14
vs. 1.82 (0.91-3.67) 0.09
Number at risk
636 377 227 136 71 34 12
105 54 22 16 11 2 1
40 17 10 7 5 3 1
Time (months)
C
Probability of Event−Free Survival
MyG^wt/TP53^wt
MyG^mut/TP53^wt
HR (95%CI) P
vs. 0.54 (0.23-1.24) 0.14
Number at risk
235 116 58 23 11 4 2
32 19 8 4 1 1 1
Time (months)
D
Probability of Overall Survival
MyG^wt/TP53^wt
MyG^mut/TP53^wt
HR (95%CI) P
vs. 0.67 (0.27-1.68) 0.40
Number at risk
235 134 72 30 13 4 2
32 20 9 4 1 1 1
Time (months)
E
Probability of Event−Free Survival
MyG^wt/TP53^wt
MyG^mut/TP53^wt
TP53^mut
HR (95%CI) P
vs. 0.64 (0.33-1.26) 0.20
vs. 1.49 (0.91-2.44) 0.11
vs. 2.33 (1.04-5.18) 0.04
Number at risk
319 154 96 69 43 22 8
36 15 9 8 7 1 0
37 13 8 5 5 3 1
Time (months)
F
Probability of Overall Survival
MyG^wt/TP53^wt
MyG^mut/TP53^wt
TP53^mut
HR (95%CI) P
vs. 0.73 (0.32-1.67) 0.45
vs. 1.34 (0.72-2.51) 0.36
vs. 1.84 (0.68-4.98) 0.23
Number at risk
319 191 121 87 48 27 9
36 18 9 8 7 1 0
37 17 10 7 5 3 1
Time (months)
G
Probability of Event−Free Survival
MyG^wt/TP53^wt
MyG^mut/TP53^wt
HR (95%CI) P
vs. 0.75 (0.40-1.43) 0.39
Number at risk
82 38 24 16 9 3 1
37 12 3 3 2 0 0
Time (months)
H
Probability of Overall Survival
MyG^wt/TP53^wt
MyG^mut/TP53^wt
HR (95%CI) P
vs. 1.02 (0.48-2.14) 0.96
Number at risk
82 52 34 19 10 3 1
37 16 4 4 3 0 0
Time (months)



Supplementary Figure 1. Kaplan-Meier analysis of EFS and OS in ALL cohorts. Plots A-D are grouped by immunophenotype and Philadelphia chromosome status. Plots (A, B) show EFS and OS in the overall ALL cohort, and plots (C, D) show EFS and OS after censoring for transplantation. Plots E-L are grouped by *TP53* and MyG mutation status, with Kapla-Meier EFS and OS analysis in the overall ALL cohort (E, F), Ph+ B-ALL (G, H), in Ph- B-ALL (I, J), and in T-ALL (K, L) after censoring of transplantation.

Supplementary Table 1. Distribution of MyG mutations in ph+ B-ALL, ph -B-ALL, and T-ALL.

	ALL	Ph-BALL	Ph+BALL	TALL	*P1*	*P2*	*P3*
	N=783	N=394	N=267	N=122			
MyG:	111 (14.20%)	41 (10.40%)	32 (12.00%)	38 (31.10%)	0.611	<0.001	<0.001
MDS:	69 (8.81%)	18 (4.57%)	27 (10.10%)	24 (19.70%)	0.013	<0.001	0.015
DTA:	42 (5.36%)	12 (3.05%)	11 (4.12%)	19 (15.60%)	0.601	<0.001	<0.001
DNA methylation:	38 (4.85%)	22 (5.58%)	3 (1.12%)	13 (10.70%)	0.009	0.082	<0.001
DNMT3A	16 (2.04%)	5 (1.27%)	1 (0.37%)	10 (8.20%)	0.41	0.001	<0.001
TET2	7 (0.89%)	2 (0.51%)	2 (0.75%)	3 (2.46%)	1	0.266	0.27
IDH1	13 (1.66%)	12 (3.05%)	0 (0.00%)	1 (0.82%)	0.007	0.318	0.318
IDH2	10 (1.28%)	3 (0.76%)	0 (0.00%)	7 (5.74%)	0.277	0.003	0.001
histone modification:	28 (3.58%)	6 (1.52%)	10 (3.75%)	12 (9.84%)	0.117	<0.001	0.044
ASXL1	23 (2.94%)	5 (1.27%)	9 (3.37%)	9 (7.38%)	0.138	0.004	0.138
EZH2	6 (0.77%)	1 (0.25%)	1 (0.37%)	4 (3.28%)	1	0.037	0.053
RNA splicing machinery：	8 (0.10%)	5 (0.11%)	0 (0.00%)	3 (0.16%)	0.249	0.487	0.065
SF3B1	1 (0.13%)	1 (0.25%)	0 (0.00%)	0 (0.00%)	1	1	1
U2AF1	7 (0.89%)	4 (1.02%)	0 (0.00%)	3 (2.46%)	0.228	0.364	0.091
transcription:	43 (5.49%)	10 (2.54%)	20 (7.49%)	13 (10.70%)	0.007	0.001	0.399
BCOR	13 (1.83%)	5 (1.40%)	2 (0.84%)	6 (5.26%)	0.708	0.042	0.042
BCORL1	9 (1.27%)	3 (0.84%)	4 (1.67%)	2 (1.75%)	0.898	0.898	1
RUNX1	22 (2.81%)	2 (0.51%)	15 (5.62%)	5 (4.10%)	<0.001	0.014	0.702
CEBPA	1 (0.13%)	0 (0.00%)	1 (0.37%)	0 (0.00%)	0.808	1	1
cohesion complexes:	4 (0.51%)	3 (0.76%)	0 (0.00%)	1 (0.82%)	0.47	1	0.47
RAD21	2 (0.28%)	2 (0.56%)	0 (0.00%)	0 (0.00%)	1	1	1
SMC3	2 (0.26%)	1 (0.25%)	0 (0.00%)	1 (0.82%)	1	0.627	0.627

P1: Ph- B-ALL vs. Ph+ B-ALL; P2: Ph- B-ALL vs. T-ALL; P3: Ph+ B-ALL vs. T-ALL

(The genes listed in the table were all examined in 783 patients, except for BCOR, BCORL1, RAD21, and SMC3, which were detected in 710, 710, 709, 782 patients.)

Supplementary Table 2. Multivariate cox analysis of prognostic factors in OS and EFS in ALL, Ph+B-ALL, Ph- B-ALL and T-ALL.

	EFS			OS		
ALL	HR	95%CI	*P*	HR	95%CI	*P*
Age	1.014	1.006 - 1.023	0.001	1.021	1.012 - 1.031	<0.001
male	1.385	1.092 - 1.756	0.007	1.326	1.000 - 1.759	0.05
WBC > 30 × 10^9/L	1.209	0.955 - 1.531	0.115	1.225	0.925 - 1.622	0.158
PLT	0.997	0.995 - 0.999	0.001	0.997	0.995 - 0.999	0.006
TP53 mutant	2.101	1.321 - 3.344	0.002	2.023	1.136 - 3.600	0.017
MyG mutant	0.693	0.467 - 1.029	0.069	0.746	0.467 - 1.191	0.219
HSCT in CR1	0.716	0.524 - 0.978	0.036	0.757	0.553 - 1.035	0.081
Ph+ B-ALL						
Age	1.022	1.004 - 1.041	0.019	1.028	1.006 - 1.050	0.012
male	1.408	0.892 - 2.224	0.142	1.191	0.709 - 2.002	0.509
WBC > 30 × 10^9/L	2.294	1.375 - 3.828	0.001	2.037	1.129 - 3.675	0.018
PLT	0.996	0.992 - 1.000	0.036	0.994	0.989 - 0.999	0.029
MyG mutant	0.514	0.221 - 1.196	0.122	0.654	0.259 - 1.655	0.37
HSCT in CR1	0.749	0.430 - 1.303	0.307	0.652	0.361 - 1.177	0.156
Ph- B-ALL						
Age	1.017	1.006 - 1.029	0.003	1.024	1.011 - 1.039	0.001
male	1.195	0.866 - 1.647	0.278	1.086	0.734 - 1.609	0.679
WBC > 30 × 10^9/L	1.176	0.823 - 1.681	0.372	1.302	0.845 - 2.006	0.232
PLT	0.995	0.992 - 0.997	0	0.995	0.992 - 0.999	0.004
TP53 mutant	1.717	1.041 - 2.832	0.034	1.573	0.828 - 2.988	0.167
MyG mutant	0.604	0.314 - 1.160	0.13	0.569	0.245 - 1.318	0.188
HSCT in CR1	0.897	0.583 - 1.381	0.622	0.987	0.630 - 1.548	0.955
T-ALL						
Age	1.014	1.005 - 1.022	0.001	1.021	1.011 - 1.031	<0.001
male	1.385	1.093 - 1.756	0.007	1.321	0.997 - 1.751	0.053
WBC > 30 × 10^9/L	1.159	0.918 - 1.464	0.216	1.173	0.889 - 1.548	0.26
PLT	0.997	0.995 - 0.999	<0.001	0.997	0.995 - 0.999	0.005
MyG mutant	0.724	0.488 - 1.073	0.107	0.776	0.487 - 1.236	0.286
HSCT in CR1	0.734	0.538 - 1.002	0.051	0.776	0.568 - 1.061	0.112