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Original Article

Impact of mutational variant allele frequency on prognosis in myelodysplastic syndromes

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Abstract: The clinical relevance of variant allele frequency (VAF) of recurrent mutations in myelodysplastic syndromes (MDS) has been increasingly reported. However, the prognostic value of mutational VAF across the genetic spectrum of MDS has not been extensively evaluated. In this study, we profiled the mutational spectrum of 382 newly diagnosed MDS patients using targeted next-generation sequencing. Exploratory analysis found that mutational VAF of some genes including *TET2*, *TP53*, and *SF3B1* had significant associations with patient survival. Specifically, *TET2* VAF ≥ 32% (HR 1.69, P = 0.025) and *TP53* VAF ≥ 27% (HR 3.58, P < 0.001) were independently associated with shorter overall survival (OS). In contrast, *SF3B1* VAF ≥ 15% had an independent association with better prognosis (HR 0.52, P = 0.048). In addition, high *TET2* VAF was associated with an increased response to hypomethylating agents relative to low *TET2* VAF (P = 0.009). Patients with high *TP53* VAF more often possessed complex karyotypes than those with low VAF (P = 0.034). And patients with high *SF3B1* VAF were more frequently classified as MDS with ring sideroblasts (MDS-RS) category than those with low VAF (P = 0.012). Meanwhile, we found that for some other genes like *EZH2* and *NRAS*, once their mutations appeared, it meant poor survival regardless of mutational VAF. These findings suggest that mutational VAF of certain genes should be considered into the routine prognostic prediction and risk stratification of MDS patients.

Keywords: Myelodysplastic syndromes, mutation, next-generation sequencing, variant allele frequency, prognosis

Introduction

Myelodysplastic syndromes (MDS) are a group of clonal myeloid malignancies with diverse clinical manifestations and molecular features [1]. In the indolent stage, the disease is characterized by mild asymptomatic cytopenias, but tends to progress to an aggressive stage with profound cytopenias and leukemic transformation. Given that MDS patients exhibit heterogeneous outcomes with a range of life expectancies from a few months to many years [2], it is critical to identify risk factors for poor survival.

Genetic factors play an important role in MDS prognosis [3-6]. Specifically, mutations of *TP53* and *EZH2* have been consistently associated with poor prognosis in multiple studies [3, 7-11]. Patient survival has also been associated with mutations of *TET2* [12-14] and *SF3B1* [6, 7, 9, 15]; but such associations have not been replicated in other studies [3, 10, 15-17].

In addition to mutation status (yes vs no), mutational variant allele frequency (VAF) (also known as mutation allelic burden) is also associated with MDS prognosis [11, 18-21]. Poorer survival has been associated with higher VAF of *TP53* mutations [11, 18-20], and *TET2* mutations [21, 22].

MDS phenotypes and treatment responses have also been linked to genetic mutations [3-6]. *SF3B1* mutations are more frequently detected in MDS with ring sideroblasts (MDS-RS) category [23, 24], whereas patients with

TP53 mutations often have complex karyotypes [8, 13]. MDS patients with *TET2* mutations tend to respond better to hypomethylating agents (HMAs) [25, 26]. Similar to the association between mutational VAF and patient survival, recent studies have indicated that mutational VAF could also influence the phenotypes and therapeutic response to HMAs [11, 26, 27]. Specifically, *SF3B1* VAF has been correlated with the presence of ring sideroblasts (RS) in the bone marrow [11, 27], and *TP53* VAF has been associated with complex cytogenetics [11]. In addition, high *TET2* VAF is associated with an enhanced response to HMAs [26].

In this study, we examined the impact of mutational VAF on the prognosis of MDS using targeted next-generation sequencing (NGS). We went on to demonstrate that high VAF levels of *TET2* and *TP53* mutations are independent predictors for poor prognosis, whereas high *SF3B1* mutational VAF may be a protective factor.

Materials and methods

Patients

This study included all patients with a diagnosis of *de novo* MDS, based on the 2016 World Health Organization (WHO) classification [28], at the First Affiliated Hospital, Zhejiang University School of Medicine between March 2009 and November 2019. All patients were subjected to metaphase cytogenetic and mutational analysis prior to treatment. Patients with secondary MDS and unevaluable karyotypes were excluded from data analysis. This study was approved by the Ethics Committee of the First Affiliated Hospital, and conducted in compliance with the Helsinki Declaration.

Mutational analysis

Genomic DNA was extracted from bone marrow mononuclear cells, and analyzed using a customized targeted NGS approach that combined multiplex PCR-based target enrichment and library generation with ultra-deep high-throughput parallel sequencing using the Ion Proton Platform or MiSeq [29, 30]. The analysis included 15 genes (e.g., *TET2*, *ASXL1*, *U2AF1*, *SF3B1*, *RUNX1*, *TP53*, *DNMT3A*, *IDH1*, *NRAS*, *CBL*, *SRSF2*, *EZH2*, *ETV6*, *IDH2*, and *JAK2*) prior to November, 2016 (n = 80), and 37 genes (15 genes listed above, plus *SETBP1*, *BCOR*, *KMT2D*, *CREBBP*, *EP300*, *ZRSR2*, *CUX1*, *KRAS*, *NPM1*, *WT1*, *PHF6*, *PTPN11*, *BCORL1*, *CEBPA*, *CSF3R*, *FLT3*, *GATA2*, *DNMT3B*, *ATM*, *KIT*, *GATA1*, and *IKZF1*) afterwards (n = 302). Exons known to be hotspots or related with hematologic malignancies were targeted, and candidate variations were obtained through background database filtering of normal samples. Mutational VAF was defined as the number of variant reads divided by the number of total reads, and reported as a percentage. Mutations with VAF < 1% were excluded for analysis. Mutations were annotated using the COSMIC, 1000 Genomes, PolyPhen-2, and dbSNP databases.

Clonal hierarchy analysis

Mutations with the highest VAF were considered as the dominant clones. Mutations were considered to be co-dominant if the difference in VAF levels with the dominant clones was ≤ 5% [22].

Follow-up and treatment response

Overall survival (OS) was defined as the period from the date of initial diagnosis to the date of death or the last follow-up, regardless of the cause. Patients who underwent transplantation were censored at the date of transplantation.

Response to monotherapy using HMAs was assessed in the patients who completed at least two treatment cycles. Patients were classified as responders if they were in complete remission (CR), partial remission (PR), or marrow CR (mCR), or if they achieved hematological improvement (HI), in accordance with modified International Working Group criteria [31]. Patients with stable disease, treatment failure, or disease progression were considered non-responders [31].

Statistical analysis

The optimal mutational VAF cut-off of each individual gene for survival stratification was identified by the web application Cutoff Finder based on the R language (http://molpath.charite.de/cutoff/): OS in two separated groups by each cut-off (high VAF vs low VAF + wild-type) was compared using the log-rank test, and the optimal VAF cut-off was selected based on the lowest *p* value [32]. More specific pairwise com-

Table 1. Clinical characteristics of 382 MDS patients

Variable	Value
Age in years, median (range)	58 (14-88)
Male, n (%)	241 (63.09)
Blood counts at diagnosis	
HB (g/dL), mean ± SD	80.2 ± 30.2
ANC ($\times 10^9$/L), mean ± SD	1.9 ± 3.7
PLT ($\times 10^9$/L), mean ± SD	98.7 ± 129.7
Marrow blasts in %, mean ± SD	5.4 ± 5.1
Abnormal karyotype, n (%)	156 (40.84)
2016 WHO classification of MDS, n (%)	
MDS-SLD	48 (12.57)
MDS-RS	30 (7.85)
MDS-MLD	125 (32.72)
MDS-EB-1	83 (21.72)
MDS-EB-2	77 (20.16)
MDS-U	18 (4.71)
MDS with isolated del (5q)	1 (0.26)
IPSS-R category, n (%)	
Very low	13 (3.40)
Low	99 (25.92)
Intermediate	111 (29.06)
High	96 (25.13)
Very high	63 (16.49)
Initial treatment, n (%)	
Supportive care	209 (54.71)
HMAs monotherapy	100 (26.18)
HMAs+other agents	69 (18.06)
Chemotherapy	4 (1.05)
HSCT, n (%)	31 (8.12)
Follow-up duration in months, median (IQR)	26.13 (10.07-48.67)
Outcome, n (%)	
Leukemic transformation	75 (19.63)
Death	145 (37.96)

ANC, absolute neutrophil count; HB, hemoglobin; HSCT, hematopoietic stem cell transplantation; HMAs, Hypomethylating agents; IPSS, International Prognostic Scoring System; MDS-EB-1, myelodysplastic syndromes with excess blasts-1; MDS-EB-2, MDS with excess blasts-2; MDS-MLD, MDS with multilineage dysplasia; MDS-RS, MDS with ring sideroblasts; MDS-SLD, MDS with single lineage dysplasia; MDS-U, MDS unclassifiable; PLT, platelets.

parisons were further conducted among three groups (high VAF vs low VAF vs wild-type) by mutation status and the optimal VAF cut-off. In patients with multiple mutations of a certain gene, the mutation with the highest VAF was chosen for calculation. VAF analysis was performed only on genes mutated in more than 10 cases.

Survival curves were constructed using the Kaplan-Meier method and compared using the log-rank test. In addition to mutational variables, candidate variables in the multivariate Cox analyses included age (≥ 65 vs < 65 years), sex, 2016 WHO classification, the revised International Prognostic Scoring System (IPSS-R; >3.5 vs ≤ 3.5 points), transplantation status, and treatment allocation. Differences between HMAs responders and non-responders were assessed using the Fisher's exact test for categorical variables and the Mann-Whitney's test for continuous variables. All analyses were performed using SPSS 23.0 (IBM, NY, USA). A two-sided $P < 0.05$ was considered statistically significant.

Results

Clinical characteristics of patients

A total of 382 MDS patients (241 men and 141 women; median age, 58 years; age range, 14-88 years) were included in the analysis (Table S1). Clinical characteristics are summarized in **Table 1**. Just over half of patients received supportive care and one quarter were treated with HMAs monotherapy. Almost one-fifth of cases received HMAs with combinations of other agents and only 4 cases were treated with chemotherapy. During the median follow-up of 26.13 months (IQR 10.07-48.67 months), 75 (19.63%) patients developed secondary leukemia and 145 (37.96%) died.

Genomic spectrum

Genes with >5% mutation frequency in the study population included: *TET2* (14.66%), *ASXL1* (12.04%), *U2AF1* (11.78%), *SF3B1* (11.26%), *RUNX1* (8.90%), *TP53* (8.64%), *SETBP1* (7.62%), *BCOR* (7.28%), *KMT2D* (7.28%), *DNMT3A* (7.07%), *CREBBP* (5.96%), *EP300* (5.30%), and *EZH2* (5.24%) (**Figure 1** and Table S2).

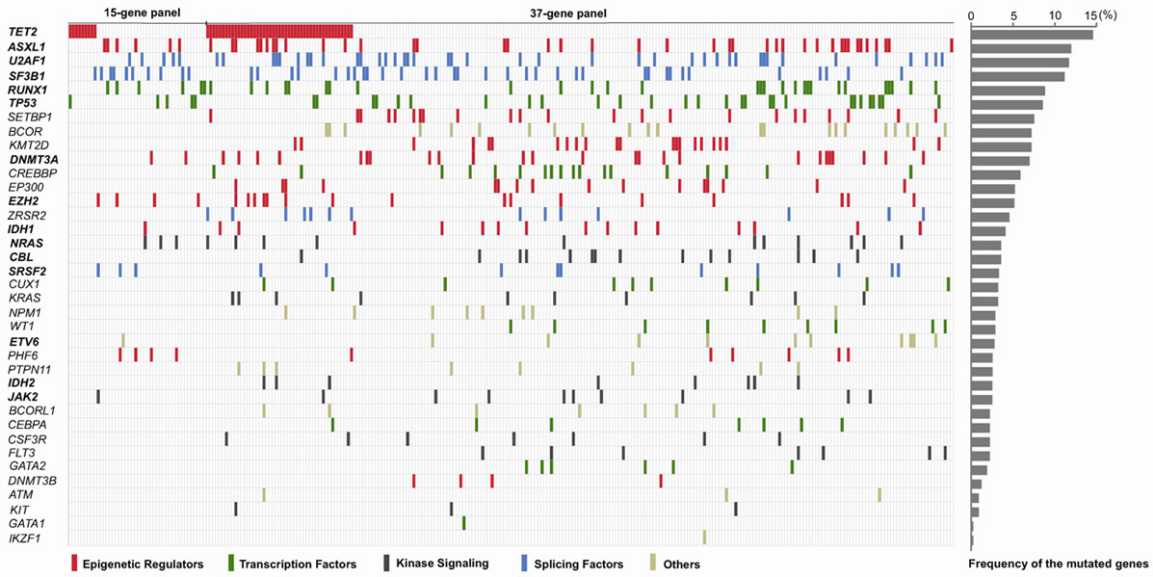

Figure 1. Genomic spectrum observed across 382 patients with myelodysplastic syndromes (MDS) using next-generation sequencing of a 15-gene panel (n = 80) or a 37-gene panel (n = 302). The genes assessed across the entire cohort are highlighted in bold on the left. Each column represents an individual patient, and each colored box refers to a mutated gene along with the corresponding functional group. The bar diagram depicts the frequency of mutations in the 37 genes identified in the cohort.

VAF cut-off values for OS stratification

The optimal VAF cut-off was 32.00% for *TET2* (HR 1.76, 95% CI 1.12-2.75, P = 0.012), 26.26% for *TP53* (HR 6.10, 95% CI 3.73-9.98, P < 0.001), 14.19% for *SF3B1* (HR 0.42, 95% CI 0.22-0.80, P = 0.007), 2.60% for *EZH2* (HR 2.30, 95% CI 1.27-4.17, P = 0.005), and 1.36% for *NRAS* (HR 2.37, 95% CI 1.16-4.85, P = 0.015) (Figure S1A-E). No optimal VAF cut-off was available for other genes (Figure S2A-N).

Association between TET2 and OS

In the 56 patients with *TET2* mutations, VAF was ≥ 32% in 44 patients (78.57%). *TET2* mutations were classified as the dominant clones in 77.27% (34/44) of the patients with *TET2* VAF ≥ 32% versus in 25.00% (3/12) of the patients with *TET2* VAF < 32% (P = 0.001; **Figure 2A**).

There was a statistically non-significant trend for shorter OS with *TET2* mutations versus without (20.37 vs 37.13 months; HR 1.45, 95% CI 0.95-2.48, P = 0.084; Table S3; **Figure 3A**). When the analysis was conducted by dividing the *TET2* gene status into 3 categories (VAF ≥ 32%, VAF < 32%, and wild-type), OS differed significantly (P = 0.034). Median OS in patients with *TET2* wild-type (37.13 months) was significantly longer than that in patients with *TET2* VAF ≥ 32% (17.70 months; HR 1.72, 95% CI 1.14-3.39, P = 0.016; **Figure 3B**) and similar to that in patients with *TET2* VAF < 32% (38.20 months; HR 0.65, 95% CI 0.28-1.79, P = 0.457; **Figure 3C**). There was a statistically non-significant trend for shorter OS in patients with *TET2* VAF ≥ 32% than in those with *TET2* VAF < 32% (17.70 vs 38.20 months; HR 2.67, 95% CI 0.89-5.15, P = 0.093; **Figure 3D**).

In multivariate Cox analysis, *TET2* mutation status *per se* was not associated with OS (HR 1.32, 95% CI 0.86-2.04, P = 0.209; **Table 2**). When *TET2* gene status was stratified at 32% VAF cut-off, high *TET2* VAF (≥ 32%) was an independent predictor of poor prognosis (HR 1.69, 95% CI 1.07-2.69, P = 0.025; **Table 2**).

Among the 100 patients receiving monotherapy using HMAs, 69 cases were available for response assessment (48 responders and 21 non-responders) (Table S4). The response rate did not differ between patients with *TET2* mutations (9/17, 52.94%) and without *TET2* mutations (39/52, 75%) (P = 0.128; Table S5). However, patients with *TET2* VAF ≥ 32% (9/12, 75%) had a higher response rate than those with *TET2* VAF < 32% (0/5, 0%) (P = 0.009; Table S6; **Figure 2B**). Such a difference rema-

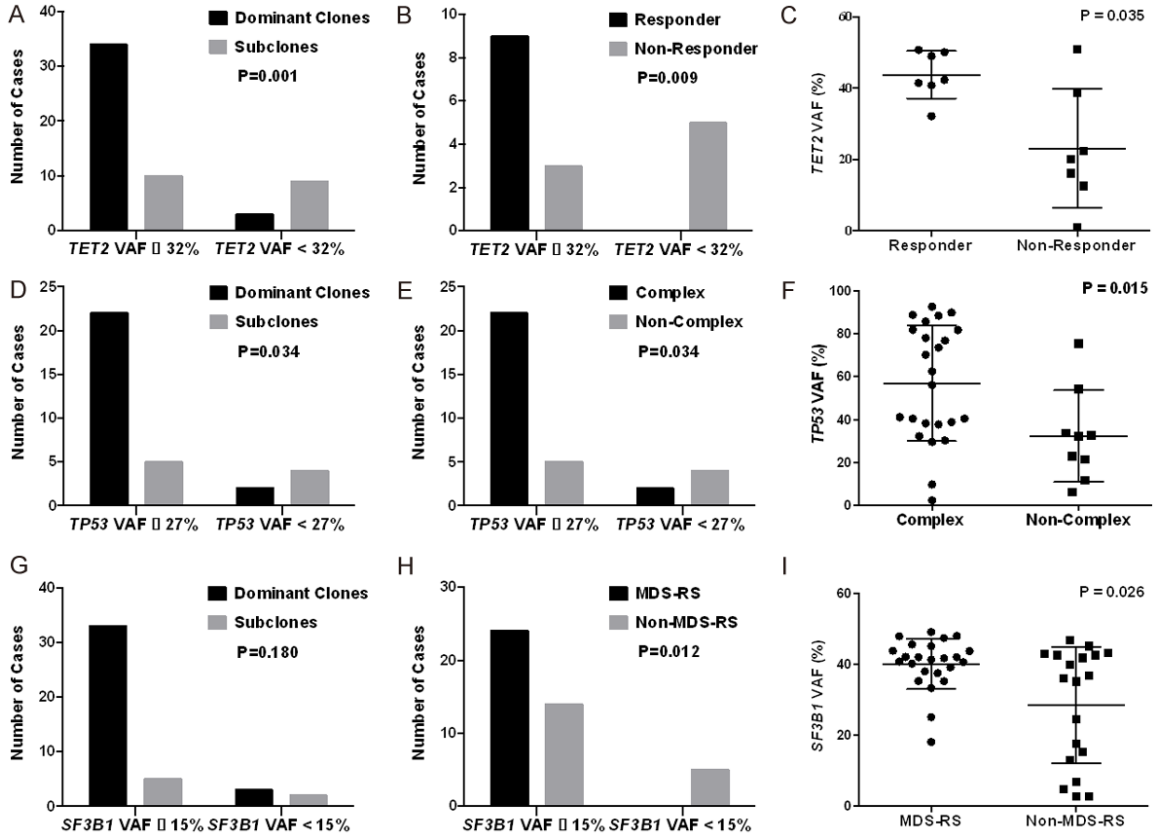

Figure 2. Associations of variant allele frequency (VAF) of *TET2*, *TP53*, and *SF3B1* mutations with response to hypomethylating agents (HMAs) or clinical phenotypes of myelodysplastic syndrome (MDS). A. Occurrence of dominant clones of *TET2* mutations in patients with *TET2* VAF ≥ 32% or < 32%. B. Numbers of patients with *TET2* VAF ≥ 32% or < 32% who responded to HMAs. C. Median *TET2* VAF in responders or non-responders (defined in Methods). D. Occurrence of dominant clones of *TP53* mutations in patients with *TP53* VAF ≥ 27% or < 27%. E. Presence of complex karyotypes in patients with *TP53* VAF ≥ 27% or < 27%. F. Median *TP53* VAF in patients with complex or non-complex karyotypes. G. Occurrence of dominant clones of *SF3B1* mutations in patients with *SF3B1* VAF ≥ 15% or < 15%. H. MDS with ring sideroblasts (MDS-RS) in patients with *SF3B1* VAF ≥ 15% or < 15%. I. Median *SF3B1* VAF in patients with MDS-RS or non-MDS-RS.

ined statistically significant after excluding cases with *ASXL1* mutations (7/9, 77.8% vs 0/5, 0%; P = 0.021). In patients with *TET2* mutations but no *ASXL1* mutations, responders also had significantly higher median *TET2* VAF than non-responders (42.37% vs 20.22%; P = 0.035; **Figure 2C**).

Association between TP53 and OS

In the 33 MDS patients with *TP53* mutations, VAF was ≥ 27% in 27 (81.82%) cases. *TP53* mutations were dominant clones in 81.48% (22/27) of patients with *TP53* VAF ≥ 27% versus in 33.33% (2/6) in patients with *TP53* VAF < 27% (P = 0.034; **Figure 2D**).

Complex cytogenetics were more frequent in patients with *TP53* mutations than in those without (72.73% vs 7.74%; P < 0.001), as well as in those with *TP53* VAF ≥ 27% than in those with *TP53* VAF < 27% (81.48% vs 33.33%; P = 0.034; **Figure 2E**). In reciprocal, patients with complex karyotypes had significantly larger median *TP53* VAF than those without complex karyotypes (59.25% vs 32.31%; P = 0.015; **Figure 2F**).

OS was significantly shorter in patients with *TP53* mutations (10.07 vs 43.97 months in patients with wild-type *TP53*; HR 4.25, 95% CI 2.72-6.62, P < 0.001; Table S3; **Figure 4A**). The association between OS and *TP53* was also apparent when *TP53* gene status was stratified into 3 categories (VAF ≥ 27%, VAF < 27%, and wild-type) (P < 0.001). Patients with wild-type *TP53* had longer median OS (43.97 months) than those with *TP53* VAF ≥ 27% (9.50 months;

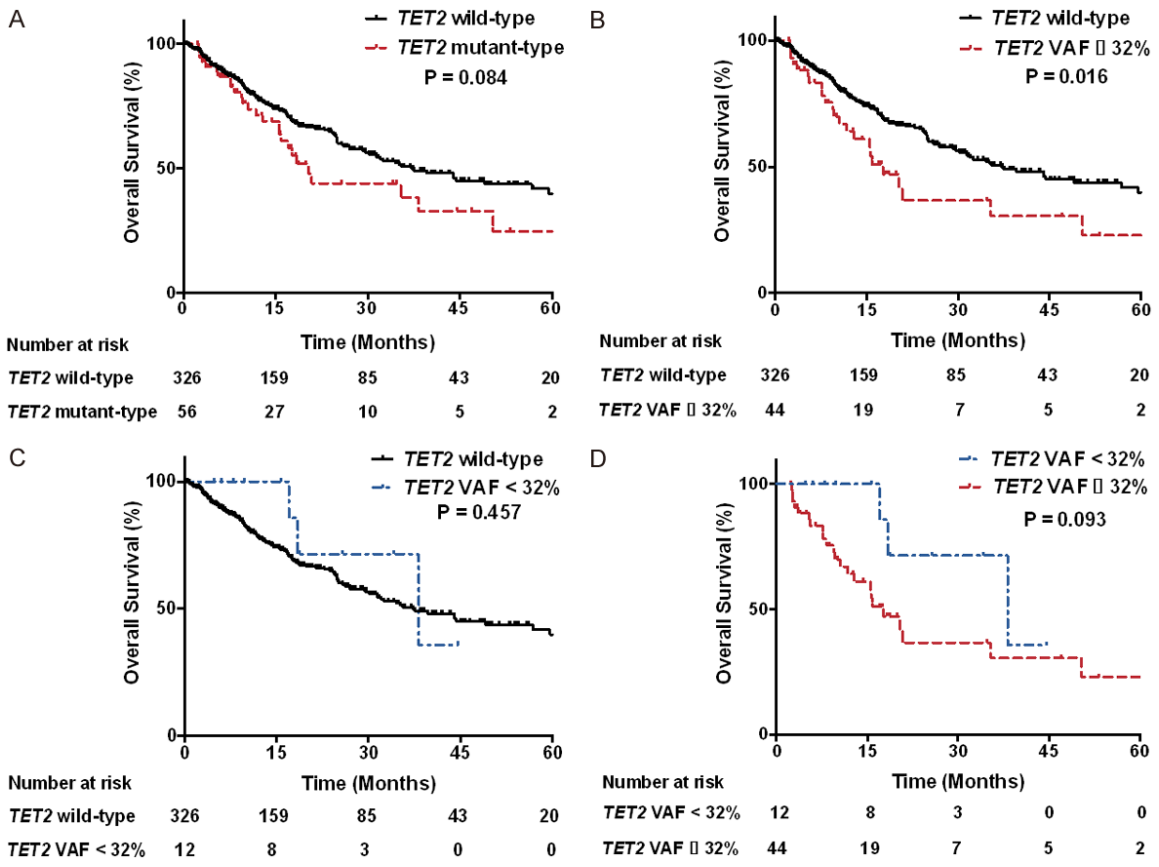

Figure 3. Association of overall survival (OS) with *TET2* mutation status or variant allele frequency (VAF). OS stratified by (A) *TET2* mutation status, (B) *TET2* VAF ≥ 32% or wild-type, (C) *TET2* VAF < 32% or wild-type, (D) *TET2* VAF ≥ 32% or < 32%.

Table 2. Associations of mutation status and mutational VAF levels of the *TET2*, *SF3B1*, and *TP53* genes with overall survival

Comparison	Univariate (log-rank tests)			Multivariate (Cox models)		
	HR	95% CI	p	HR	95% CI	P
TET2						
TET2 mutant type vs wild-type	1.45	0.95-2.48	0.084	1.32	0.86-2.04	0.209
TET2 VAF ≥ 32% vs wild-type	1.72	1.14-3.39	0.016	1.69	1.07-2.69	0.025
TET2 VAF < 32% vs wild-type	0.65	0.28-1.79	0.457	0.50	0.16-1.59	0.243
TET2 VAF ≥ 32% vs < 32%	2.67	0.89-5.15	0.093	--	--	--
TP53						
TP53 mutant type vs wild-type	4.25	2.72-6.62	< 0.001	2.73	1.73-4.31	< 0.001
TP53 VAF ≥ 27% vs wild-type	2.47	1.93-3.16	< 0.001	3.58	2.16-5.94	< 0.001
TP53 VAF < 27% vs wild-type	1.72	0.56-7.40	0.279	1.30	0.48-3.55	0.610
TP53 VAF ≥ 27% vs < 27%	2.87	1.30-6.83	0.023	--	--	--
SF3B1						
SF3B1 mutant type vs wild-type	0.51	0.37-0.90	0.017	0.59	0.33-1.05	0.073
SF3B1 VAF ≥ 15% vs wild-type	0.42	0.33-0.84	0.007	0.52	0.27-0.99	0.048
SF3B1 VAF < 15% vs wild-type	1.36	0.38-5.38	0.598	1.05	0.33-3.30	0.935
SF3B1 VAF ≥ 15% vs < 15%	0.29	0.02-0.92	0.044	--	--	--

CI, confidence interval; HR, Hazards ratio; VAF, variant allele frequency.

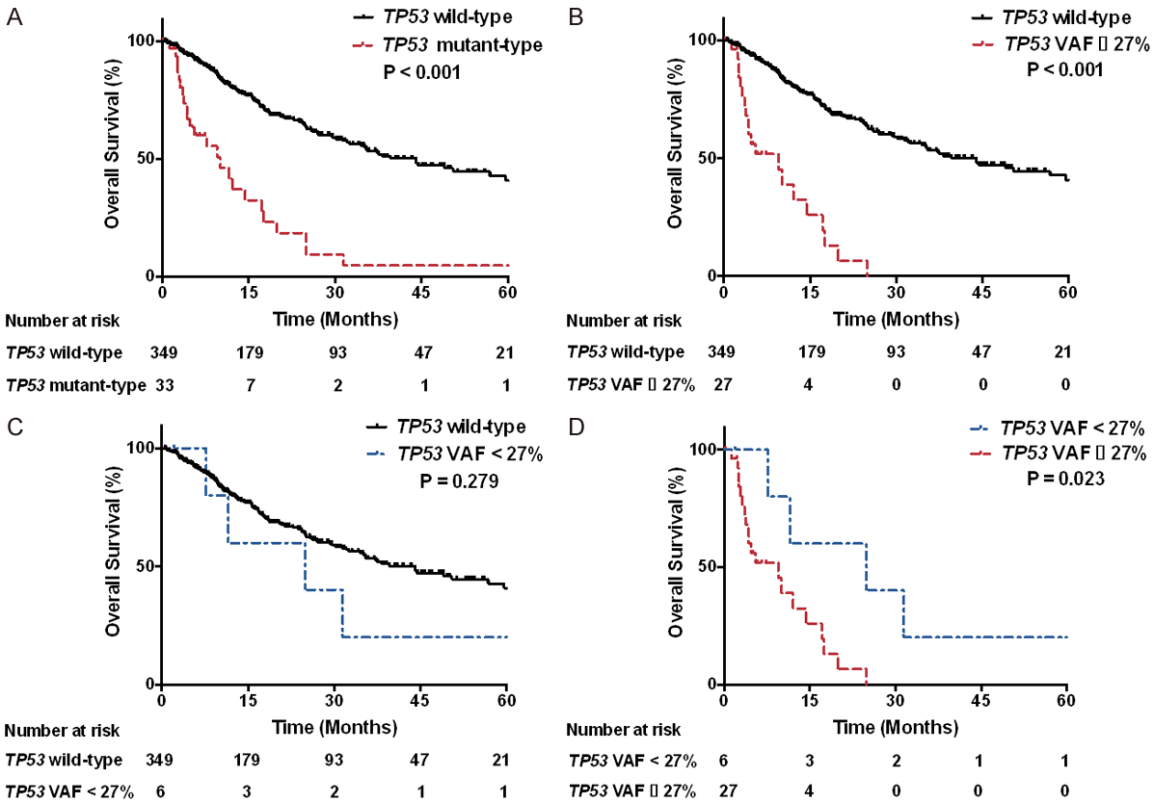

Figure 4. Association of overall survival (OS) with *TP53* mutation status or variant allele frequency (VAF). OS stratified by (A) *TP53* mutation status, (B) *TP53* VAF ≥ 27% or wild-type, (C) *TP53* VAF < 27% or wild-type, (D) *TP53* VAF ≥ 27% or < 27%.

HR 2.47, 95% CI 1.93-3.16, P < 0.001; **Figure 4B**) but not those with *TP53* VAF < 27% (24.93 months; HR 1.72, 95% CI 0.56-7.40, P = 0.279; **Figure 4C**). Patients with *TP53* VAF ≥ 27% had shorter OS than those with *TP53* VAF < 27% (9.50 vs 24.93 months; HR 2.87, 95% CI 1.30-6.83, P = 0.023; **Figure 4D**).

After adjusting for age, sex, WHO classification, the IPSS-R, transplantation status, and treatment allocation, OS remained associated with both *TP53* mutation status (HR 2.73, 95% CI 1.73-4.31, P < 0.001; **Table 2**) and high *TP53* VAF (≥ 27%) (HR 3.58, 95% CI 2.16-5.94, P < 0.001; **Table 2**).

Association between SF3B1 and OS

In the patients with *SF3B1* mutations (n = 43), *SF3B1* VAF was ≥ 15% in 38 patients (88.37%). Majority of *SF3B1* mutations were dominant clones in patients with *SF3B1* VAF ≥ 15% (33/38, 86.84%) as well as in those with *SF3B1* VAF < 15% (3/5, 60%) (P = 0.180, **Figure 2G**).

SF3B1 mutations were more prevalent in patients with MDS-RS than in patients with non-MDS-RS (80% vs 5.4%; P < 0.001). 63.16% of the patients with *SF3B1* VAF ≥ 15% were MDS-RS, whereas none of the patients with *SF3B1* VAF < 15% were MDS-RS (P = 0.012; **Figure 2H**). Patients with MDS-RS had higher median *SF3B1* VAF than those with non-MDS-RS (41.6% vs 36.1%; P = 0.026; **Figure 2I**).

Median OS was longer in the patients with *SF3B1* mutations (not reached) versus in those without (30.17 months; HR 0.51, 95% CI 0.37-0.90, P = 0.017; Table S3; **Figure 5A**). The association between OS and *SF3B1* VAF levels (VAF ≥ 15%, VAF < 15%, and wild-type) was also apparent (P = 0.021). Patients with *SF3B1* VAF ≥ 15% had longer OS (not reached) versus patients with wild-type *SF3B1* (30.17 months, HR 0.42, 95% CI 0.33-0.84, P = 0.007; **Figure 5B**), as well as those with *SF3B1* VAF < 15% (26.97 months; HR 0.29, 95% CI 0.02-0.92, P = 0.044; **Figure 5D**). OS did not differ significantly in patients with *SF3B1* VAF < 15% versus wild-

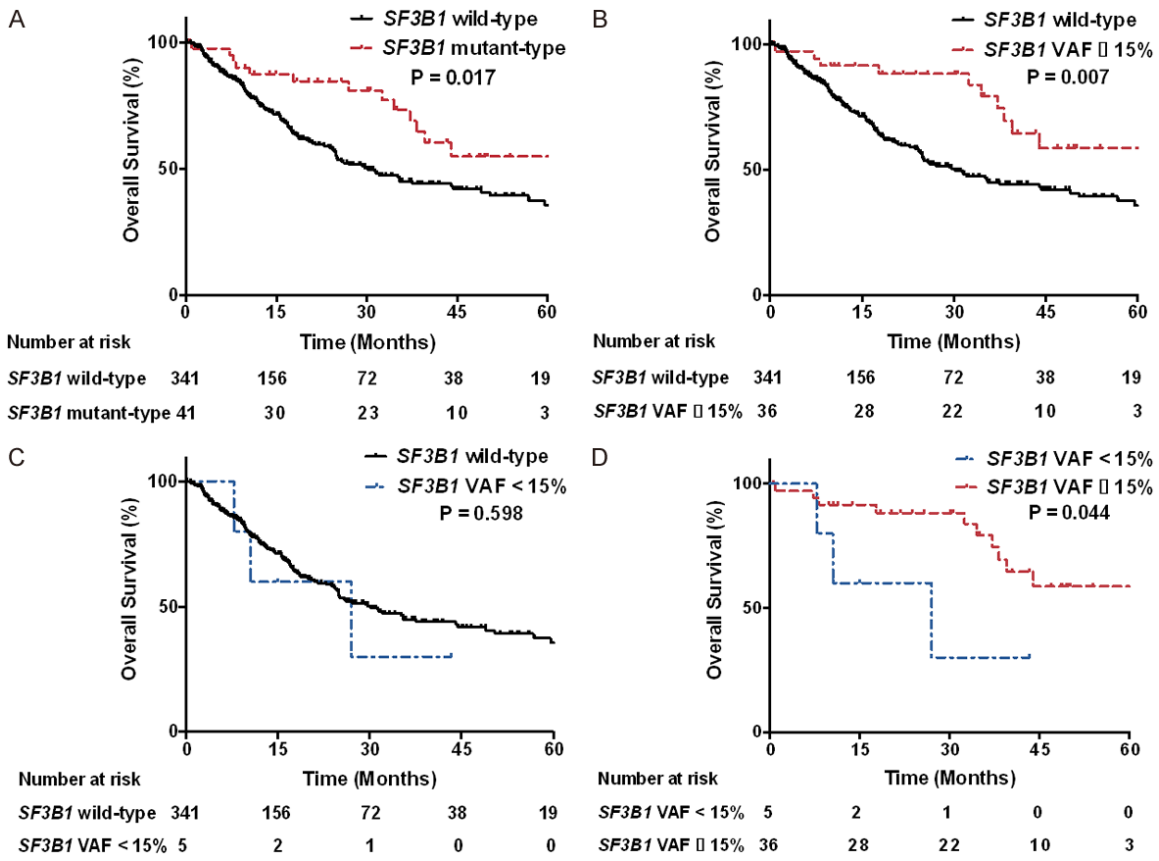

Figure 5. Association of overall survival (OS) with *SF3B1* mutation status or variant allele frequency (VAF). OS stratified by (A) *SF3B1* mutation status, (B) *SF3B1* VAF ≥ 15% or wild-type, (C) *SF3B1* VAF < 15% or wild-type, (D) *SF3B1* VAF ≥ 15% or < 15%.

type *SF3B1* (26.97 vs 30.17 months; HR 1.36, 95% CI 0.38-5.38, P = 0.598; **Figure 5C**).

In the multivariate regression, mutation status of *SF3B1* was not associated with OS (HR 0.59, 95% CI 0.33-1.05, P = 0.073; **Table 2**). Instead, high *SF3B1* VAF was an independent protective factor for MDS prognosis (HR 0.52, 95% CI 0.27-0.99, P = 0.048; **Table 2**).

Association between EZH2/NRAS and OS

OS was shorter in patients with *EZH2* mutations (P = 0.005) and *NRAS* mutations (P = 0.038) (Table S3). Analysis with Cutoff Finder identified optimal VAF cut-off at 2.6% for *EZH2* and 1.36% for *NRAS* mutations, but there were no cases with *EZH2* VAF < 2.6% and only one case with *NRAS* VAF < 1.36% in our cohort. Therefore, it could be considered that the associations between OS with *NRAS* and *EZH2* mutations would not be influenced by mutational VAF.

Discussion

The results from the current study suggest independent associations between shorter OS with high mutational VAF of the *TET2* and *TP53* genes in MDS patients. In contrast, high mutational VAF of the *SF3B1* gene seemed to be a protective factor.

TET2 is one of the most frequently mutated genes in MDS. The association between *TET2* mutations and poor prognosis has been reported in some [12-14], but not all studies [3, 6, 15-17, 33]. In the current study, OS was not associated with *TET2* mutation status *per se,* but with *TET2* VAF instead. Specifically, shorter OS was associated with *TET2* mutations, but only if the mutational VAF was ≥ 32%. In our recently published research, higher *TET2* VAF was associated with worse prognosis in lower-risk MDS patients [21]. The current study extended such a finding to MDS patients regardless of the risk stratification. Such an associa-

tion was previously observed in a group of patients with myeloid neoplasms [22], suggesting a broader implication of *TET2* VAF in hematological diseases. Also consistent with a previous study [26], we found an association between *TET2* VAF with better response to HMAs in the current study, highlighting the clinical significance of incorporating *TET2* VAF into routine prognosis prediction and treatment decision-making in MDS patients.

TP53 mutations have been associated with complex karyotypes and poor prognosis in MDS [7, 9, 34, 35]. The current study showed a higher percentage of complex cytogenetics in patients with high *TP53* VAF. Further, we found shorter OS in patients with high VAF level of *TP53* mutations relative to patients bearing wild-type *TP53*, but not in patients with low VAF level. Patients with high *TP53* VAF also had significantly shorter survival than those with low *TP53* VAF. More importantly, multivariate analysis identified high *TP53* VAF as an independent predictor for poor survival. These observations corroborate the findings of several previous studies [11, 18-20], and highlight the prognostic value of *TP53* VAF.

SF3B1 mutations have been reported in association with MDS-RS category [23, 24]. Indeed, *SF3B1* mutations have been associated with improved survival in MDS patients by majority [6, 7, 9, 15], if not all studies [3, 17]. In the current study, patients with high *SF3B1* VAF were more frequently classified as MDS-RS category and had longer OS than patients with low *SF3B1* VAF. In contrast to patients with wide-type *SF3B1*, those with high *SF3B1* VAF had a more favorable prognosis. In the multivariate regression analyses, OS was independently associated with high *SF3B1* VAF but not mutation status *per se*.

Our study shows that the associations of mutations in *TET2*, *TP53*, and *SF3B1* with survival, clinical phenotypes and even the treatment response of MDS might be strongly influenced by mutational VAF. These findings highlight the potential importance and necessity of incorporating VAF in risk stratification and therapeutic decisions of MDS. However, the detailed mechanism by which higher VAF mutations in these genes leading to greater effect remains elusive. As one of the mechanistic explanations, mutational VAF might represent clonal burden, and only mutations with sufficiently large clones could produce realistic impact on patient survival. Moreover, high VAF mutations are often dominant, whereas low VAF mutations were mostly subclonal.

However, VAF does not influence all the associations of mutations with prognosis across the genetic spectrum of MDS. In a previous study using serial sequencing, *NRAS* mutations with low VAF were associated with leukemic transformation as large VAF mutations [36]. In the current study, we identified associations between shorter OS with *NRAS* and *EZH2* mutations, regardless of mutational VAF [36]. These findings suggest that for some genes like *NRAS* and *EZH2*, their mutations with low VAF might pose a similar risk as their presence with high mutational VAF.

There were several limitations including population size and the lack of external validations in this study. Moreover, VAF is not the only factor that influence the clinical and prognostic impact of the mutations, other mutational characteristics including mutation location, mutation type (missense vs others), and co-mutated genes might also play important roles [2, 37]. More studies are needed to confirm our findings and explore the significance of diverse mutational characteristics in MDS.

In conclusion, the current study indicates that the prognostic impact of *TET2*, *TP53*, and *SF3B1* mutations in MDS highly depends on their mutational VAF. These findings encourage the consideration of mutational VAF of certain genes into prognosis prediction and decision-making in the treatment of MDS patients.

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Disclosure of conflict of interest

None.

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Table S1. Clinical characteristics of each patient in the cohort

Number	Sex	Age	Diagnosis	Cytogenetics	IPSS-R scores	Initial treatment
MDS-15-001	M	68	MDS-MLD	Normal	2.5	Supportive care
MDS-15-002	M	47	MDS-MLD	Normal	2	Supportive care
MDS-15-003	F	61	MDS-U	Normal	2	Supportive care
MDS-15-004	M	71	MDS-RS	Normal	2.5	Supportive care
MDS-15-005	M	73	MDS-MLD	Normal	2	HMAs monotherapy
MDS-15-006	M	63	MDS-MLD	Normal	5	HMAs+other agents
MDS-15-007	F	69	MDS-RS	Normal	2.5	HMAs monotherapy
MDS-15-008	F	47	MDS-MLD	Normal	2.5	HMAs+other agents
MDS-15-009	F	61	MDS-RS	Normal	2	Supportive care
MDS-15-010	F	66	MDS-RS	47, XX, +8 [17]	4.5	HMAs monotherapy
MDS-15-011	F	46	MDS-MLD	47, XX, +8 [20]	4	Supportive care
MDS-15-012	F	33	MDS-U	Normal	2	Supportive care
MDS-15-013	M	77	MDS-MLD	Normal	2.5	HMAs monotherapy
MDS-15-014	F	49	MDS-SLD	Normal	2.5	Supportive care
MDS-15-015	M	73	MDS-MLD	Normal	3	HMAs monotherapy
MDS-15-016	M	56	MDS-MLD	Normal	3.5	HMAs+other agents
MDS-15-017	F	41	MDS-SLD	Normal	3	Supportive care
MDS-15-018	F	59	MDS-SLD	Normal	3.5	HMAs monotherapy
MDS-15-019	F	64	MDS-MLD	Normal	3	HMAs monotherapy
MDS-15-020	M	36	MDS-U	Normal	4	HMAs monotherapy
MDS-15-021	M	53	MDS-U	Normal	4	Supportive care
MDS-15-022	M	51	MDS-RS	Normal	3	Supportive care
MDS-15-023	M	57	MDS-MLD	Normal	2.5	Supportive care
MDS-15-024	F	55	MDS-MLD	Normal	3.5	HMAs+other agents
MDS-15-025	F	64	MDS-EB-1	Normal	3.5	Supportive care
MDS-15-026	M	52	MDS-MLD	Normal	4	Supportive care
MDS-15-027	F	73	MDS-MLD	Normal	4	Supportive care
MDS-15-028	M	25	MDS-MLD	Normal	4	Supportive care
MDS-15-029	M	77	MDS-EB-1	Normal	4.5	HMAs monotherapy
MDS-15-030	F	61	MDS-MLD	Normal	4	Supportive care
MDS-15-031	M	57	MDS-MLD	47, XY, +8 [10]	4	HMAs monotherapy
MDS-15-032	M	52	MDS-EB-1	47, XY, +8 [10]	5.5	HMAs monotherapy
MDS-15-033	F	52	MDS-EB-1	47, XX, +11 [2]/46, XX [8]	6	HMAs+other agents
MDS-15-034	M	49	MDS-MLD	46, XY, -16, +mar [10]	5.5	HMAs monotherapy
MDS-15-035	F	57	MDS-EB-1	Normal	5	HMAs+other agents
MDS-15-036	M	60	MDS-EB-1	47, XY, +8 [10]	4	HMAs+other agents
MDS-15-037	F	53	MDS-EB-1	Normal	4	HMAs+other agents
MDS-15-038	F	61	MDS-EB-1	Normal	4.5	HMAs monotherapy
MDS-15-039	F	61	MDS-EB-1	Normal	5.5	HMAs monotherapy
MDS-15-040	F	22	MDS-EB-1	Normal	5.5	HMAs monotherapy
MDS-15-041	F	56	MDS-EB-1	Normal	4.5	HMAs+other agents
MDS-15-042	F	31	MDS-EB-1	Normal	4.5	HMAs+other agents
MDS-15-043	M	67	MDS-EB-1	Normal	4.5	HMAs monotherapy
MDS-15-044	F	69	MDS-EB-1	Normal	6	Supportive care
MDS-15-045	M	59	MDS-EB-1	Normal	5	HMAs monotherapy
MDS-15-046	M	62	MDS-EB-1	Normal	5	HMAs+other agents
MDS-15-047	M	34	MDS-EB-1	Normal	6	HMAs monotherapy
MDS-15-048	M	33	MDS-EB-2	Normal	5.5	HMAs+other agents
MDS-15-049	F	41	MDS-EB-1	Normal	4.5	Supportive care
MDS-15-050	M	68	MDS-EB-1	47, XY, del(5)(q23), -11, del(13)(q14q22), +2mar [1]/49, idem, -7, +19, +21, +1mar [3]/46, XY [2]	7.5	HMAs+other agents
MDS-15-051	M	45	MDS-EB-1	47, XY, +8, del(11)(q14) [10]	6	Supportive care
MDS-15-052	M	23	MDS-EB-1	46, XY, +8 [10]	6.5	HMAs monotherapy
MDS-15-053	F	23	MDS-EB-1	46, XX, -11, +mar [10]	5	HMAs monotherapy

MDS-15-054	M	55	MDS-EB-2	45, x, -y [3]/46, xy [17]	4.5	HMAs+other agents
MDS-15-055	M	22	MDS-MLD	46, XY, +5 [2]/46, xy [18]	3	HMAs monotherapy
MDS-15-056	F	53	MDS-EB-2	Normal	4	HMAs+other agents
MDS-15-057	M	38	MDS-EB-2	Normal	5	HMAs+other agents
MDS-15-058	M	61	MDS-EB-2	Normal	5	HMAs+other agents
MDS-15-059	F	62	MDS-EB-2	47, XX, +8 [12]	7	HMAs+other agents
MDS-15-060	M	34	MDS-EB-2	46, XY, del(20)(q11) [10]	5	HMAs+other agents
MDS-15-061	M	65	MDS-EB-2	46, XY, del(11)(q21) [8]/46, XY [2]	4	HMAs+other agents
MDS-15-062	M	37	MDS-EB-2	Normal	4.5	HMAs+other agents
MDS-15-063	M	60	MDS-EB-2	Normal	5	HMAs+other agents
MDS-15-064	M	58	MDS-EB-2	Normal	5.5	HMAs+other agents
MDS-15-065	F	57	MDS-EB-2	Normal	6	HMAs+other agents
MDS-15-066	M	54	MDS-EB-2	Normal	6	HMAs+other agents
MDS-15-067	M	57	MDS-EB-2	Normal	6.5	HMAs monotherapy
MDS-15-068	F	65	MDS-EB-2	Normal	7	HMAs+other agents
MDS-15-069	M	56	MDS-EB-2	46, XY, del(20)(q11) [7]/46, XY [4]	4.5	HMAs+other agents
MDS-15-070	F	60	MDS-EB-2	46, XX [19]/92, XXXX [1]	6.5	HMAs+other agents
MDS-15-071	M	52	MDS-EB-1	43~47, XY, der(2)(q31), -4, del(5)(q21), -8 [5], -9, -14 [5], del(15)(q23), -20 [4], +2~3mar [10]	9	HMAs monotherapy
MDS-15-072	M	64	MDS-EB-2	43, XY, del(5)(q31), -7, -11, -12 [1]	9	HMAs+other agents
MDS-15-073	M	65	MDS-EB-2	Normal	6.5	HMAs monotherapy
MDS-15-074	F	40	MDS-EB-2	45, XX, -7 [7]/46, XX [4]	8.5	HMAs+other agents
MDS-15-075	F	68	MDS-EB-1	Normal	5	HMAs+other agents
MDS-15-076	F	59	MDS-SLD	Normal	2	Supportive care
MDS-15-077	M	43	MDS-SLD	Normal	3.5	HMAs+other agents
MDS-15-078	M	58	MDS-EB-1	Normal	3.5	HMAs+other agents
MDS-15-079	M	25	MDS-EB-1	Normal	4	HMAs monotherapy
MDS-15-080	F	65	MDS-U	Normal	4.5	Supportive care
MDS-37-081	M	60	MDS-EB-2	Normal	5	Supportive care
MDS-37-082	M	30	MDS-MLD	Normal	2.5	Supportive care
MDS-37-083	M	67	MDS-EB-1	Normal	6	HMAs monotherapy
MDS-37-084	M	55	MDS-MLD	46, XY, der(12)(p13) [10]	3	HMAs monotherapy
MDS-37-085	F	27	MDS-EB-1	46, XX, t(3;3)(q21;q26) [11]/46, XX [1]	5	HMAs monotherapy
MDS-37-086	F	51	MDS-EB-2	45, XX, -7 [3]/46, XX, del(20)(q11) [12]	7.5	HMAs+other agents
MDS-37-087	F	58	MDS-MLD	Normal	2.5	Supportive care
MDS-37-088	M	58	MDS-RS	Normal	2.5	Supportive care
MDS-37-089	M	42	MDS-EB-1	Normal	4.5	HMAs+other agents
MDS-37-090	F	51	MDS-MLD	45, XX, der(3)(q23), -12 [2]/46, XX, del(5)(q15) [3]/46, XX [5]	5	HMAs monotherapy
MDS-37-091	M	66	MDS-EB-1	46, XY, del(20)(q11) [6]/47, sl1, del(20)(q11) [1]/47, sl2, +8 [1]/50, sdl1, +8, +2mar [2]	7	HMAs monotherapy
MDS-37-092	F	68	MDS-RS	46, XX, -3, del(5)(q21), +mar [5]/46, XX [5]	7	Supportive care
MDS-37-093	M	28	MDS-MLD	47, XY, +8 [10]	4.5	Supportive care
MDS-37-094	M	56	MDS-EB-2	46, XY, -2*2, der(3)(q27), der(14)(q32), +2mar [5]/47, idem, +mar3 [1]/46, XY [1]	10	HMAs monotherapy
MDS-37-095	F	66	MDS-MLD	46, XX, del(20)(q11) [10]	3	Supportive care
MDS-37-096	M	65	MDS-EB-2	Normal	6.5	HMAs monotherapy
MDS-37-097	M	29	MDS-EB-2	Normal	6	HMAs+other agents
MDS-37-098	M	52	MDS-U	Normal	3.5	Supportive care
MDS-37-099	M	44	MDS-MLD	47, XY, +8 [6]/46, XY [4]	3.5	Supportive care
MDS-37-100	M	74	MDS-MLD	47, XY, +8 [10]	5	Supportive care
MDS-37-101	M	48	MDS-EB-1	Normal	6	HMAs monotherapy
MDS-37-102	M	63	MDS-EB-2	43, XY, -3, der(7)(p13), der(8)(p23), der(12)(p13), -17, -18 [10]	9.5	Supportive care
MDS-37-103	M	72	MDS-RS	Normal	2.5	Supportive care
MDS-37-104	F	69	MDS-MLD	Normal	3	Supportive care
MDS-37-105	M	52	MDS-MLD	46, XY, +8 [10]	5.5	Supportive care
MDS-37-106	M	58	MDS-MLD	53, XY, +9, +10, +19, +20, +21, +22, +mar [3]/53, idem, der(11)(p15) [5]/46, XY [2]	8	HMAs monotherapy

MDS-37-107	M	35	MDS-EB-1	48, XY, +8, +19 [3]/46, XY [7]	6.5	Supportive care
MDS-37-108	M	30	MDS-EB-1	47, XY, +8 [5]/46, XY [5]	6	Supportive care
MDS-37-109	F	33	MDS-SLD	Normal	2	Supportive care
MDS-37-110	M	71	MDS-MLD	Normal	3.5	HMAs monotherapy
MDS-37-111	M	67	MDS-MLD	44~53, XY, der(1)(q44) [1], der(2)(p14), -4 [8], -6 [3], der(7)(q22), -7 [4], +9 [1], +10 [1], -12 [3], -13 [5], +14 [1], +4~5mar [1]	6	Supportive care
MDS-37-112	M	50	MDS-RS	Normal	2	Supportive care
MDS-37-113	F	69	MDS-MLD	Normal	3	Supportive care
MDS-37-114	F	79	MDS-SLD	Normal	2	Supportive care
MDS-37-115	M	69	MDS-MLD	Normal	3	Supportive care
MDS-37-116	M	29	MDS-EB-1	Normal	3.5	Supportive care
MDS-37-117	F	81	MDS-SLD	Normal	2.5	Supportive care
MDS-37-118	F	61	MDS-MLD	46, XX, del(20)(q11) [3]/46, XX [7]	3.5	Supportive care
MDS-37-119	M	75	MDS-U	Normal	4.5	Supportive care
MDS-37-120	F	54	MDS-SLD	45, XX, -18 [3]/46, XX [12]	4.5	HMAs monotherapy
MDS-37-121	F	52	MDS-SLD	Normal	2	HMAs monotherapy
MDS-37-122	M	67	MDS-SLD	Normal	1	Supportive care
MDS-37-123	M	63	MDS-EB-1	Normal	4	HMAs monotherapy
MDS-37-124	M	73	MDS-EB-2	Normal	5.5	HMAs+other agents
MDS-37-125	F	57	MDS-MLD	46, XX, del(20)(q11) [4]/46, idem, del(16)(p11) [6]	4	Supportive care
MDS-37-126	F	57	MDS-MLD	Normal	4	Supportive care
MDS-37-127	F	69	MDS-RS	Normal	2	Supportive care
MDS-37-128	M	59	MDS-MLD	47, XY, +mar [1]/45, XY, -15 [3]/46, XY [16]	5	HMAs monotherapy
MDS-37-129	M	64	MDS-RS	Normal	3	Supportive care
MDS-37-130	M	46	MDS-MLD	48, XY, +9, del(17)(p13), +mar [2]/46, XY [8]	6	HMAs monotherapy
MDS-37-131	M	55	MDS-U	Normal	3.5	HMAs monotherapy
MDS-37-132	F	29	MDS-MLD	Normal	3	Supportive care
MDS-37-133	M	42	MDS-U	Normal	3.5	Supportive care
MDS-37-134	M	49	MDS-EB-2	Normal	5	HMAs+other agents
MDS-37-135	F	63	MDS-SLD	Normal	3	Supportive care
MDS-37-136	M	69	MDS-MLD	44~48, XY, -4, -5, -7 [4], +8, -17, -18 [3], -21 [5], +3~5mar [8]	7.5	Supportive care
MDS-37-137	F	62	MDS-MLD	Normal	4.5	HMAs monotherapy
MDS-37-138	M	46	MDS-MLD	46, XY, der(20)(q11) [9]/46, XY [1]	3.5	Supportive care
MDS-37-139	M	28	MDS-SLD	Normal	2.5	Supportive care
MDS-37-140	M	64	MDS-MLD	Normal	2.5	Supportive care
MDS-37-141	M	74	MDS-EB-2	Normal	6.5	Supportive care
MDS-37-142	M	61	MDS-MLD	47, XY, +8 [9]/46, XY [1]	3.5	Supportive care
MDS-37-143	M	69	MDS-MLD	45~48, X, -Y [8], -6 [8], -7, +8, -13 [7], -15 [3], -18 [3], +2~3mar [11]	5.5	Supportive care
MDS-37-144	M	66	MDS-MLD	Normal	2	Chemotherapy
MDS-37-145	F	21	MDS-EB-1	47, XX, -5, +2mar [2]/46, idem, -X, -8, +mar [8]	9	HMAs+other agents
MDS-37-146	M	33	MDS-EB-1	41, XY, -5, -8, -21*2, -22, +1mar, 1ace [2]/41, sl, -19 [5]/42, sdl, +19 [5]/42, sdl, +18 [3]/46, XY [2]	8.5	HMAs+other agents
MDS-37-147	F	67	MDS-EB-2	Normal	5	HMAs monotherapy
MDS-37-148	F	70	MDS-RS	Normal	2	Supportive care
MDS-37-149	F	71	MDS-RS	48, XX, t(2;12)(q13;p13), del(5)(q22), +8, -13, der(20)(q13), +2mar, 1 min [6]/47, sl1, -21 [4]	5	Supportive care
MDS-37-150	M	65	MDS-EB-1	46, XY, t(3;12)(p25;q24) [7]/46, idem, t(9;10)(q32,P15) [3]	6.5	Supportive care
MDS-37-151	M	51	MDS-MLD	47, XY, +8 [9]/46, XY [1]	2.5	Supportive care
MDS-37-152	F	56	MDS-MLD	Normal	3.5	Supportive care
MDS-37-153	M	67	MDS-MLD	Normal	3.5	Supportive care
MDS-37-154	M	61	MDS-MLD	Normal	4.5	Supportive care
MDS-37-155	M	66	MDS-MLD	Normal	3.5	Supportive care
MDS-37-156	M	32	MDS-MLD	Normal	3	HMAs+other agents
MDS-37-157	F	60	MDS-SLD	47, XX, +8 [3]/46, XX [17]	6	HMAs monotherapy
MDS-37-158	M	57	MDS-EB-1	45~52, XY, +1 [1], +2 [2], del(5)(q31) [3] +8, -10 [3], -11 [3], +15 [1]	8.5	Supportive care
MDS-37-159	F	64	MDS-SLD	Normal	1.5	Supportive care
MDS-37-160	F	70	MDS-EB-2	46, XX, der(5)(q32) [16]/46, XX [4]	6	HMAs monotherapy

MDS-37-161	M	67	MDS-EB-1	Normal	4.5	Supportive care
MDS-37-162	M	57	MDS-MLD	44, XY, -18, -20 [1]/44, sdl. +20 [1]/48, XY [8]	4	HMAs monotherapy
MDS-37-163	M	39	MDS-EB-2	46, XY, der(14)(p11) [5]/46, XY, der(17)(q36) [2]/46, XY [6]	5	HMAs+other agents
MDS-37-164	M	60	MDS-MLD	44~46, XY, der(3)(p11), del(5)(q31), der(11)(p15) [6], -15 [5], -17 [6], der(17)(p13) [4]/46, XY [2]	4.5	Supportive care
MDS-37-165	M	67	MDS-EB-1	42~44, XY, -Y [3], -4 [5], -7, -12, +2~3mar [6]/46, XY [3]	8	Supportive care
MDS-37-166	F	64	MDS-EB-1	Normal	5	Supportive care
MDS-37-167	M	57	MDS-RS	46, XY, del(20)(q11) [7]/46, XY [3]	2	Supportive care
MDS-37-168	M	25	MDS-MLD	45~46, XY, +8 [7], -13 [3], -14 [3], -15 [3], del(20)(q11) [8]/46, XY [1]	3.5	Supportive care
MDS-37-169	F	37	MDS-RS	Normal	4	Supportive care
MDS-37-170	M	66	MDS-EB-2	39, XY, -7, -12, -13, der(14;15)(q10;q10), -17, -18, -19, -20, +mar [3]/39, idem, -17, +mar [1]/46, XY [6]	10	HMAs monotherapy
MDS-37-171	M	37	MDS-MLD	49, XY, +9, +16, +21 [3]/46, XY [7]	4.5	Supportive care
MDS-37-172	M	64	MDS-RS	Normal	2.5	Supportive care
MDS-37-173	M	49	MDS-EB-2	46, XY, del(8)8q22) [3]/46, XY [9]	6.5	Supportive care
MDS-37-174	F	63	MDS-MLD	47, XX, +8 [10]	3.5	Supportive care
MDS-37-175	F	68	MDS-EB-2	Normal	7	HMAs monotherapy
MDS-37-176	M	27	MDS-MLD	47, XX, +8 [10]	4	HMAs monotherapy
MDS-37-177	M	67	MDS-RS	Normal	3.5	HMAs monotherapy
MDS-37-178	F	69	MDS-RS	Normal	3.5	HMAs monotherapy
MDS-37-179	M	72	MDS-U	Normal	3	Supportive care
MDS-37-180	F	68	MDS-EB-1	Normal	6	Supportive care
MDS-37-181	F	53	MDS-MLD	Normal	3.5	Supportive care
MDS-37-182	M	55	MDS-U	Normal	3	Supportive care
MDS-37-183	M	57	MDS-MLD	Normal	2	HMAs monotherapy
MDS-37-184	M	78	MDS-EB-2	Normal	6	HMAs monotherapy
MDS-37-185	M	39	MDS-U	Normal	4	Supportive care
MDS-37-186	F	33	MDS-SLD	Normal	1.5	Supportive care
MDS-37-187	F	61	MDS-EB-1	46, XX, del(5)(q21), del(7)(q22) [4]/46, idem, t(15;17)(q22;q12) [6]	4.5	HMAs monotherapy
MDS-37-188	F	42	MDS-SLD	Normal	3.5	Supportive care
MDS-37-189	F	35	MDS-MLD	47, XX, +8 [10]	3	Supportive care
MDS-37-190	M	55	MDS-RS	Normal	2.5	Supportive care
MDS-37-191	M	28	MDS-MLD	Normal	2	Chemotherapy
MDS-37-192	F	62	MDS-RS	Normal	2.5	Supportive care
MDS-37-193	M	63	MDS-SLD	Normal	2.5	Supportive care
MDS-37-194	M	59	MDS-SLD	Normal	2.5	Supportive care
MDS-37-195	F	31	MDS-EB-1	47, XX, +6 [6]/48, idem, +21 [2]/47, XX +8 [2]	5	HMAs monotherapy
MDS-37-196	F	49	MDS-SLD	47, XX, +14 [2]/49, idem, +8, +16 [2]/46, XX [6]	4	HMAs monotherapy
MDS-37-197	M	29	MDS-MLD	Normal	3	Supportive care
MDS-37-198	M	57	MDS-EB-2	45, XY, -Y [3]/46, XY, t(3;12)(p25;q24) [2]/46, XY [5]	6	HMAs monotherapy
MDS-37-199	M	74	MDS-EB-1	43, XX, del(5)(q15), -7, -8, dic(12)(p10), -17 [5]/46, XY [5]	8.5	Supportive care
MDS-37-200	M	27	MDS-SLD	Normal	2	HMAs monotherapy
MDS-37-201	F	78	MDS-EB-1	46, XX, del(4)(q26), del(5)(q21) [6]/46, idem, del(12)(p13) [4]	6	Supportive care
MDS-37-202	M	62	MDS-MLD	46, XY, -3, -11, +2mar [1]/46, idem, der(19)(q13;3) [9]	6.5	Supportive care
MDS-37-203	F	65	MDS-EB-2	46, XX, del(5)(q15) [6]/46, XX [4]	4.5	Supportive care
MDS-37-204	F	56	MDS-MLD	Normal	3.5	Supportive care
MDS-37-205	M	56	MDS-MLD	Normal	2.5	HMAs monotherapy
MDS-37-206	F	36	MDS-MLD	Normal	1	Supportive care
MDS-37-207	F	52	MDS-MLD	Normal	4	Supportive care
MDS-37-208	F	61	MDS-EB-2	43, XX, del(5)(q31), -7, -8, -10, -12, -13, -17*2, +4mar [9]/43, XX, -5, -8, -18, -12, -13, -17*2, +4mar [1]	8.5	HMAs monotherapy
MDS-37-209	M	71	MDS-EB-1	Normal	5.5	Supportive care
MDS-37-210	M	77	MDS-MLD	46, XY, del(11)(q23) [8]/46, XY [2]	1.5	HMAs monotherapy
MDS-37-211	F	21	MDS-EB-1	46, XX, t(9;22;11)(q34;q11;p12) [9]/46, XX [1]	5.5	Supportive care
MDS-37-212	M	56	MDS-SLD	46, XY, inv(9)(p12q13) [9]/46, XY [1]	2.5	Supportive care
MDS-37-213	M	14	MDS-SLD	Normal	2	Supportive care
MDS-37-214	F	59	MDS-MLD	47, XX, +8 [2]/46, XX [8]	3.5	HMAs monotherapy

MDS-37-215	M	68	MDS-SLD	Normal	1	Supportive care
MDS-37-216	M	57	MDS-EB-2	Normal	4	HMAs monotherapy
MDS-37-217	M	35	MDS-EB-2	46, XY, -11, +r [4]/45, sl, -17 [2]/92, sl*2 [2]/45, x, -Y, -17, +mar [2]	6	HMAs+other agents
MDS-37-218	F	49	MDS-MLD	46, XX, del(20)(q11) [2]/47, xx, del(1)(q12), +18 [1]	3	Supportive care
MDS-37-219	M	62	MDS with isolated del (5q)	46, XY, del(5)(q21) [8]/46, XY [2]	2.5	Supportive care
MDS-37-220	M	56	MDS-EB-2	Normal	5	HMAs+other agents
MDS-37-221	M	51	MDS-EB-2	Normal	6	HMAs+other agents
MDS-37-222	M	57	MDS-MLD	Normal	1.5	Supportive care
MDS-37-223	M	66	MDS-U	45, X, -Y [8]/46, XY [2]	3	Supportive care
MDS-37-224	M	67	MDS-EB-1	46, XY, del(5)(q31), del(20)(q11) [4]/65~66, XXY, idem, -2 [3], -3, -5, -7, +15, -21 [3], +mar [4]/46, XY [1]	8.5	Supportive care
MDS-37-225	M	58	MDS-EB-1	47, XY, +8 [6]/46, XY [4]	6	HMAs monotherapy
MDS-37-226	M	64	MDS-MLD	Normal	4	HMAs monotherapy
MDS-37-227	M	74	MDS-EB-1	Normal	5.5	HMAs monotherapy
MDS-37-228	F	73	MDS-EB-2	47, XX, +8 [10]	5.5	HMAs monotherapy
MDS-37-229	F	44	MDS-MLD	Normal	2	Supportive care
MDS-37-230	M	38	MDS-MLD	Normal	3	Supportive care
MDS-37-231	F	66	MDS-RS	Normal	2	Supportive care
MDS-37-232	M	51	MDS-RS	46, XY, del(20)(q11) [10]	3.5	Supportive care
MDS-37-233	F	51	MDS-MLD	47, XX, -7, +8, der(7)t(1;7)(q10;q10) [10]	6.5	HMAs+other agents
MDS-37-234	M	66	MDS-MLD	Normal	4.5	Supportive care
MDS-37-235	F	55	MDS-U	Normal	3.5	Supportive care
MDS-37-236	M	74	MDS-MLD	Normal	2.5	HMAs monotherapy
MDS-37-237	M	75	MDS-MLD	Normal	1	Supportive care
MDS-37-238	M	59	MDS-SLD	44~46, XY, del(5)(q21) [5], -7 [4], -11/del(11)(q22) [3], del(20)(q11) [5]/46, XY [5]	5.5	HMAs monotherapy
MDS-37-239	F	56	MDS-RS	46, XY, del(8)(q22) [7]/47, XX, +8 [2]/46, XX [1]	4	HMAs+other agents
MDS-37-240	F	59	MDS-SLD	47, XX, +8 [4]/47, idem, del(20)(q11) [2]/46, XX [4]	4	Supportive care
MDS-37-241	M	64	MDS-EB-2	Normal	4.5	HMAs+other agents
MDS-37-242	F	25	MDS-EB-1	Normal	4.5	HMAs+other agents
MDS-37-243	F	59	MDS-EB-2	Normal	6.5	Supportive care
MDS-37-244	M	76	MDS-SLD	Normal	2.5	Supportive care
MDS-37-245	M	66	MDS-EB-1	48, XY, -5, -17, -19, -20, +6mar [1]/47, XY, -5, -17*2, -19, -20, +6mar [3]/46, XY [6]	8.5	HMAs monotherapy
MDS-37-246	M	65	MDS-EB-1	Normal	5.5	HMAs monotherapy
MDS-37-247	M	53	MDS-SLD	Normal	2	Supportive care
MDS-37-248	M	53	MDS-MLD	Normal	2.5	Supportive care
MDS-37-249	M	59	MDS-EB-1	46, XY, der(6)(q21) [2]/46, XY [18]	5	HMAs monotherapy
MDS-37-250	M	55	MDS-EB-1	Normal	5.5	HMAs+other agents
MDS-37-251	M	70	MDS-MLD	Normal	4.5	Supportive care
MDS-37-252	M	60	MDS-EB-1	46, XY, del(5)(q31) [9]/46, XY [1]	5	Supportive care
MDS-37-253	M	77	MDS-RS	Normal	2	Supportive care
MDS-37-254	M	72	MDS-MLD	Normal	3	Supportive care
MDS-37-255	M	62	MDS-EB-2	Normal	6.5	HMAs monotherapy
MDS-37-256	M	48	MDS-MLD	48, XY, +8, +9 [4]/46, XY [6]	5.5	Supportive care
MDS-37-257	F	39	MDS-SLD	Normal	2	Supportive care
MDS-37-258	M	64	MDS-EB-1	Normal	5.5	HMAs monotherapy
MDS-37-259	F	50	MDS-U	Normal	3	Supportive care
MDS-37-260	M	53	MDS-MLD	46, XY, del(5)(q15) [2]/46, XY [8]	4	Supportive care
MDS-37-261	M	55	MDS-EB-1	Normal	5	Supportive care
MDS-37-262	F	42	MDS-MLD	47, XX, +9 [2]/46, XX [18]	4.5	Supportive care
MDS-37-263	M	36	MDS-U	46, XY, inv(9)(p12q13) [10]	3	Supportive care
MDS-37-264	M	69	MDS-MLD	45, XY, del(5)(q15), -6, der(7)t(1:7)(p22;p22), add(11)(q21) [2]/46, XY [8]	5.5	HMAs monotherapy
MDS-37-265	F	74	MDS-MLD	47, XX, +8 [9]/47, idem, der(3)(p21), ?del(12)(q11) [1]	6.5	Supportive care
MDS-37-266	F	64	MDS-MLD	46, XY, del(5)(q31) [2]/46, XY [8]	4.5	Supportive care

MDS-37-267	M	69	MDS-MLD	46, XY, dup(1)(q22?q25) [8]/46, XY [2]	4.5	Supportive care
MDS-37-268	M	53	MDS-SLD	Normal	2.5	Supportive care
MDS-37-269	M	20	MDS-MLD	Normal	2.5	Supportive care
MDS-37-270	F	23	MDS-EB-1	44, XX, der(5)(q15), -7, -20 [3]/46, XX [7]	6.5	HMAs+other agents
MDS-37-271	M	65	MDS-EB-1	Normal	5	Supportive care
MDS-37-272	F	55	MDS-EB-2	44-45, XX, -5/del(5)(q15), -7, -13/del(13)(q14q21), -16 [3], -18 [6], -20 [7], -21 [3], +1-3mar [10]	8.5	HMAs monotherapy
MDS-37-273	M	72	MDS-EB-1	46, XY, t(2;6)(q32;q26), del(3)(p23), del(12)(p13) [9]/46, XY [1]	7.5	HMAs monotherapy
MDS-37-274	M	60	MDS-EB-2	61-72, XYY, -2 [5], -3 [4], -4 [3], +6 [6], -7 [3], del(7)(p15), +del(7)(p15), +8 [3], -9 [3], -11 [3], -12 [7], +13 [6], -16, -17 [8], -18 [9], -20 [6], -21 [4], -22 [4], +3u7mor [13]/46, xy [1]	9	Supportive care
MDS-37-275	M	56	MDS-EB-2	Normal	6	Supportive care
MDS-37-276	M	76	MDS-EB-2	48, XY, +2mar [2]/46-48, idem, der(2)(q2?5), -5, -11 [4]	9.5	HMAs monotherapy
MDS-37-277	M	61	MDS-EB-2	47, XY, +8 [9]/46, XY [1]	5.5	HMAs monotherapy
MDS-37-278	F	67	MDS-EB-2	46, XX, der(1)(p36), der(5)(q15), -7, +mar [10]	9	Supportive care
MDS-37-279	F	37	MDS-SLD	46, XX, ider(20)del(20)(q11.2) [18]/46, XX [2]	3	HMAs monotherapy
MDS-37-280	M	82	MDS-EB-2	47, XY, +8 [6]/46, XY [14]	6	HMAs+other agents
MDS-37-281	M	78	MDS-EB-1	Normal	5	HMAs+other agents
MDS-37-282	M	60	MDS-MLD	Normal	4	Supportive care
MDS-37-283	M	54	MDS-EB-2	Normal	6	HMAs+other agents
MDS-37-284	M	61	MDS-EB-2	Normal	4.5	HMAs monotherapy
MDS-37-285	F	78	MDS-EB-2	Normal	5.5	HMAs monotherapy
MDS-37-286	F	31	MDS-EB-2	Normal	6	Supportive care
MDS-37-287	M	66	MDS-EB-1	45-46, XY, t(2;19)(p22;q13), -4-5/del(5)(q21), -7, ?del(9)(q21q22) [9], +12 [1], deL(12)(p13) [2], -13 [4], +15 [1]	7.5	HMAs+other agents
MDS-37-288	M	72	MDS-EB-1	45, XY, -5, -7, -12, +3mar [3]/46, sl, +mar [3]/48, sdl, +2mar [1]/46, XY, -5, -7, +8, -9, -12, der(21)(p11), -22, +4mar [3]/46, XY [3]	8	HMAs monotherapy
MDS-37-289	M	51	MDS-EB-1	45, XY, -7 [8]/46, XY [2]	8	Supportive care
MDS-37-290	M	70	MDS-EB-1	46, XY, del(20)(q11) [10]	5.5	Supportive care
MDS-37-291	F	53	MDS-MLD	47, XX, +8 [20]	2.5	HMAs monotherapy
MDS-37-292	M	51	MDS-EB-2	49-52, XY, del(1)(p13p22), +del(1)(p13p22) [8], -5 [3], +8, +9 [1], +15 [8], +1-4mar [9]/46, XY [1]	8.5	HMAs+other agents
MDS-37-293	M	65	MDS-EB-2	Normal	5.5	HMAs monotherapy
MDS-37-294	M	17	MDS-SLD	45, XY, -7 [10]	6	Supportive care
MDS-37-295	F	45	MDS-MLD	46, XX, t(9;22;11)(q34;q11) [1]/46, sl, del(20)(q11) [1]/48, sdl, +8, +14 [6], XX [2]	6.5	Chemotherapy
MDS-37-296	M	37	MDS-EB-2	47, XY, +8 [10]	7.5	HMAs+other agents
MDS-37-297	F	64	MDS-MLD	Normal	5	Supportive care
MDS-37-298	M	58	MDS-EB-1	Normal	4.5	Supportive care
MDS-37-299	M	88	MDS-EB-1	44, XY, der(1)(q31), der(4)(q35), -5, -6, -11, -12, -13, +3mar [9]/46, XY [1]	6.5	HMAs monotherapy
MDS-37-300	F	62	MDS-EB-2	Normal	6	Supportive care
MDS-37-301	M	23	MDS-MLD	Normal	2	Supportive care
MDS-37-302	F	49	MDS-EB-1	Normal	5.5	HMAs+other agents
MDS-37-303	M	55	MDS-MLD	46, XY, del(20)(q11) [12]/46, XY [1]	3	Supportive care
MDS-37-304	F	22	MDS-EB-2	Normal	7	HMAs+other agents
MDS-37-305	M	67	MDS-RS	Normal	2	Supportive care
MDS-37-306	M	37	MDS-EB-2	Normal	5	HMAs+other agents
MDS-37-307	F	57	MDS-RS	Normal	2	Supportive care
MDS-37-308	F	56	MDS-MLD	Normal	1.5	Supportive care
MDS-37-309	F	57	MDS-EB-2	47, XX, +8 [10]	6	HMAs+other agents
MDS-37-310	M	75	MDS-RS	Normal	2.5	Supportive care
MDS-37-311	M	56	MDS-EB-2	Normal	4.5	HMAs+other agents
MDS-37-312	M	66	MDS-SLD	Normal	2.5	Supportive care
MDS-37-313	M	36	MDS-EB-2	46, XY, del(9)(q13q22) [10]	7.5	HMAs monotherapy
MDS-37-314	M	31	MDS-MLD	47, XY, +8 [9]/46, XY [1]	5.5	Supportive care
MDS-37-315	F	68	MDS-MLD	46, XX, der(9)(q34) [4]/46, XX [16]	5.5	Supportive care
MDS-37-316	M	68	MDS-U	Normal	4.5	Supportive care
MDS-37-317	M	76	MDS-MLD	46, XY, del(7)(q22) [9]/46, XY [1]	4.5	HMAs+other agents

MDS-37-318	M	62	MDS-MLD	46, X, der(Y)t(Y;?1)(q12;?q22) [10]	4	Supportive care
MDS-37-319	F	32	MDS-EB-2	Normal	5	HMAs+other agents
MDS-37-320	F	54	MDS-SLD	46-51, XX, +1, del(5)(q21q34), +11 [7], -13 [5], +14 [7], -18 [8], -20 [5], -22 [5], +1~3mar [9, 10]	6	HMAs monotherapy
MDS-37-321	M	77	MDS-EB-1	45, XY, der(1)(q?32), ?t(2;5)(p23;q31), der(7)(p22), -17 [8]/46, idem, +8 [1]/46, XY [1]	6.5	Supportive care
MDS-37-322	M	69	MDS-MLD	Normal	3.5	Supportive care
MDS-37-323	M	73	MDS-EB-2	Normal	7	HMAs monotherapy
MDS-37-324	M	31	MDS-SLD	Normal	2	Supportive care
MDS-37-325	F	67	MDS-SLD	46, XX, der(1)(p36), del(4)(q25), -5, -6, -7, -17, +4mar [9]/46, XY [1]	6.5	Supportive care
MDS-37-326	M	15	MDS-EB-1	44, XY, -5, -17 [1]/45, sl, +mar1 [5]/47, idem, +mar3 [1]/46, XY [4]	8.5	HMAs monotherapy
MDS-37-327	M	63	MDS-EB-2	45, XY, -16 [3]/45, XY, -17 [3]/46, XY [15]	7	HMAs monotherapy
MDS-37-328	M	65	MDS-SLD	Normal	6	Supportive care
MDS-37-329	F	33	MDS-MLD	Normal	3.5	Supportive care
MDS-37-330	F	60	MDS-EB-1	46, XX, t(1;21)(p11;q22), del(5)(q31), del(20)(q11) [1]/46, idem, ?inv(2)(p11q37) [8]/46, XX [1]	6	Supportive care
MDS-37-331	M	72	MDS-EB-2	42-45, XY, del(1)(q24) [2], -5, der(12)(p11) [3], -13, -14 [5], -17 [4], -19 [5], -22, +3, -5mar [6]/46, XY [1]	9.5	Supportive care
MDS-37-332	M	69	MDS-MLD	46, XY, del(20)(q12) [3]/46, XY [7]	2.5	Supportive care
MDS-37-333	M	62	MDS-SLD	Normal	1.5	Supportive care
MDS-37-334	M	69	MDS-MLD	46, XY, del(20)(q11) [10]	3	Supportive care
MDS-37-335	M	73	MDS-EB-2	Normal	7	HMAs+other agents
MDS-37-336	F	69	MDS-SLD	41-49, XX, add(3)(q21), -5, +8, -11, -20, +22, +mar1 -3 [cp17]/46, XX [3]	6	Supportive care
MDS-37-337	M	25	MDS-MLD	Normal	1.5	Supportive care
MDS-37-338	F	54	MDS-MLD	46, XX, der(1)t(1;11)(p34;q13), der(5)t(5;11)(q15;q12), del(20)(q11.2) [20]	6.5	Supportive care
MDS-37-339	M	70	MDS-EB-1	46, XY, der(7)t(1;7)(q21;q11) [4]/46, XY [6]	5	Supportive care
MDS-37-340	M	76	MDS-EB-1	Normal	4	HMAs monotherapy
MDS-37-341	M	52	MDS-EB-1	Normal	4.5	HMAs monotherapy
MDS-37-342	F	54	MDS-MLD	46, XX, +8 [20]	2.5	Supportive care
MDS-37-343	M	33	MDS-MLD	46, XY, der(20)(q11;q13)idic(p11) [10]	2.5	Supportive care
MDS-37-344	F	64	MDS-EB-1	Normal	4.5	Supportive care
MDS-37-345	M	36	MDS-SLD	Normal	4	Supportive care
MDS-37-346	M	61	MDS-SLD	Normal	3.5	Supportive care
MDS-37-347	M	23	MDS-SLD	Normal	1.5	Supportive care
MDS-37-348	M	44	MDS-MLD	Normal	1.5	Supportive care
MDS-37-349	M	54	MDS-MLD	Normal	2	Supportive care
MDS-37-350	F	60	MDS-MLD	Normal	4.5	Supportive care
MDS-37-351	M	41	MDS-MLD	Normal	2.5	Chemotherapy
MDS-37-352	F	65	MDS-EB-1	46, XX, -11, der(17)(p13), +mar [5]/46, XX [5]	7.5	HMAs+other agents
MDS-37-353	M	56	MDS-MLD	Normal	3	Supportive care
MDS-37-354	F	45	MDS-MLD	Normal	3.5	Supportive care
MDS-37-355	M	52	MDS-MLD	Normal	2	Supportive care
MDS-37-356	F	44	MDS-MLD	Normal	4	Supportive care
MDS-37-357	M	77	MDS-SLD	Normal	2	Supportive care
MDS-37-358	F	60	MDS-RS	47, XX, t(3;3)(q21;q26), +8 [10]	5	Supportive care
MDS-37-359	F	55	MDS-RS	48, XX, +8, +15 [8]/46, XX [2]	6	Supportive care
MDS-37-360	F	56	MDS-MLD	47, XX, +8 [2]/46, XX [18]	4.5	Supportive care
MDS-37-361	M	66	MDS-MLD	Normal	4	Supportive care
MDS-37-362	M	63	MDS-EB-1	Normal	5	Supportive care
MDS-37-363	F	44	MDS-SLD	47, XX, +8 [2]/47, idem, der(13)(p11) [8]	2	Supportive care
MDS-37-364	M	71	MDS-EB-1	47, XY, +8 [20]	5	HMAs monotherapy
MDS-37-365	M	50	MDS-SLD	Normal	2	Supportive care
MDS-37-366	M	60	MDS-EB-2	47, XY, +21 [3]/46, XY, ?t(3;18)(q24;q21) [1]/46, XY [16]	7.5	HMAs monotherapy
MDS-37-367	M	23	MDS-SLD	Normal	2	Supportive care
MDS-37-368	M	77	MDS-EB-1	Normal	3	HMAs+other agents
MDS-37-369	F	62	MDS-EB-2	Normal	5	HMAs monotherapy

MDS-37-370	F	42	MDS-MLD	Normal	4.5	Supportive care
MDS-37-371	F	65	MDS-MLD	Normal	2	Supportive care
MDS-37-372	M	56	MDS-EB-2	Normal	4.5	HMAs monotherapy
MDS-37-373	F	64	MDS-EB-2	Normal	5.5	HMAs monotherapy
MDS-37-374	F	39	MDS-MLD	48, XX, +8, +21 [20]	3.5	HMAs monotherapy
MDS-37-375	M	69	MDS-SLD	53-55, XY, +Y [8], +1, +2 [3], +6, +8/+8*2, +10 [2], +12 [2]	5	Supportive care
MDS-37-376	M	45	MDS-MLD	46, XY, del(20)(q11) [8]/46, XY [2]	2.5	Supportive care
MDS-37-377	M	29	MDS-EB-2	Normal	6.5	HMAs+other agents
MDS-37-378	M	59	MDS-RS	46, XY, del(5)(q12q35), ?del(8)(q21), del(9)(q21) [7]/46, XY [3]	4	Supportive care
MDS-37-379	M	32	MDS-U	47, XY, +8 [10]	4	Supportive care
MDS-37-380	F	64	MDS-MLD	Normal	3.5	Supportive care
MDS-37-381	F	69	MDS-SLD	46, XX, del(5)(q21) [5]/47, XX, del(3)(p12), +8 [1]/46, XX [4]	4.5	HMAs monotherapy
MDS-37-382	F	48	MDS-EB-1	Normal	3.5	HMAs+other agents

F, female; HMA, hypomethylating agent; IPSS-R, revised International Prognostic Scoring System; M, male; MDS-EB-1, myelodysplastic syndromes with excess blasts-1; MDS-EB-2, MDS with excess blasts-2; MDS-MLD, MDS with multilineage dysplasia; MDS-RS, MDS with ring sideroblasts; MDS-SLD, MDS with single lineage dysplasia; MDS-U, MDS unclassifiable.

Table S2. Description of mutations detected in the cohort using next-generation sequencing

Number	RefSeq	Gene	Allele Change	Amino Acid Change	VAF
MDS-15-007	NM_001127208	TET2	c.3393_3314insT	p.S1132FfsTer10	12.70
MDS-15-025	NM_001127208	TET2	c.3409+1G>A	–	44.50
MDS-15-025	NM_001127208	TET2	c.2899C>T	p.Q967X	28.59
MDS-15-030	NM_001127208	TET2	c.3315_3316insA	p.E1106fs*23	45.15
MDS-15-030	NM_001127208	TET2	c.5353A>T	p.K1785X	44.10
MDS-15-037	NM_001127208	TET2	c.2604T>G	p.F868L	54.20
MDS-15-044	NM_001127208	TET2	c.2068C>T	p.Q690X	52.20
MDS-15-045	NM_001127208	TET2	c.5543C>G	p.S1848Ter	16.20
MDS-15-049	NM_001127208	TET2	c.2153delT	p.L719fs*32	45.60
MDS-15-053	NM_001127208	TET2	c.2440C>T	p.R814C	50.79
MDS-15-078	NM_001127208	TET2	c.5476G>T	p.E1826Ter	38.70
MDS-37-110	NM_001127208	TET2	c.5618T>C	p.I1873T	42.37
MDS-37-115	NM_001127208	TET2	c.4393C>T	p.R1465X	51.83
MDS-37-118	NM_001127208	TET2	c.2604T>G	p.F868L	51.45
MDS-37-123	NM_001127208	TET2	c.3646C>T	p.R1216X	20.22
MDS-37-128	NM_001127208	TET2	c.4793delA	p.Y1598fs	32.20
MDS-37-134	NM_001127208	TET2	c.2604T>G	p.F868L	51.00
MDS-37-136	NM_001127208	TET2	c.2604T>G	p.F868L	36.20
MDS-37-138	NM_001127208	TET2	c.2604T>G	p.F868L	48.10
MDS-37-140	NM_001127208	TET2	c.3955-2A>G	–	4.70
MDS-37-141	NM_001127208	TET2	c.2746C>T	p.Q916X	50.50
MDS-37-142	NM_001127208	TET2	c.5298delC	p.Y1766X	40.40
MDS-37-144	NM_001127208	TET2	c.3626T>C	p.L1209P	89.90
MDS-37-160	NM_001127208	TET2	c.2230C>T	p.Q744X	40.80
MDS-37-170	NM_017628	TET2	c.3451G>T	p.E1151X	50.00
MDS-37-175	NM_001127208	TET2	c.500C>G	p.S167X	36.00
MDS-37-177	NM_001127208	TET2	c.4138C>T	p.H1380Y	1.30
MDS-37-177	NM_001127208	TET2	c.5178delT	p.H1727Mfs*18	41.50
MDS-37-177	NM_001127208	TET2	c.2338A>T	p.K780X	40.70
MDS-37-184	NM_001127208	TET2	c.1630C>T	p.R544X	27.10
MDS-37-184	NM_001127208	TET2	c.1924C>T	p.Q642X	1.60
MDS-37-184	NM_001127208	TET2	c.2440C>T	p.R814C	49.50
MDS-37-192	NM_001127208	TET2	c.5618T>C	p.I1873T	42.40
MDS-37-196	NM_001127208	TET2	c.1411dupA	p.S471Kfs*8	38.70
MDS-37-198	NM_001127208	TET2	c.1207C>T	p.Q403X	47.10
MDS-37-226	NM_001127208	TET2	c.5709_5711delGCA	p.Q1903delQ	24.20

MDS-37-227	NM_001127208	TET2	c.1776T>G	p.Y592X	49.00
MDS-37-234	NM_001127208	TET2	c.4303C>T	p.Q1435X	46.80
MDS-37-234	NM_001127208	TET2	c.4139A>G	p.H1380R	48.50
MDS-37-241	NM_017628	TET2	c.3451G>T	p.E1151X	50.90
MDS-37-244	NM_001127208	TET2	c.1630C>T	p.R544X	42.60
MDS-37-244	NM_001127208	TET2	c.2689C>T	p.Q897X	3.80
MDS-37-246	NM_001127208	TET2	c.986_987delTT	p.F329X	44.20
MDS-37-246	NM_001127208	TET2	c.3430dupG	p.E1144Gfs*13	45.30
MDS-37-247	NM_001127208	TET2	c.2440C>T	p.R814C	51.80
MDS-37-248	NM_001127208	TET2	c.4627_4644del18l	p.R1543_Q1548delRPQQQQ	50.00
MDS-37-251	NM_001127208	TET2	c.4471A>T	p.K1491X	45.70
MDS-37-251	NM_001127208	TET2	c.419delA	p.N140Mfs*5	45.30
MDS-37-253	NM_001127208	TET2	c.521delC	p.P174Lfs*9	9.50
MDS-37-258	NM_001127208	TET2	c.4546C>T	p.R1516X	51.00
MDS-37-261	NM_001127208	TET2	c.3812dupG	p.C1271Wfs*29	23.00
MDS-37-261	NM_001127208	TET2	c.3425_3426insTTCA	p.K1142Nfs*4	31.80
MDS-37-273	NM_001127208	TET2	c.5162T>G	p.L1721W	50.53
MDS-37-278	NM_001127208	TET2	c.5162T>G	p.L1721W	49.55
MDS-37-285	NM_001127208	TET2	c.5162T>G	p.L1721W	50.09
MDS-37-295	NM_001127208	TET2	c.5162T>G	p.L1721W	48.26
MDS-37-296	NM_001127208	TET2	c.3664G>T	p.E1222X	5.49
MDS-37-296	NM_001127208	TET2	c.5083delG	p.G1695fs	48.03
MDS-37-305	NM_001127208	TET2	c.3343delC	p.P1115fs	1.03
MDS-37-323	NM_001127208	TET2	c.4347delT	p.S1449fs	22.43
MDS-37-334	NM_001127208	TET2	c.5617A>C	p.I1873L	6.79
MDS-37-347	NM_001127208	TET2	c.1900delT	p.Y634fs	1.14
MDS-37-347	NM_001127208	TET2	c.2878C>T	p.Q960X	1.21
MDS-37-347	NM_001127208	TET2	c.3076G>T	p.E1026X	40.54
MDS-37-347	NM_001127208	TET2	c.5681C>T	p.P1894L	4.21
MDS-37-348	NM_001127208	TET2	c.2440C>T	p.R814C	50.54
MDS-37-351	NM_001127208	TET2	c.5162T>G	p.L1721W	47.27
MDS-37-353	NM_001127208	TET2	c.5162T>G	p.L1721W	48.19
MDS-37-364	NM_001127208	TET2	c.3230_3231insCGGG	p.H1077fs	1.00
MDS-37-380	NM_001127208	TET2	c.5597_5601del	p.P1866fs	1.43
MDS-37-381	NM_001127208	TET2	c.5602_5605del	p.H1868fs	1.00
MDS-37-381	NM_001127208	TET2	c.5473C>G	p.Q1825E	48.90
MDS-15-005	NM_015338	ASXL1	c.1774C>T	p.Q592X	27.01
MDS-15-006	NM_015338	ASXL1	c.2074C>T	p.Q693X	16.18
MDS-15-013	NM_015338	ASXL1	c.2160delC	p.L721CfsX4	31.58
MDS-15-029	NM_015338	ASXL1	c.2077C>T	p.R693X	33.67
MDS-15-052	NM_015338	ASXL1	c.1926-1927insG	p.G646WfsTer12	15.89
MDS-15-064	NM_015338	ASXL1	c.2128delG	p.G710EfsTer15	39.30
MDS-37-083	NM_015338	ASXL1	c.2077C>T	p.R693X	36.00
MDS-37-107	NM_015338	ASXL1	c.2077C>T	p.R693X	49.49
MDS-37-108	NM_015338	ASXL1	c.1249C>T	p.R417X	21.00
MDS-37-115	NM_015338	ASXL1	c.1900_1922del23	p.E635Rfs	25.30
MDS-37-141	NM_015338	ASXL1	c.1900_1922del23	p.E635Rfs*15	69.50
MDS-37-155	NM_015338	ASXL1	c.2128dupG	p.T711Nfs*77	42.90
MDS-37-156	NM_015338	ASXL1	c.1210C>T	p.R404X	5.00
MDS-37-172	NM_015338	ASXL1	c.3195G>A	p.W1065X	38.60
MDS-37-179	NM_015338	ASXL1	c.1900_1922del23	p.E635Rfs*15	11.20
MDS-37-195	NM_015338	ASXL1	c.2464dupA	p.T822Nfs*11	40.00
MDS-37-216	NM_015338	ASXL1	c.1926_1930delAGGGG	p.G644Wfs*12	14.50
MDS-37-231	NM_015338	ASXL1	c.2893C>T	p.R965X	43.30
MDS-37-234	NM_015338	ASXL1	c.1900_1922del23	p.E635Rfs*15	18.10
MDS-37-246	NM_015338	ASXL1	c.1772dupA	p.Y591X	46.60

MDS-37-255	NM_015338	ASXL1	c.2036dupG	p.G680Rfs*38	27.60
MDS-37-261	NM_015338	ASXL1	c.1903G>T	p.E635X	41.30
MDS-37-265	NM_015338	ASXL1	c.1898dupA	p.H633Qfs*2	14.10
MDS-37-267	NM_015338	ASXL1	c.1900_1922del23	p.E635Rfs*15	55.60
MDS-37-273	NM_015338	ASXL1	c.1888_1910del	p.H630fs	25.97
MDS-37-286	NM_015338	ASXL1	c.1876dupG	p.R625fs	44.35
MDS-37-289	NM_015338	ASXL1	c.1888_1910del	p.H630fs	35.92
MDS-37-291	NM_015338	ASXL1	c.1975_1976del	p.G659fs	44.08
MDS-37-296	NM_015338	ASXL1	c.2077C>T	p.R693X	26.82
MDS-37-301	NM_015338	ASXL1	c.2242C>T	p.Q748X	40.68
MDS-37-306	NM_015338	ASXL1	c.2157delG	p.E719fs	16.62
MDS-37-312	NM_015338	ASXL1	c.1888_1910del	p.H630fs	9.45
MDS-37-316	NM_015338	ASXL1	c.2791G>T	p.E931X	51.17
MDS-37-317	NM_015338	ASXL1	c.2839_2893del	p.E947fs	33.42
MDS-37-318	NM_015338	ASXL1	c.2110delG	p.G704fs	1.23
MDS-37-322	NM_015338	ASXL1	c.1772dupA	p.Y591_Q592delinsX	43.25
MDS-37-326	NM_015338	ASXL1	c.1210C>T	p.R404X	31.84
MDS-37-328	NM_015338	ASXL1	c.3150_3163del	p.M1050fs	26.93
MDS-37-332	NM_015338	ASXL1	c.1927dupG	p.G642fs	23.93
MDS-37-339	NM_015338	ASXL1	c.4281delT	p.P1427fs	1.92
MDS-37-341	NM_015338	ASXL1	c.1888_1910del	p.H630fs	33.63
MDS-37-351	NM_015338	ASXL1	c.1888_1910del	p.H630fs	44.21
MDS-37-353	NM_015338	ASXL1	c.2324T>G	p.L775X	40.61
MDS-37-380	NM_015338	ASXL1	c.2023_2039del	p.P675fs	1.74
MDS-37-381	NM_015338	ASXL1	c.2879G>A	p.W960X	1.03
MDS-37-382	NM_015338	ASXL1	c.1815C>A	p.C605X	1.00
MDS-15-024	NM_006758	U2AF1	c.101C>A	p.S34Y	25.00
MDS-15-033	NM_006758	U2AF1	c.101C>A	p.S34Y	39.90
MDS-15-047	NM_006758	U2AF1	c.101C>T	p.S34F	50.00
MDS-15-055	NM_006758	U2AF1	c.101C>T	p.S34F	50.00
MDS-15-064	NM_006758	U2AF1	c.101C>A	p.S34Y	47.10
MDS-37-082	NM_001025203	U2AF1	c.101C>T	p.S34F	35.09
MDS-37-083	NM_001025203	U2AF1	c.470A>C	p.Q157P	44.71
MDS-37-093	NM_001025203	U2AF1	c.101C>A	p.S34Y	25.61
MDS-37-096	NM_001025203	U2AF1	c.470A>C	p.Q157P	24.02
MDS-37-101	NM_001025203	U2AF1	c.101C>T	p.S34F	38.99
MDS-37-101	NM_001025203	U2AF1	c.470A>G	p.Q157R	32.63
MDS-37-104	NM_001025203	U2AF1	c.101C>T	p.S34F	48.47
MDS-37-105	NM_001025203	U2AF1	c.101C>A	p.S34Y	45.73
MDS-37-107	NM_001025203	U2AF1	c.101C>T	p.S34F	45.78
MDS-37-118	NM_001025203	U2AF1	c.101C>A	p.S34Y	42.40
MDS-37-124	NM_001025203	U2AF1	c.101C>T	p.S34F	25.60
MDS-37-125	NM_001025203	U2AF1	c.101C>T	p.S34F	41.40
MDS-37-137	NM_001025203	U2AF1	c.101C>T	p.S34F	35.30
MDS-37-142	NM_001025203	U2AF1	c.101C>T	p.S34F	38.70
MDS-37-161	NM_001025203	U2AF1	c.470A>C	p.Q157P	39.90
MDS-37-168	NM_001025203	U2AF1	c.101C>T	p.S34F	24.90
MDS-37-177	NM_001025203	U2AF1	c.101C>A	p.S34Y	34.20
MDS-37-195	NM_001025203	U2AF1	c.101C>A	p.S34Y	46.00
MDS-37-196	NM_001025203	U2AF1	c.101C>A	p.S34Y	41.10
MDS-37-198	NM_001025203	U2AF1	c.101C>T	p.S34F	50.00
MDS-37-216	NM_001025203	U2AF1	c.101C>T	p.S34F	42.50
MDS-37-225	NM_001025203	U2AF1	c.101C>T	p.S34F	38.80
MDS-37-240	NM_001025203	U2AF1	c.101C>T	p.S34F	30.70
MDS-37-250	NM_001025203	U2AF1	c.101C>T	p.S34F	34.90
MDS-37-258	NM_001025203	U2AF1	c.101C>T	p.S34F	45.90
MDS-37-260	NM_001025203	U2AF1	c.101C>T	p.S34F	38.60

MDS-37-261	NM_001025203	U2AF1	c.101C>T	p.S34F	33.80
MDS-37-265	NM_001025203	U2AF1	c.101C>T	p.S34F	31.80
MDS-37-269	NM_001025203	U2AF1	c.101C>T	p.S34F	27.40
MDS-37-282	NM_006758	U2AF1	c.101C>T	p.S34F	33.99
MDS-37-283	NM_006758	U2AF1	c.101C>T	p.S34F	37.09
MDS-37-286	NM_006758	U2AF1	c.101C>A	p.S34Y	43.74
MDS-37-291	NM_006758	U2AF1	c.101C>T	p.S34F	42.81
MDS-37-296	NM_006758	U2AF1	c.101C>A	p.S34Y	25.98
MDS-37-313	NM_006758	U2AF1	c.101C>A	p.S34Y	37.26
MDS-37-332	NM_006758	U2AF1	c.101C>T	p.S34F	36.15
MDS-37-351	NM_006758	U2AF1	c.101C>T	p.S34F	45.40
MDS-37-361	NM_006758	U2AF1	c.101C>T	p.S34F	43.11
MDS-37-369	NM_006758	U2AF1	c.101C>T	p.S34F	31.43
MDS-37-374	NM_006758	U2AF1	c.101C>A	p.S34Y	57.89
MDS-37-376	NM_006758	U2AF1	c.101C>A	p.S34Y	40.00
MDS-15-004	NM_012433	SF3B1	c.1866G>C	p.E622D	40.88
MDS-15-007	NM_012433	SF3B1	c.2098A>G	p.K700E	41.40
MDS-15-009	NM_012433	SF3B1	c.2098A>G	p.K700E	35.40
MDS-15-010	NM_012433	SF3B1	c.2098A>G	p.K700E	43.83
MDS-15-022	NM_012433	SF3B1	c.2098A>G	p.K700E	40.31
MDS-15-026	NM_012433	SF3B1	c.2098A>G	p.K700E	35.20
MDS-15-036	NM_012433	SF3B1	c.1873C>T	p.R625C	36.10
MDS-15-046	NM_012433	SF3B1	c.2098A>G	p.K700E	45.20
MDS-15-065	NM_012433	SF3B1	c.2098A>G	p.K700E	46.80
MDS-15-070	NM_012433	SF3B1	c.1873C>T	p.R625C	43.00
MDS-37-081	NM_012433	SF3B1	c.1998G>C	p.K666N	40.00
MDS-37-085	NM_012433	SF3B1	c.2098A>C	p.K700E	42.68
MDS-37-088	NM_012433	SF3B1	c.2098A>G	p.K700E	45.21
MDS-37-095	NM_012433	SF3B1	c.2098A>G	p.K700E	36.92
MDS-37-103	NM_012433	SF3B1	c.2098A>G	p.K700E	39.22
MDS-37-112	NM_012433	SF3B1	c.2098A>G	p.K700E	40.68
MDS-37-117	NM_012433	SF3B1	c.1873C>T	p.R625C	13.03
MDS-37-127	NM_012433	SF3B1	c.1874G>A	p.R625H	18.20
MDS-37-129	NM_012433	SF3B1	c.2098A>G	p.K700E	48.10
MDS-37-148	NM_012433	SF3B1	c.2098A>G	p.K700E	4.60
MDS-37-148	NM_012433	SF3B1	c.1874G>T	p.R625L	42.10
MDS-37-156	NM_012433	SF3B1	c.2098A>G	p.K700E	6.90
MDS-37-163	NM_012433	SF3B1	c.2098A>G	p.K700E	41.90
MDS-37-167	NM_012433	SF3B1	c.2098A>G	p.K700E	43.90
MDS-37-177	NM_012433	SF3B1	c.2098A>G	p.K700E	41.80
MDS-37-178	NM_012433	SF3B1	c.2098A>G	p.K700E	35.30
MDS-37-184	NM_012433	SF3B1	c.1997A>C	p.K666T	2.90
MDS-37-187	NM_012433	SF3B1	c.2098A>G	p.K700E	2.80
MDS-37-190	NM_012433	SF3B1	c.2098A>G	p.K700E	48.00
MDS-37-192	NM_012433	SF3B1	c.2098A>G	p.K700E	45.70
MDS-37-221	NM_012433	SF3B1	c.2098A>G	p.K700E	17.70
MDS-37-223	NM_012433	SF3B1	c.2098A>G	p.K700E	42.60
MDS-37-231	NM_012433	SF3B1	c.1866G>C	p.E622D	47.50
MDS-37-232	NM_012433	SF3B1	c.2098A>G	p.K700E	38.10
MDS-37-237	NM_012433	SF3B1	c.2098A>G	p.K700E	24.70
MDS-37-239	NM_012433	SF3B1	c.2098A>G	p.K700E	25.20
MDS-37-253	NM_012433	SF3B1	c.2098A>G	p.K700E	33.40
MDS-37-290	NM_012433	SF3B1	c.2225G>A	p.G742D	1.24
MDS-37-290	NM_012433	SF3B1	c.2098A>G	p.K700E	4.85
MDS-37-305	NM_012433	SF3B1	c.2098A>G	p.K700E	42.15
MDS-37-307	NM_012433	SF3B1	c.2098A>G	p.K700E	37.58
MDS-37-310	NM_012433	SF3B1	c.2098A>G	p.K700E	42.18

MDS-37-318	NM_012433	SF3B1	c.2098A>G	p.K700E	43.33
MDS-37-358	NM_012433	SF3B1	c.2098A>G	p.K700E	49.22
MDS-37-381	NM_012433	SF3B1	c.2098A>G	p.K700E	15.35
MDS-15-006	NM_001754	RUNX1	c.320G>A	p.R107H	11.47
MDS-15-013	NM_001754	RUNX1	c.327_329delCAA	p.N109del	34.13
MDS-15-031	NM_001754	RUNX1	c.1208-1209delAC	p.Y403SfsTer196	27.10
MDS-15-065	NM_001754	RUNX1	c.706_707dupAT	p.M236IfsTer2	42.90
MDS-15-079	NM_001754	RUNX1	c.485G>A	p.R162K	45.25
MDS-15-080	NM_001754	RUNX1	c.1396A>T	p.M466L	51.50
MDS-37-082	NM_001001890	RUNX1	c.124G>C	p.G42R	42.55
MDS-37-115	NM_001001890	RUNX1	c.529C>T	p.R177X	46.04
MDS-37-157	NM_001001890	RUNX1	c.511G>A	p.D171N	18.30
MDS-37-157	NM_001001890	RUNX1	c.1059C>A	p.Y353X	37.10
MDS-37-179	NM_001001890	RUNX1	c.884C>G	p.S295X	3.80
MDS-37-179	NM_001001890	RUNX1	c.427+2T>C	--	5.70
MDS-37-179	NM_001001890	RUNX1	c.547_548insAA	p.L183Qfs*2	5.80
MDS-37-179	NM_001001890	RUNX1	c.520C>G	p.R174G	6.00
MDS-37-184	NM_001001890	RUNX1	c.172C>A	p.H58N	5.70
MDS-37-184	NM_001001890	RUNX1	c.595_596delAG	p.S199*fs*1	33.50
MDS-37-195	NM_001001890	RUNX1	c.415C>T	p.R139X	44.20
MDS-37-203	NM_001001890	RUNX1	c.422C>A	p.S141X	22.80
MDS-37-219	NM_001001890	RUNX1	c.1193C>T	p.P398L	3.70
MDS-37-226	NM_001001890	RUNX1	c.496C>G	p.R166G	40.20
MDS-37-244	NM_001001890	RUNX1	c.1274C>T	p.P425L	25.60
MDS-37-244	NM_001001890	RUNX1	c.724G>T	p.E242X	3.30
MDS-37-246	NM_001001890	RUNX1	c.856_859dupCAAT	p.Y287Sfs*269	44.20
MDS-37-281	NM_001754	RUNX1	c.883_884insTT	p.S295fs	40.06
MDS-37-282	NM_001754	RUNX1	c.884dupC	p.S295fs	32.37
MDS-37-283	NM_001754	RUNX1	c.493G>T	p.G165C	38.94
MDS-37-291	NM_001754	RUNX1	c.602G>A	p.R201Q	2.13
MDS-37-297	NM_001754	RUNX1	c.593A>G	p.D198G	1.21
MDS-37-301	NM_001754	RUNX1	c.103dupA	p.S35fs	45.37
MDS-37-302	NM_001754	RUNX1	c.494G>T	p.G165V	11.83
MDS-37-303	NM_001754	RUNX1	c.592G>A	p.D198N	6.39
MDS-37-303	NM_001754	RUNX1	c.808dupA	p.T270fs	8.74
MDS-37-315	NM_001754	RUNX1	c.292delC	p.L98fs	41.82
MDS-37-317	NM_001754	RUNX1	c.294_300del	p.L98fs	40.20
MDS-37-317	NM_001754	RUNX1	c.160G>T	p.E54X	1.22
MDS-37-323	NM_001754	RUNX1	c.469A>T	p.R157X	1.22
MDS-37-323	NM_001754	RUNX1	c.1178dupG	p.G393fs	7.46
MDS-37-339	NM_001754	RUNX1	c.938dupT	p.L313fs	2.99
MDS-37-339	NM_001754	RUNX1	c.965C>G	p.S322X	6.30
MDS-37-341	NM_001754	RUNX1	c.958C>T	p.R320X	5.44
MDS-37-344	NM_001754	RUNX1	c.346_347del	p.F116fs	2.89
MDS-37-353	NM_001754	RUNX1	c.496C>G	p.R166G	8.39
MDS-37-361	NM_001754	RUNX1	c.290_309del	p.F97fs	2.53
MDS-37-361	NM_001754	RUNX1	c.1264G>T	p.E422X	7.48
MDS-37-361	NM_001754	RUNX1	c.497G>A	p.R166Q	2.56
MDS-37-374	NM_001754	RUNX1	c.610C>T	p.R204X	27.82
MDS-15-037	NM_000546	TP53	c.427G>A	p.V143M	18.70
MDS-15-037	NM_000546	TP53	c.467G>C	p.R156P	21.40
MDS-15-043	NM_000546	TP53	c.91G>A	p.V31I	11.80
MDS-15-050	NM_000546	TP53	c.524G>A	p.R175H	73.50
MDS-15-071	NM_000546	TP53	c.451C>G	p.P151A	62.40
MDS-15-072	NM_000546	TP53	c.715_718dupAACA	p.S240KfsTer25	56.10
MDS-37-090	NM_000546	TP53	c.733G>A	p.G245S	75.34
MDS-37-092	NM_000546	TP53	c.524G>A	p.R175H	81.75

MDS-37-102	NM_000546	TP53	c.733G>A	p.G245S	92.54
MDS-37-106	NM_000546	TP53	c.817C>T	p.R273C	89.79
MDS-37-136	NM_000546	TP53	c.659A>G	p.Y220C	30.30
MDS-37-148	NM_000546	TP53	c.527G>T	p.C176F	22.90
MDS-37-165	NM_000546	TP53	c.629delA	p.N210Tfs*37	88.70
MDS-37-169	NM_000546	TP53	c.374C>T	p.T125M	22.50
MDS-37-169	NM_000546	TP53	c.838A>G	p.R280G	33.60
MDS-37-175	NM_000546	TP53	c.524G>A	p.R175H	54.10
MDS-37-199	NM_000546	TP53	c.438G>A	p.W146X	40.40
MDS-37-209	NM_000546	TP53	c.652delG	p.V218Cfs*29	6.30
MDS-37-224	NM_000546	TP53	c.475G>C	p.A159P	88.40
MDS-37-238	NM_000546	TP53	c.919+1G>A	--	31.70
MDS-37-238	NM_000546	TP53	c.781_782+4del6	--	32.80
MDS-37-245	NM_000546	TP53	c.376-1G>A	--	81.70
MDS-37-264	NM_000546	TP53	c.722C>T	p.S241F	2.80
MDS-37-264	NM_000546	TP53	c.853G>T	p.E285X	28.30
MDS-37-264	NM_000546	TP53	c.848G>C	p.R283P	32.30
MDS-37-272	NM_000546	TP53	c.413C>T	p.A138V	77.95
MDS-37-276	NM_000546	TP53	c.329G>T	p.R110L	38.81
MDS-37-276	NM_000546	TP53	c.844C>T	p.R282W	36.89
MDS-37-287	NM_000546	TP53	c.524G>A	p.R175H	29.62
MDS-37-288	NM_000546	TP53	c.659A>G	p.Y220C	34.34
MDS-37-288	NM_000546	TP53	c.524G>A	p.R175H	38.25
MDS-37-292	NM_000546	TP53	c.818G>A	p.R273H	9.84
MDS-37-320	NM_000546	TP53	c.799_809delinsA	p.R267fs	85.64
MDS-37-321	NM_000546	TP53	c.376-2A>G	--	40.45
MDS-37-326	NM_000546	TP53	c.215_224del	p.P72fs	41.14
MDS-37-330	NM_000546	TP53	c.527G>T	p.C176F	2.44
MDS-37-331	NM_000546	TP53	c.613T>G	p.Y205D	76.74
MDS-37-335	NM_000546	TP53	c.749C>T	p.P250L	32.31
MDS-37-336	NM_000546	TP53	c.749C>T	p.P250L	34.96
MDS-37-336	NM_000546	TP53	c.1123C>A	p.Q375K	37.73
MDS-37-375	NM_000546	TP53	c.818G>A	p.R273H	70.15
MDS-37-082	NM_015559	SETBP1	c.2602G>T	p.D868Y	9.89
MDS-37-083	NM_015559	SETBP1	c.2608G>A	p.G870S	5.47
MDS-37-083	NM_015559	SETBP1	c.2612T>C	p.I871T	30.41
MDS-37-099	NM_015559	SETBP1	c.2608G>A	p.G870S	1.95
MDS-37-101	NM_015559	SETBP1	c.2602G>A	p.D868N	29.07
MDS-37-107	NM_015559	SETBP1	c.2608G>A	p.G870S	47.59
MDS-37-109	NM_015559	SETBP1	c.1379A>G	p.K460R	46.30
MDS-37-111	NM_015559	SETBP1	c.1879C>T	p.R627C	49.72
MDS-37-115	NM_015559	SETBP1	c.1379A>G	p.K460R	50.33
MDS-37-129	NM_015559	SETBP1	c.1828G>A	p.V610I	46.20
MDS-37-157	NM_015559	SETBP1	c.2608G>A	p.G870S	1.50
MDS-37-161	NM_015559	SETBP1	c.2608G>A	p.G870S	25.60
MDS-37-172	NM_015559	SETBP1	c.2612T>C	p.I871T	34.40
MDS-37-205	NM_015559	SETBP1	c.1879C>T	p.R627C	49.10
MDS-37-219	NM_015559	SETBP1	c.2608G>A	p.G870S	29.00
MDS-37-232	NM_015559	SETBP1	c.2602G>A	p.D868N	30.40
MDS-37-265	NM_015559	SETBP1	c.4010G>C	p.S1337T	52.10
MDS-37-289	NM_015559	SETBP1	c.2602G>A	p.D868N	42.01
MDS-37-297	NM_015559	SETBP1	c.2602G>A	p.D868N	93.85
MDS-37-301	NM_015559	SETBP1	c.2608G>A	p.G870S	43.21
MDS-37-311	NM_015559	SETBP1	c.2612T>C	p.I871T	38.31
MDS-37-318	NM_015559	SETBP1	c.2602G>A	p.D868N	3.79
MDS-37-318	NM_015559	SETBP1	c.2612T>C	p.I871T	4.59
MDS-37-352	NM_015559	SETBP1	c.2602G>A	p.D868N	38.07

MDS-37-352	NM_015559	SETBP1	c.2608G>A	p.G870S	1.33
MDS-37-374	NM_015559	SETBP1	c.2608G>A	p.G870S	39.95
MDS-37-109	NM_017745	BCOR	c.4159C>T	p.R1387C	54.20
MDS-37-125	NM_017745	BCOR	c.1448C>T	p.P483L	52.20
MDS-37-146	NM_017745	BCOR	c.4697_4699delTCT	p.F1566delF	8.60
MDS-37-165	NM_017745	BCOR	c.1448C>T	p.P483L	98.90
MDS-37-176	NM_017745	BCOR	c.4639+1G>A	–	27.00
MDS-37-190	NM_017745	BCOR	c.4164dupG	p.Q1389Afs*38	17.30
MDS-37-213	NM_017745	BCOR	c.4326+1G>A	–	25.50
MDS-37-223	NM_017745	BCOR	c.1448C>T	p.P483L	100.00
MDS-37-226	NM_017745	BCOR	c.2428C>T	p.R810X	80.60
MDS-37-228	NM_017745	BCOR	c.702T>G	p.Y234X	12.40
MDS-37-282	NM_001123383	BCOR	c.1136_1139del	p.V379fs	66.12
MDS-37-283	NM_001123383	BCOR	c.4416_4438del	p.A1472fs	73.10
MDS-37-311	NM_001123383	BCOR	c.4730_4737del	p.E1577fs	73.35
MDS-37-313	NM_001123383	BCOR	c.4326+1G>A	–	86.20
MDS-37-317	NM_001123383	BCOR	c.4717+1G>A	–	1.62
MDS-37-323	NM_001123383	BCOR	c.2769dupA	p.F924fs	13.13
MDS-37-323	NM_001123383	BCOR	c.1375A>T	p.K459X	5.76
MDS-37-339	NM_001123383	BCOR	c.2054dupT	p.L685fs	11.94
MDS-37-339	NM_001123383	BCOR	c.2428C>T	p.R810X	1.94
MDS-37-349	NM_001123383	BCOR	c.2565delG	p.L855fs	3.02
MDS-37-360	NM_001123383	BCOR	c.349G>T	p.E117X	2.77
MDS-37-360	NM_001123383	BCOR	c.2997+2T>G	–	2.95
MDS-37-365	NM_001123383	BCOR	c.524_527del	p.K175fs	11.10
MDS-37-377	NM_001123383	BCOR	c.4834dupC	p.L1612fs	6.70
MDS-37-380	NM_001123383	BCOR	c.836delT	p.L279fs	13.42
MDS-37-107	NM_003482	KMT2D	c.6643T>A	p.S2215T	45.50
MDS-37-110	NM_003482	KMT2D	c.12329C>T	p.T4110T	50.50
MDS-37-143	NM_003482	KMT2D	c.1201G>A	p.V401M	50.50
MDS-37-150	NM_003482	KMT2D	c.13450C>T	p.R4484X	9.30
MDS-37-151	NM_003482	KMT2D	c.8774C>T	p.A2925V	52.80
MDS-37-160	NM_003482	KMT2D	c.7046C>T	p.P2349L	45.90
MDS-37-178	NM_003482	KMT2D	c.1954C>T	p.R652C	54.40
MDS-37-181	NM_003482	KMT2D	c.7490C>T	p.A2497V	45.20
MDS-37-187	NM_003482	KMT2D	c.11729_11734del6	p.Q3910_Q3911delQQ	48.40
MDS-37-191	NM_003482	KMT2D	c.3392C>T	p.P1131L	52.80
MDS-37-207	NM_003482	KMT2D	c.2088_2114del27	p.T698_P706del9	69.30
MDS-37-209	NM_003482	KMT2D	c.7888delC	p.H2630Mfs*61	6.60
MDS-37-209	NM_003482	KMT2D	c.12220delC	p.Q4074Nfs*22	14.40
MDS-37-233	NM_003482	KMT2D	c.6682A>G	p.T2228A	52.10
MDS-37-235	NM_003482	KMT2D	c.15671G>A	p.R5224H	51.30
MDS-37-236	NM_003482	KMT2D	c.15671G>A	p.R5224H	48.80
MDS-37-242	NM_003482	KMT2D	c.5372C>T	p.A1791V	45.80
MDS-37-249	NM_003482	KMT2D	c.3775C>T	p.L1259F	49.60
MDS-37-255	NM_003482	KMT2D	c.4007T>C	p.I1336T	50.00
MDS-37-262	NM_003482	KMT2D	c.11342G>A	p.S3781N	55.00
MDS-37-264	NM_003482	KMT2D	c.11124C>G	p.S3708R	47.30
MDS-37-362	NM_003482	KMT2D	c.8585_8586insGTCTGCC	p.P2862fs	45.01
MDS-37-375	NM_003482	KMT2D	c.14941A>T	p.K4981X	34.74
MDS-15-039	NM_022552	DNMT3A	c.2645G>A	p.R882H	41.77
MDS-15-066	NM_022552	DNMT3A	c.2645G>A	p.R882H	44.90
MDS-37-083	NM_022552	DNMT3A	c.2141C>G	p.S714C	41.51
MDS-37-088	NM_022552	DNMT3A	c.2644C>T	p.R882C	47.56
MDS-37-089	NM_022552	DNMT3A	c.1643T>C	p.M548T	42.02
MDS-37-113	NM_022552	DNMT3A	c.2723A>G	p.Y908C	4.03
MDS-37-120	NM_022552	DNMT3A	c.2644C>T	p.R882C	33.26

MDS-37-143	NM_022552	DNMT3A	c.2031-1G>A	–	35.30
MDS-37-162	NM_022552	DNMT3A	c.2644C>T	p.R882C	26.40
MDS-37-166	NM_022552	DNMT3A	c.2645G>A	p.R882H	43.10
MDS-37-190	NM_022552	DNMT3A	c.1667+1G>A	–	47.00
MDS-37-198	NM_022552	DNMT3A	c.2645G>A	p.R882H	49.60
MDS-37-215	NM_022552	DNMT3A	c.2645G>A	p.R882H	10.40
MDS-37-216	NM_022552	DNMT3A	c.2204A>G	p.Y735C	47.60
MDS-37-230	NM_022552	DNMT3A	c.2644C>T	p.R882C	7.00
MDS-37-236	NM_022552	DNMT3A	c.2074_2081dup	p.I695Rfs*13	27.40
MDS-37-258	NM_022552	DNMT3A	c.2635A>G	p.N879D	47.30
MDS-37-285	NM_022552	DNMT3A	c.1084C>T	p.Q362X	3.51
MDS-37-298	NM_022552	DNMT3A	c.2645G>A	p.R882H	40.04
MDS-37-307	NM_022552	DNMT3A	c.1904G>A	p.R635Q	39.58
MDS-37-310	NM_022552	DNMT3A	c.1285A>T	p.K429X	42.17
MDS-37-311	NM_022552	DNMT3A	c.2644C>T	p.R882C	35.82
MDS-37-312	NM_022552	DNMT3A	c.958C>T	p.R320X	10.66
MDS-37-327	NM_022552	DNMT3A	c.1627G>T	p.G543C	44.12
MDS-37-339	NM_022552	DNMT3A	c.1005delA	p.K335fs	1.00
MDS-37-368	NM_022552	DNMT3A	c.1985C>G	p.A662G	1.00
MDS-37-381	NM_022552	DNMT3A	c.2074C>T	p.Q692X	1.89
MDS-37-381	NM_022552	DNMT3A	c.2206C>T	p.R736C	2.20
MDS-37-121	NM_004380	CREBBP	c.760G>A	p.A254T	47.05
MDS-37-139	NM_004380	CREBBP	c.6332A>G	p.N2111S	44.80
MDS-37-152	NM_004380	CREBBP	c.7222A>G	p.M2408V	50.50
MDS-37-160	NM_004380	CREBBP	c.1651C>A	p.L551I	49.70
MDS-37-161	NM_004380	CREBBP	c.1651C>A	p.L551I	46.80
MDS-37-171	NM_004380	CREBBP	c.760G>A	p.A254T	56.80
MDS-37-173	NM_004380	CREBBP	c.5333C>A	p.S1778X	43.60
MDS-37-179	NM_004380	CREBBP	c.5533_5534delAA	p.N1845Hfs*120	5.40
MDS-37-186	NM_004380	CREBBP	c.1651C>A	p.L551I	47.80
MDS-37-188	NM_004380	CREBBP	c.1651C>A	p.L551I	48.50
MDS-37-201	NM_004380	CREBBP	c.4240G>A	p.V1414I	47.30
MDS-37-204	NM_004380	CREBBP	c.1651C>A	p.L551I	49.40
MDS-37-231	NM_004380	CREBBP	c.1651C>A	p.L551I	45.90
MDS-37-247	NM_004380	CREBBP	c.4835A>G	p.N1612S	49.40
MDS-37-252	NM_004380	CREBBP	c.760G>A	p.A254T	48.00
MDS-37-264	NM_004380	CREBBP	c.760G>A	p.A254T	46.10
MDS-37-286	NM_004380	CREBBP	c.5566C>T	p.Q1856X	46.06
MDS-37-361	NM_004380	CREBBP	c.5541delA	p.K1847fs	47.10
MDS-37-141	NM_001429	EP300	c.2240C>T	p.P747L	51.80
MDS-37-152	NM_001429	EP300	c.4817C>T	p.A1606V	45.30
MDS-37-153	NM_001429	EP300	c.5150A>G	p.N1717S	51.20
MDS-37-159	NM_001429	EP300	c.1519A>G	p.S507G	51.60
MDS-37-166	NM_001429	EP300	c.2539C>T	p.P847S	44.00
MDS-37-193	NM_001429	EP300	c.3377A>G	p.N1126S	47.80
MDS-37-211	NM_001429	EP300	c.4817C>T	p.A1606V	53.00
MDS-37-236	NM_001429	EP300	c.1519A>G	p.S507G	50.70
MDS-37-246	NM_001429	EP300	c.1519A>G	p.S507G	51.10
MDS-37-250	NM_001429	EP300	c.1913A>G	p.Y638C	6.20
MDS-37-250	NM_001429	EP300	c.1913A>G	p.S507G	51.40
MDS-37-251	NM_001429	EP300	c.2642delC	p.P881Lfs*65	50.60
MDS-37-252	NM_001429	EP300	c.1519A>G	p.S507G	49.50
MDS-37-261	NM_001429	EP300	c.1913A>G	p.Y638C	63.40
MDS-37-263	NM_001429	EP300	c.5957C>T	p.P1986L	49.20
MDS-37-306	NM_001429	EP300	c.1413_1414insA	p.L471fs	18.28
MDS-37-359	NM_001429	EP300	c.931C>T	p.Q311X	1.00
MDS-37-359	NM_001429	EP300	c.1058dupG	p.R353fs	1.13

MDS-37-359	NM_001429	EP300	c.1567C>T	p.Q523X	21.02
MDS-15-001	NM_004456	EZH2	c.1258C>T	p.Q420X	31.96
MDS-15-013	NM_004456	EZH2	c.2035G>A	p.V678M	16.69
MDS-15-040	NM_004456	EZH2	c.1957C>G	p.Q653E	93.83
MDS-15-077	NM_004456	EZH2	c.2069G>A	p.R690H	48.40
MDS-37-100	NM_001203247	EZH2	c.763G>A	p.A255T	15.13
MDS-37-123	NM_001203247	EZH2	c.2069G>A	p.R690H	81.68
MDS-37-141	NM_001203247	EZH2	c.944dupT	p.D316Rfs*26	45.40
MDS-37-141	NM_001203247	EZH2	c.458A>G	p.Y153C	45.60
MDS-37-155	NM_004456	EZH2	c.1411-1G>A	–	9.30
MDS-37-155	NM_001203247	EZH2	c.66_67insGAG	p.E22dupE	8.00
MDS-37-155	NM_001203247	EZH2	c.2160dupA	p.E721Rfs*5	62.70
MDS-37-157	NM_001203247	EZH2	c.2065C>T	p.H689Y	38.30
MDS-37-179	NM_001203247	EZH2	c.1320dupT	p.R441*fs*1	5.20
MDS-37-219	NM_001203247	EZH2	c.1077delC	p.N360Ifs*59	65.50
MDS-37-227	NM_001203247	EZH2	c.2161G>T	p.E721X	47.60
MDS-37-246	NM_001203247	EZH2	c.1963G>A	p.G655R	95.70
MDS-37-255	NM_001203247	EZH2	c.1491-3C>G	–	30.20
MDS-37-255	NM_001203247	EZH2	c.2147T>A	p.I716N	3.20
MDS-37-278	NM_001203247	EZH2	c.1991A>G	p.D664G	13.72
MDS-37-295	NM_001203247	EZH2	c.2217_2220delinsGAGGT	p.I739_R741delinsMRX	19.38
MDS-37-316	NM_001203247	EZH2	c.1627dupT	p.C543fs	98.02
MDS-37-318	NM_001203247	EZH2	c.2172dupT	p.D725_Y726delinsX	5.56
MDS-37-353	NM_001203247	EZH2	c.73C>T	p.R25X	74.39
MDS-37-362	NM_001203247	EZH2	c.2172dupT	p.D725_Y726delinsX	43.97
MDS-37-144	NM_005089	ZRSR2	c.558-1G>T	–	96.90
MDS-37-161	NM_005089	ZRSR2	c.771+1G>A	–	47.70
MDS-37-171	NM_005089	ZRSR2	c.1252delC	p.H418Tfs*99	42.00
MDS-37-179	NM_005089	ZRSR2	c.312+1G>T	–	64.00
MDS-37-196	NM_005089	ZRSR2	c.1146C>A	p.N382K	50.80
MDS-37-199	NM_005089	ZRSR2	c.813delT	p.Y271*fs*1	81.30
MDS-37-246	NM_005089	ZRSR2	c.557+1G>A	–	97.00
MDS-37-273	NM_005089	ZRSR2	c.827+1G>A	–	15.08
MDS-37-293	NM_005089	ZRSR2	c.827+1G>A	–	95.01
MDS-37-323	NM_005089	ZRSR2	c.106C>T	p.R36X	38.40
MDS-37-341	NM_005089	ZRSR2	c.203+1G>A	–	18.49
MDS-37-347	NM_005089	ZRSR2	c.1082delC	p.S361fs	92.25
MDS-37-364	NM_005089	ZRSR2	c.505C>T	p.R169X	20.59
MDS-37-368	NM_005089	ZRSR2	c.252_258del	p.E84fs	4.82
MDS-15-035	NM_005896	IDH1	c.315C>T	p.G105G	49.10
MDS-37-081	NM_005896	IDH1	c.395G>A	p.R132H	1.68
MDS-37-121	NM_001282386	IDH1	c.394C>T	p.R132C	16.56
MDS-37-134	NM_005896	IDH1	c.395G>A	p.R132H	6.20
MDS-37-147	NM_005896	IDH1	c.394C>G	p.R132G	39.10
MDS-37-153	NM_005896	IDH1	c.297A>G	p.I99M	50.30
MDS-37-163	NM_005896	IDH1	c.297A>G	p.I99M	51.10
MDS-37-191	NM_005896	IDH1	c.1163G>A	p.R388H	49.40
MDS-37-203	NM_005896	IDH1	c.394C>T	p.R132C	10.60
MDS-37-215	NM_005896	IDH1	c.394C>G	p.R132G	10.20
MDS-37-228	NM_005896	IDH1	c.394C>T	p.R132C	15.90
MDS-37-270	NM_005896	IDH1	c.395G>A	p.R132H	3.10
MDS-37-280	NM_001282386	IDH1	c.394C>G	p.R132G	34.30
MDS-37-285	NM_001282386	IDH1	c.394C>T	p.R132C	22.30
MDS-37-322	NM_001282386	IDH1	c.395G>A	p.R132H	38.88
MDS-37-366	NM_001282386	IDH1	c.395G>A	p.R132H	39.89
MDS-15-035	NM_002524	NRAS	c.38G>A	G13D	48.10
MDS-15-046	NM_002524	NRAS	c.182A>G	p.Q61R	43.60

MDS-15-058	NM_002524	NRAS	c.38G>A	G13D	8.80
MDS-37-141	NM_002524	NRAS	c.35G>A	p.G12D	7.30
MDS-37-144	NM_002524	NRAS	c.181C>A	p.Q61K	45.00
MDS-37-175	NM_002524	NRAS	c.34G>A	p.G12S	12.90
MDS-37-180	NM_002524	NRAS	c.35G>A	p.G12D	28.50
MDS-37-280	NM_002524	NRAS	c.182A>C	p.Q61P	4.64
MDS-37-283	NM_002524	NRAS	c.35G>T	p.G12V	34.32
MDS-37-295	NM_002524	NRAS	c.183A>T	p.Q61H	1.33
MDS-37-298	NM_002524	NRAS	c.38G>A	p.G13D	1.38
MDS-37-320	NM_002524	NRAS	c.37G>C	p.G13R	5.15
MDS-37-327	NM_002524	NRAS	c.35G>A	p.G12D	4.85
MDS-37-327	NM_002524	NRAS	c.182A>G	p.Q61R	36.68
MDS-37-358	NM_002524	NRAS	c.182A>G	p.Q61R	44.44
MDS-37-146	NM_005188	CBL	c.125_127dupACC	p.H42dupH	47.40
MDS-37-160	NM_005188	CBL	c.2350G>A	p.V784M	49.80
MDS-37-161	NM_005188	CBL	c.1250C>G	p.P417R	12.50
MDS-37-163	NM_005188	CBL	c.1259G>A	p.R420Q	86.70
MDS-37-183	NM_005188	CBL	c.362delA	p.N121lfs*2	9.70
MDS-37-195	NM_005188	CBL	c.1259G>A	p.R420Q	2.60
MDS-37-197	NM_005188	CBL	c.2316T>G	p.D772E	50.70
MDS-37-209	NM_005188	CBL	c.1484C>T	p.P495L	48.70
MDS-37-237	NM_005188	CBL	c.2432_2434delCAA	p.T811delT	49.90
MDS-37-254	NM_005188	CBL	c.2154-2A>G	–	9.10
MDS-37-265	NM_005188	CBL	c.1111T>C	p.Y371H	20.50
MDS-37-298	NM_005188	CBL	c.1111T>C	p.Y371H	1.22
MDS-37-304	NM_005188	CBL	c.1096-2A>T	–	44.73
MDS-37-322	NM_005188	CBL	c.1253T>G	p.F418C	1.33
MDS-15-001	NM_001195427	SRSF2	c.284_307delCCCCGGACTCACACCACAGCCGCC	pP95_R103del	40.25
MDS-15-016	NM_001195427	SRSF2	c.283C>A	p.P95T	50.00
MDS-15-029	NM_001195427	SRSF2	c.284C>A	p.P95H	36.88
MDS-37-154	NM_003016	SRSF2	c.284C>A	p.P95H	48.10
MDS-37-178	NM_003016	SRSF2	c.284C>G	p.P95R	7.80
MDS-37-179	NM_003016	SRSF2	c.284C>A	p.P95H	19.90
MDS-37-226	NM_003016	SRSF2	c.284C>A	p.P95H	37.40
MDS-37-234	NM_003016	SRSF2	c.284C>A	p.P95H	43.50
MDS-37-249	NM_003016	SRSF2	c.284C>A	p.P95H	41.50
MDS-37-281	NM_003016	SRSF2	c.170T>A	p.F57Y	45.65
MDS-37-315	NM_003016	SRSF2	c.284C>A	p.P95H	42.94
MDS-37-344	NM_003016	SRSF2	c.284C>G	p.P95R	3.78
MDS-37-352	NM_003016	SRSF2	c.284C>G	p.P95R	57.16
MDS-37-122	NM_181552	CUX1	c.3128C>T	p.S1043L	50.00
MDS-37-123	NM_181552	CUX1	c.1726G>A	p.E576K	85.50
MDS-37-205	NM_181552	CUX1	c.2092G>A	p.G698S	50.00
MDS-37-214	NM_181552	CUX1	c.3161C>T	p.S1054L	53.20
MDS-37-224	NM_181552	CUX1	c.3128C>T	p.S1043L	59.50
MDS-37-264	NM_181552	CUX1	530_530+1dupGG	–	26.30
MDS-37-281	NM_181552	CUX1	c.1942C>T	p.R648X	3.24
MDS-37-295	NM_181552	CUX1	1076+1G>A	–	4.00
MDS-37-328	NM_181552	CUX1	c.541G>T	p.E181X	6.81
MDS-37-378	NM_181552	CUX1	c.4465_4466del	p.H1489fs	1.00
MDS-37-083	NM_004985	KRAS	c.G34C	p.G12R	21.71
MDS-37-156	NM_033360	KRAS	c.38G>A	p.G13D	1.10
MDS-37-176	NM_033360	KRAS	c.38G>A	p.G13D	1.40
MDS-37-212	NM_033360	KRAS	c.496T>C	p.Y166H	50.70
MDS-37-273	NM_004985	KRAS	c.173C>T	p.T58I	4.27
MDS-37-279	NM_004985	KRAS	c.38G>A	p.G13D	7.62
MDS-37-285	NM_004985	KRAS	c.437C>T	p.A146V	3.35

MDS-37-297	NM_004985	KRAS	c.35G>A	p.G12D	2.30
MDS-37-327	NM_004985	KRAS	c.183A>T	p.Q61H	1.70
MDS-37-351	NM_004985	KRAS	c.35G>T	p.G12V	41.06
MDS-37-081	NM_002520	NPM1	c.860_863dupTCTG	p.W288fs	11.00
MDS-37-114	NM_002520	NPM1	c.733G>C	p.E245Q	59.33
MDS-37-137	NM_002520	NPM1	c.733G>C	p.E245Q	50.60
MDS-37-147	NM_002520	NPM1	c.860_863dupTCTG	p.W288Cfs*12	45.00
MDS-37-162	NM_002520	NPM1	c.733G>C	p.E245Q	53.50
MDS-37-166	NM_002520	NPM1	c.860_863dupTCTG	p.W288fs	40.00
MDS-37-246	NM_002520	NPM1	c.733G>C	p.E245Q	45.40
MDS-37-298	NM_002520	NPM1	c.859_860insTCTG	p.L287fs	38.05
MDS-37-313	NM_002520	NPM1	c.859_860insTCTG	p.L287fs	44.98
MDS-37-157	NM_000378	WT1	c.1090_1092delTCG	p.S364delS	18.30
MDS-37-157	NM_000378	WT1	c.1077_1086del10	p.T360Gfs*69	18.30
MDS-37-176	NM_024426	WT1	c.1109G>A	p.R370H	5.00
MDS-37-221	NM_000378	WT1	c.785C>A	p.S262X	9.80
MDS-37-252	NM_024426	WT1	c.1379T>C	p.F460S	35.60
MDS-37-283	NM_024426	WT1	c.1140delG	p.R380fs	9.09
MDS-37-302	NM_024426	WT1	c.1138_1140deinsGGGG	p.R380fs	10.38
MDS-37-302	NM_024426	WT1	c.582delG	p.R194fs	1.77
MDS-37-313	NM_024426	WT1	c.1359_1360insGT	p.K454fs	40.33
MDS-37-373	NM_024426	WT1	c.1138delinsGT	p.R380fs	31.00
MDS-37-377	NM_024426	WT1	c.1138_1139insTCTTGTAC	p.R380fs	1.00
MDS-37-377	NM_024426	WT1	c.1144_1145insTCGG	p.A382fs	9.88
MDS-15-019	NM_001987	ETV6	c.1196G>A	p.R399H	23.80
MDS-37-114	NM_001987	ETV6	c.196G>A	p.V66I	47.34
MDS-37-172	NM_001987	ETV6	c.246dupT	p.D83X	33.50
MDS-37-216	NM_001987	ETV6	c.1196G>A	p.R399H	3.30
MDS-37-252	NM_001987	ETV6	c.641C>T	p.P214L	33.80
MDS-37-297	NM_001987	ETV6	c.1106G>A	p.R369Q	61.42
MDS-37-303	NM_001987	ETV6	c.1033delG	p.V345fs	10.11
MDS-37-358	NM_001987	ETV6	c.305_306insTC	p.F102fs	1.80
MDS-37-361	NM_001987	ETV6	c.700_701insCT	p.P234fs	1.00
MDS-37-361	NM_001987	ETV6	c.704dupT	p.L235fs	1.23
MDS-37-362	NM_001987	ETV6	c.1140G>A	p.W380X	3.02
MDS-37-374	NM_001987	ETV6	c.1214_1215insCATT	p.N405fs	1.00
MDS-37-125	NM_001015877	PHF6	c.955C>T	p.R319X	26.50
MDS-37-161	NM_032458	PHF6	c.835-2A>C	–	36.00
MDS-37-214	NM_032458	PHF6	c.898A>G	p.T300A	1.90
MDS-37-282	NM_001015877	PHF6	c.820C>T	p.R274X	64.10
MDS-37-285	NM_001015877	PHF6	c.941T>C	p.I314T	22.53
MDS-37-295	NM_001015877	PHF6	c.418+1G>A	–	42.72
MDS-37-298	NM_001015877	PHF6	c.900_901insTA	p.T300fs	3.47
MDS-37-351	NM_001015877	PHF6	c.820C>T	p.R274X	94.38
MDS-37-089	NM_002834	PTPN11	c.1508G>A	p.G503E	2.65
MDS-37-146	NM_002834	PTPN11	c.1507G>A	p.G503R	6.80
MDS-37-156	NM_002834	PTPN11	c.181G>A	p.D61N	4.60
MDS-37-199	NM_002834	PTPN11	c.214G>A	p.A72T	12.80
MDS-37-242	NM_002834	PTPN11	c.215C>T	p.A72V	11.30
MDS-37-277	NM_002834	PTPN11	c.215C>T	p.A72V	3.18
MDS-37-280	NM_002834	PTPN11	c.204_205insAATCTCA	p.Y68fs	9.07
MDS-37-295	NM_002834	PTPN11	c.227A>T	p.E76V	3.32
MDS-37-297	NM_002834	PTPN11	c.1505C>T	p.S502L	7.28
MDS-37-298	NM_002834	PTPN11	c.205G>A	p.E69K	2.90
MDS-37-323	NM_002834	PTPN11	c.181G>A	p.D61N	1.22
MDS-37-351	NM_002834	PTPN11	c.1382C>G	p.A461G	1.31
MDS-15-016	NM_002168	IDH2	c.419G>A	p.R140Q	36.00

MDS-15-029	NM_002168	IDH2	c.419G>A	p.R140Q	41.69
MDS-15-039	NM_002168	IDH2	c.419G>A	p.R140Q	41.83
MDS-15-058	NM_002168	IDH2	c.418C>T	p.R140W	44.20
MDS-37-254	NM_002168	IDH2	c.178C>T	p.R60C	48.10
MDS-37-267	NM_002168	IDH2	c.418C>T	p.R140W	50.00
MDS-37-293	NM_002168	IDH2	c.515G>A	p.R172K	37.02
MDS-37-315	NM_002168	IDH2	c.419G>A	p.R140Q	15.04
MDS-37-318	NM_002168	IDH2	c.419G>A	p.R140Q	2.73
MDS-37-364	NM_002168	IDH2	c.419G>A	p.R140Q	40.13
MDS-15-001	NM_004972	JAK2	c.1849G>T	p.V617F	14.76
MDS-37-117	NM_004972	JAK2	c.1849G>T	p.V617F	6.35
MDS-37-150	NM_004972	JAK2	c.1174G>A	p.V392M	49.80
MDS-37-180	NM_004972	JAK2	c.1849G>T	p.V617F	2.60
MDS-37-186	NM_004972	JAK2	c.2959G>A	p.E987K	47.00
MDS-37-200	NM_004972	JAK2	c.1174G>A	p.V392M	46.80
MDS-37-237	NM_004972	JAK2	c.1174G>A	p.V392M	45.80
MDS-37-261	NM_004972	JAK2	c.1174G>A	p.V392M	48.00
MDS-37-318	NM_004972	JAK2	c.842G>A	p.G281D	44.66
MDS-37-330	NM_004972	JAK2	c.1849G>T	p.V617F	52.97
MDS-37-145	NM_021946	BCORL1	c.2615T>G	p.V872G	43.90
MDS-37-188	NM_021946	BCORL1	c.1541C>T	p.S514L	48.60
MDS-37-221	NM_021946	BCORL1	c.3268_3269ins10	p.R1090Pfs*23	16.20
MDS-37-235	NM_021946	BCORL1	c.5036C>T	p.S1679F	36.30
MDS-37-255	NM_021946	BCORL1	c.2669G>A	p.R890Q	30.20
MDS-37-295	NM_021946	BCORL1	c.3796C>T	p.R1266X	18.38
MDS-37-323	NM_021946	BCORL1	c.3895C>T	p.R1299X	13.60
MDS-37-323	NM_021946	BCORL1	c.4971_4972insAGGCT	p.Y1657fs	1.21
MDS-37-123	NM_004364	CEBPA	c.1066_1069delinsGCCATGG	p.N356_C357delinsAMG	40.00
MDS-37-145	NM_004364	CEBPA	c.186_187insCA	p.D63Qfs*98	42.90
MDS-37-173	NM_004364	CEBPA	c.937_939dupAAG	p.K313dupK	44.80
MDS-37-173	NM_004364	CEBPA	c.62delG	p.S21Tfs*139	52.10
MDS-37-270	NM_004364	CEBPA	c.1013T>C	p.L338P	4.10
MDS-37-283	NM_004364	CEBPA	c.430G>T	p.E144X	6.37
MDS-37-300	NM_004364	CEBPA	c.247delC	p.Q83fs	28.30
MDS-37-316	NM_004364	CEBPA	c.855C>A	p.Y285X	46.48
MDS-37-316	NM_004364	CEBPA	c.68dupC	p.P23fs	48.02
MDS-37-105	NM_000760	CSF3R	c.2197C>A	p.P733T	49.75
MDS-37-158	NM_000760	CSF3R	c.1096G>A	p.G366R	56.20
MDS-37-186	NM_000760	CSF3R	c.2125_2134del10	p.W709Ifs*90	29.70
MDS-37-241	NM_000760	CSF3R	c.1919C>A	p.T640N	14.40
MDS-37-250	NM_000760	CSF3R	c.2256_2261del	p.Y752_Q754delinsX	11.70
MDS-37-290	NM_156039	CSF3R	c.2225G>A	p.G742D	1.24
MDS-37-305	NM_156039	CSF3R	c.2098A>G	p.K700E	42.15
MDS-37-147	NM_004119	FLT3	FLT3-ITD	–	15.00
MDS-37-173	NM_004119	FLT3	c.2504A>T	p.D835V	1.80
MDS-37-211	NM_004119	FLT3	c.1423A>C	p.T475P	49.90
MDS-37-298	NM_004119	FLT3	FLT3-ITD	–	10.17
MDS-37-309	NM_004119	FLT3	FLT3-ITD	–	9.03
MDS-37-372	NM_004119	FLT3	c.2503G>T	p.D835Y	1.54
MDS-37-377	NM_004119	FLT3	FLT3-ITD	–	8.43
MDS-37-163	NM_001145661	GATA2	c.959G>A	p.G320D	44.70
MDS-37-169	NM_001145661	GATA2	c.1114G>A	p.A372T	3.10
MDS-37-173	NM_001145661	GATA2	c.1085G>A	p.R362Q	41.50
MDS-37-221	NM_001145661	GATA2	c.952G>A	p.A318T	10.20
MDS-37-233	NM_001145661	GATA2	c.1168_1174delAAGGAAG	p.K390Gfs*85	3.70
MDS-37-294	NM_032638	GATA2	c.1081C>T	p.R361C	46.29
MDS-37-107	NM_006892	DNMT3B	c.317G>A	p.R106Q	47.50

MDS-37-131	NM_006892	DNMT3B	c.1804G>A	p.V602I	55.00
MDS-37-151	NM_006892	DNMT3B	c.1126G>A	p.E376K	50.00
MDS-37-229	NM_006892	DNMT3B	c.832G>A	p.V278M	51.80
MDS-37-264	NM_000051	ATM	c.6056A>G	p.Y2019C	2.80
MDS-37-264	NM_000051	ATM	c.283C>A	;p.Q95K	28.80
MDS-37-295	NM_000051	ATM	c.9016G>A	p.A3006T	45.06
MDS-37-335	NM_000051	ATM	c.8095C>T	p.P2699S	1.33
MDS-37-125	NM_000222	KIT	c.2447A>T	p.D816V	5.00
MDS-37-141	NM_000222	KIT	c.1504_1509dupGCCTAT	p.A502_Y503dupAY	10.50
MDS-37-141	NM_000222	KIT	c.2447A>T	p.D816V	17.50
MDS-37-269	NM_000222	KIT	c.2924A>T	p.D975V	49.70
MDS-37-135	NM_002049	GATA1	c.482G>C	p.S161T	54.30
MDS-37-250	NM_006060	IKZF1	c.476A>G	p.N159S	30.20

MDS, myelodysplastic syndromes; VAF, variant allele frequency.

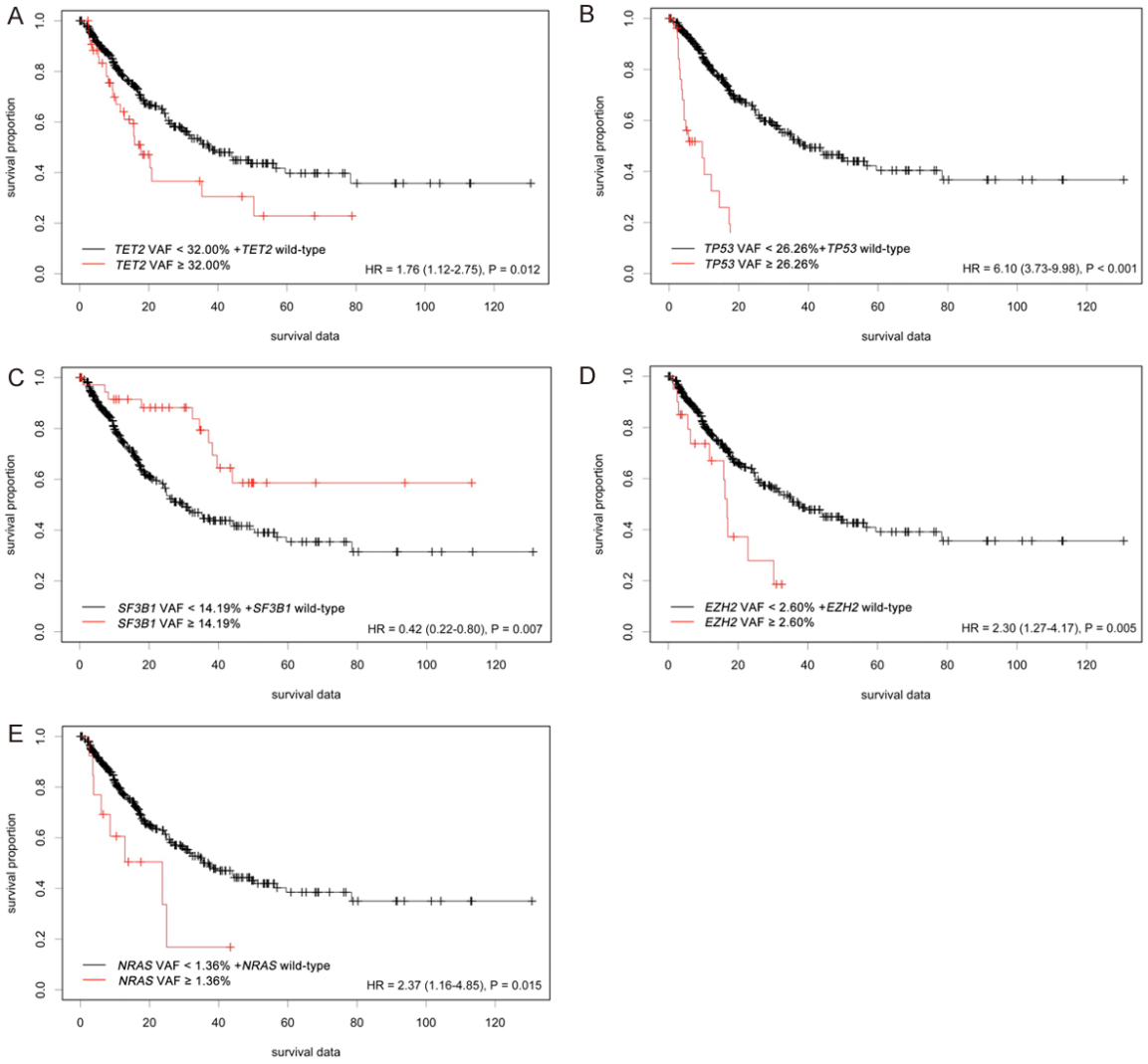
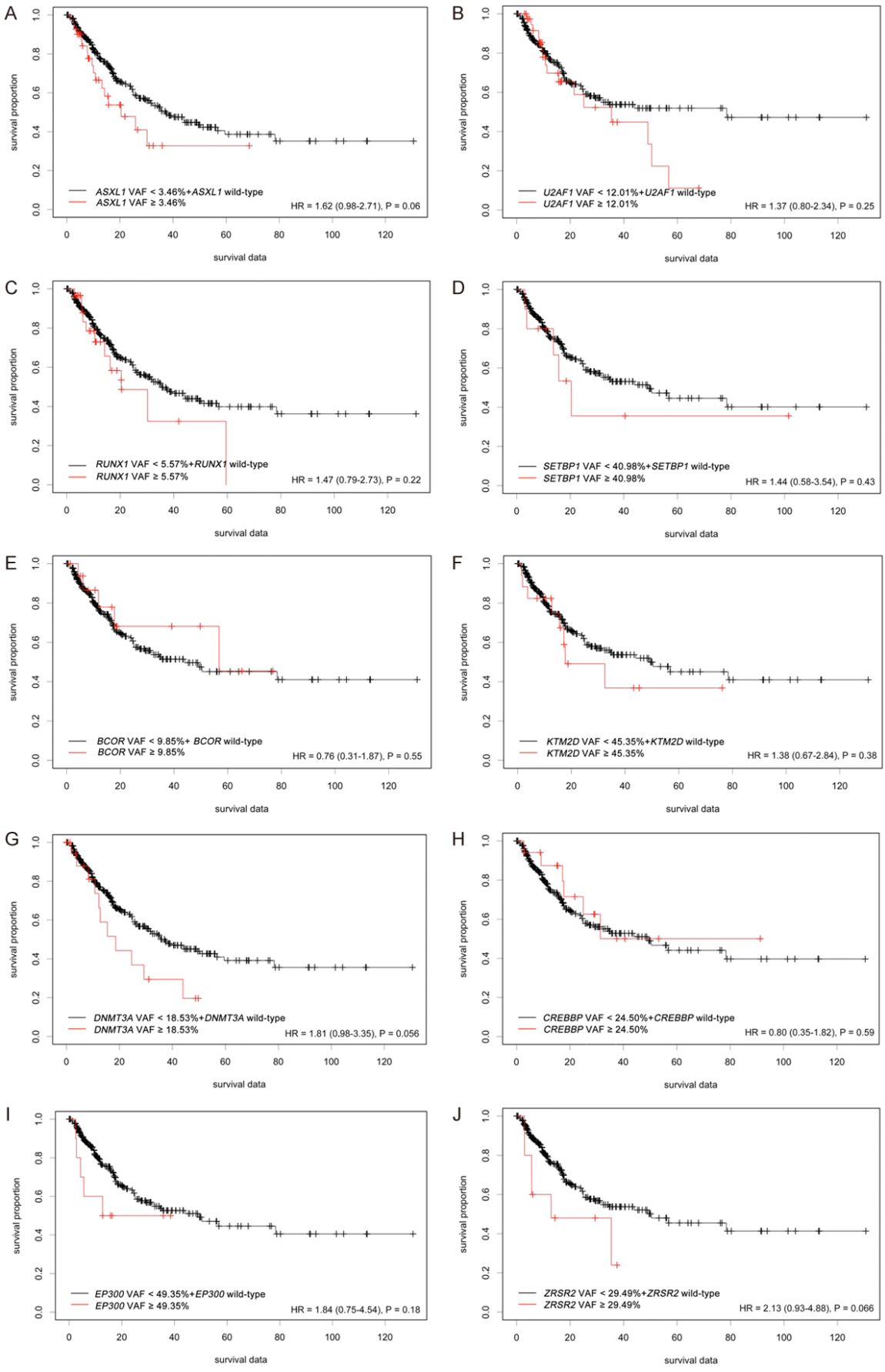


Figure S1. Determination of the optimal VAF cut-point of each gene for survival stratification by the R language-based web application Cut-off Finder, OS (months) significantly stratified by the optimal VAF cut-off (A) TET2, (B) TP53, (C) SF3B1, (D) EZH2, and (E) NRAS mutation.


A
survival proportion
survival data
ASXL1 VAF < 3.46%+ASXL1 wild-type
ASXL1 VAF ≥ 3.46%
HR = 1.62 (0.98-2.71), P = 0.06
B
U2AF1 VAF < 12.01%+U2AF1 wild-type
U2AF1 VAF ≥ 12.01%
HR = 1.37 (0.80-2.34), P = 0.25
C
RUNX1 VAF < 5.57%+RUNX1 wild-type
RUNX1 VAF ≥ 5.57%
HR = 1.47 (0.79-2.73), P = 0.22
D
SETBP1 VAF < 40.98%+SETBP1 wild-type
SETBP1 VAF ≥ 40.98%
HR = 1.44 (0.58-3.54), P = 0.43
E
BCOR VAF < 9.85%+ BCOR wild-type
BCOR VAF ≥ 9.85%
HR = 0.76 (0.31-1.87), P = 0.55
F
KTM2D VAF < 45.35%+KTM2D wild-type
KTM2D VAF ≥ 45.35%
HR = 1.38 (0.67-2.84), P = 0.38
G
DNMT3A VAF < 18.53%+DNMT3A wild-type
DNMT3A VAF ≥ 18.53%
HR = 1.81 (0.98-3.35), P = 0.056
H
CREBBP VAF < 24.50%+CREBBP wild-type
CREBBP VAF ≥ 24.50%
HR = 0.80 (0.35-1.82), P = 0.59
I
EP300 VAF < 49.35%+EP300 wild-type
EP300 VAF ≥ 49.35%
HR = 1.84 (0.75-4.54), P = 0.18
J
ZRSR2 VAF < 29.49%+ZRSR2 wild-type
ZRSR2 VAF ≥ 29.49%
HR = 2.13 (0.93-4.88), P = 0.066

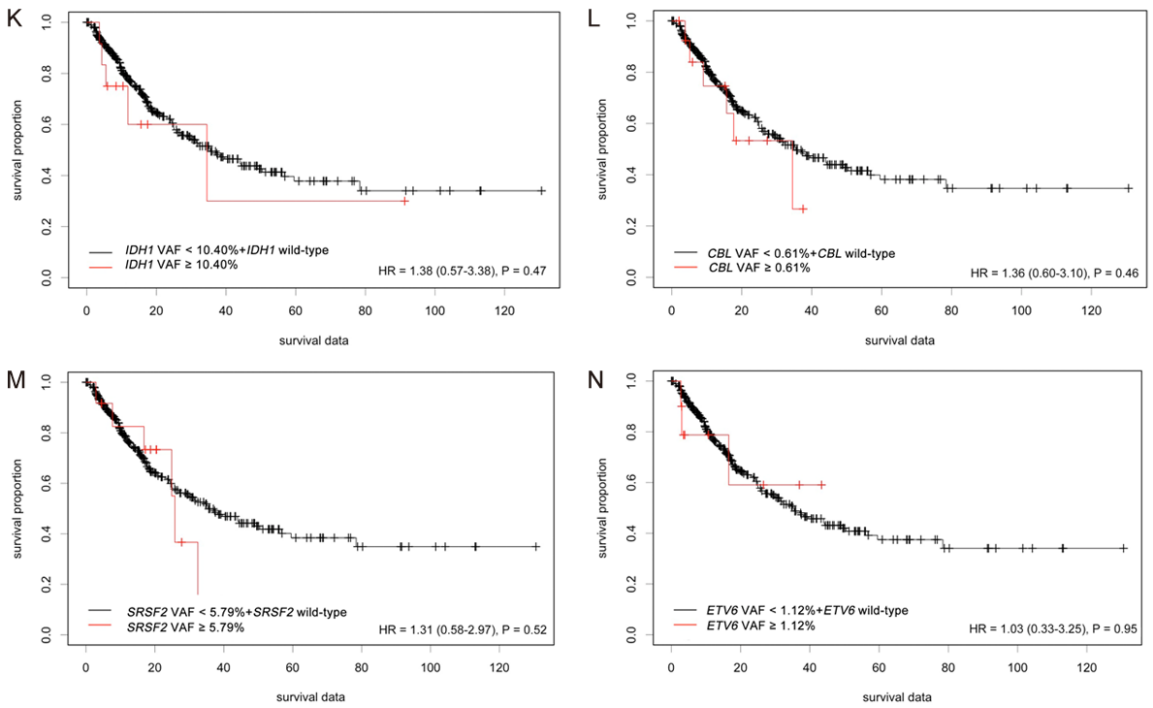


Figure S2. Determination of the optimal VAF cut-point of each gene for survival stratification by the R language-base web application Cutoff Finder. OS (moths) stratified by the optimal VAF cut-off of (A) *ASXL 1*, (B) *U2AF1*, (C) *RUNX1*, (D) *SETBP1*, (E) *BCOR*, (F) *KTM2D*, (G) *DNMT3A*, (H) *CREBBP*, (I) *EP300*, (J) *ZRSR2*, (K) *IDH1*, (L) *CBL*, (M) *SRSF2*, and (N) *ETV6* mutations.

Table S3. Univariate analysis of mutational status and overall survival

Gene	Mutant (n)	Wild-type (n)	Mutation frequency (%)	Median OS (months)		HR	95% CI	P
				Mutant	Wild-type			
TET2	56	326	14.66	20.37	37.13	1.45	0.95-2.48	0.084
ASXL1	46	336	12.04	25.80	37.13	1.45	0.86-2.79	0.146
U2AF1	45	337	11.78	27.00	37.13	1.25	0.76-2.16	0.364
SF3B1	43	339	11.26	NR	30.17	0.51	0.37-0.90	0.017
RUNX1	34	348	8.90	30.17	35.47	1.38	0.74-2.88	0.277
TP53	33	349	8.64	10.07	43.97	4.25	2.72-6.62	< 0.001
SETBP1	23	279	7.62	49.00	50.43	0.95	0.47-1.93	0.886
BCOR	22	280	7.28	56.77	43.97	1.18	0.54-2.52	0.691
KMT2D	22	280	7.28	32.47	49.00	1.17	0.55-2.55	0.674
DNMT3A	27	355	7.07	24.60	35.47	1.37	0.73-2.81	0.299
CREBBP	18	284	5.96	31.37	49.00	0.93	0.44-1.97	0.860
EP300	16	286	5.30	NR	49.00	1.03	0.45-2.37	0.947
EZH2	20	362	5.24	16.83	37.50	2.28	1.46-7.97	0.005
ZRSR2	14	288	4.64	35.37	49.00	1.49	0.60-4.32	0.344
IDH1	16	366	4.19	NR	35.37	0.85	0.38-1.96	0.719
NRAS	14	368	3.66	23.70	35.47	2.09	1.06-7.88	0.038
CBL	14	368	3.66	34.50	35.47	1.36	0.56-3.68	0.455
SRSF2	13	369	3.40	25.80	35.47	1.28	0.53-3.32	0.547
CUX1	10	292	3.31	78.43	49.00	0.98	0.36-2.65	0.971
KRAS	10	292	3.31	NR	49.00	1.36	0.45-4.50	0.549
NPM1	9	293	2.98	25.07	49.00	1.82	0.68-7.30	0.185

WT1	9	293	2.98	16.20	49.00	1.19	0.35-4.20	0.768
ETV6	11	371	2.88	NR	35.37	0.98	0.32-3.04	0.971
PHF6	8	294	2.65	56.77	43.97	0.83	0.29-2.43	0.756
PTPN11	8	294	2.65	NR	49.00	1.78	0.48-9.87	0.316
IDH2	10	372	2.62	24.87	35.47	1.77	0.73-6.19	0.166
JAK2	10	372	2.62	26.97	35.47	0.99	0.37-2.64	0.977
BCORL1	7	295	2.32	24.33	49.00	1.36	0.38-5.41	0.597
CEBPA	7	295	2.32	24.33	49.00	1.07	0.33-3.49	0.914
CSF3R	7	295	2.32	NR	49.00	0.52	0.15-2.55	0.500
FLT3	7	295	2.32	NR	49.00	1.65	0.32-11.44	0.476
GATA2	6	296	1.99	34.50	49.00	0.52	0.15-2.60	0.511
DNMT3B	4	298	1.32	NR	49.00	0.51	0.15-2.52	0.495
ATM	3	299	0.99	17.20	49.00	2.46	0.48-36.98	0.193
KIT	3	299	0.99	56.77	49.00	1.99	0.38-18.85	0.326
GATA1	1	301	0.33	10.60	49.00	4.40	0.49-1764.00	0.107
IKZF1	1	301	0.33	NR	49.00	0.00	0.01-10.96	0.563

CI, confidence interval; HR, hazard ratio; OS, overall survival.

Table S4. Response to monotherapy using hypomethylating agents

Variable	Value
Monotherapy using HMAs, n (%)	
Decitabine	62 (89.86)
Azacitidine	7 (10.14)
HMAs cycles, median (range)	4 (2-20)
Treatment response, n (%)	
CR	2 (3.23)
PR	0 (0)
mCR/HI	46 (66.67)
Stable disease without HI	14 (20.29)
Disease progression	6 (8.70)
Treatment failure	1 (1.45)
Overall response*, n (%)	48 (69.57)

CR, complete remission; HI, hematological improvement; HMAs, hypomethylating agents; mCR, marrow CR; PR, partial remission. *Overall response: CR+PR+mCR/HI.

Table S5. Associations between mutation status and response to monotherapy using hypomethylating agents

Gene	Mutant (n)	Wild-type (n)	Mutation frequency (%)	Responders		P
				Mutant n (%)	Wild-type n (%)	
TET2	17	52	24.64	9 (52.94)	39 (75.00)	0.128
U2AF1	13	56	18.84	10 (76.92)	38 (67.86)	0.740
ASXL1	9	60	13.04	8 (88.89)	40 (66.67)	0.258
RUNX1	9	60	13.04	7 (77.78)	41 (68.33)	0.712
KMT2D	6	42	12.50	5 (83.33)	26 (61.90)	0.402
ZRSR2	6	42	12.50	2 (33.33)	29 (69.05)	0.167
SETBP1	5	43	10.42	4 (80.00)	27 (62.79)	0.643

DNMT3A	7	62	10.14	5 (71.43)	43 (69.35)	1.000
EZH2	6	63	8.70	5 (83.33)	43 (68.25)	0.659
SF3B1	6	63	8.70	5 (83.33)	43 (68.25)	0.659
NPM1	4	44	8.33	4 (100.00)	27 (61.36)	0.282
TP53	5	64	7.25	3 (60.00)	45 (70.31)	0.636
BCOR	3	45	6.25	1 (33.33)	30 (66.67)	0.283
CREBBP	3	45	6.25	2 (66.67)	29 (64.44)	1.000
CUX1	3	45	6.25	1 (33.33)	30 (66.67)	0.283
KRAS	3	45	6.25	2 (66.67)	29 (64.44)	1.000
WT1	3	45	6.25	3 (100.00)	28 (62.22)	0.543
IDH1	4	65	5.80	2 (50.00)	46 (70.77)	0.580
IDH2	3	66	4.35	2 (66.67)	46 (69.70)	1.000
SRSF2	3	66	4.35	3 (100.00)	45 (68.18)	0.548
PTPN11	2	46	4.17	0 (0.00)	31 (67.39)	0.121
ETV6	2	67	2.90	1 (50.00)	47 (70.15)	0.519
ATM	1	47	2.08	0 (0.00)	31 (65.96)	0.354
BCORL1	1	47	2.08	0 (0.00)	31 (65.96)	0.354
CEBPA	1	47	2.08	0 (0.00)	31 (65.96)	0.354
DNMT3B	1	47	2.08	1 (100.00)	30 (63.83)	1.000
EP300	1	47	2.08	1 (100.00)	30 (63.83)	1.000
FLT3	1	47	2.08	0 (0.00)	31 (65.96)	0.354
PHF6	1	47	2.08	1 (100.00)	30 (63.83)	1.000
CBL	1	68	1.45	1 (100.00)	47 (69.12)	1.000
JAK2	1	68	1.45	0 (0.00)	48 (70.59)	0.304
CSF3R	0	48	0.00	--	31 (64.58)	--
GATA1	0	48	0.00	--	31 (64.58)	--
GATA2	0	48	0.00	--	31 (64.58)	--
IKZF1	0	48	0.00	--	31 (64.58)	--
KIT	0	48	0.00	--	31 (64.58)	--
NRAS	0	69	0.0	--	48 (69.57)	--

Table S6. Associations between *TET2* mutations and response to monotherapy using hypomethylating agents

Comparison	Responder, n (%)		P
TET2 mutant vs *TET2* wild-type	9/17 (52.94)	39/52 (75)	0.128
TET2 VAF ≥ 32% vs *TET2* wild-type	9/12 (75)	39/52 (75)	1.000
TET2 VAF < 32% vs *TET2* wild-type	0/5 (0)	39/52 (75)	0.002
TET2 VAF ≥ 32% vs *TET2* VAF < 32%	9/12 (75)	0/5 (0)	0.009
TET2 VAF ≥ 32% *ASXL1* wild-type vs *TET2* VAF < 32%	7/9 (77.78)	0/5 (0)	0.021

VAF, variant allele frequency.