LETTER TO THE EDITOR

Exclusion of persistent mutations in splicing factor genes and isocitrate dehydrogenase 2 improves the prognostic power of molecular measurable residual disease assessment in acute myeloid leukemia

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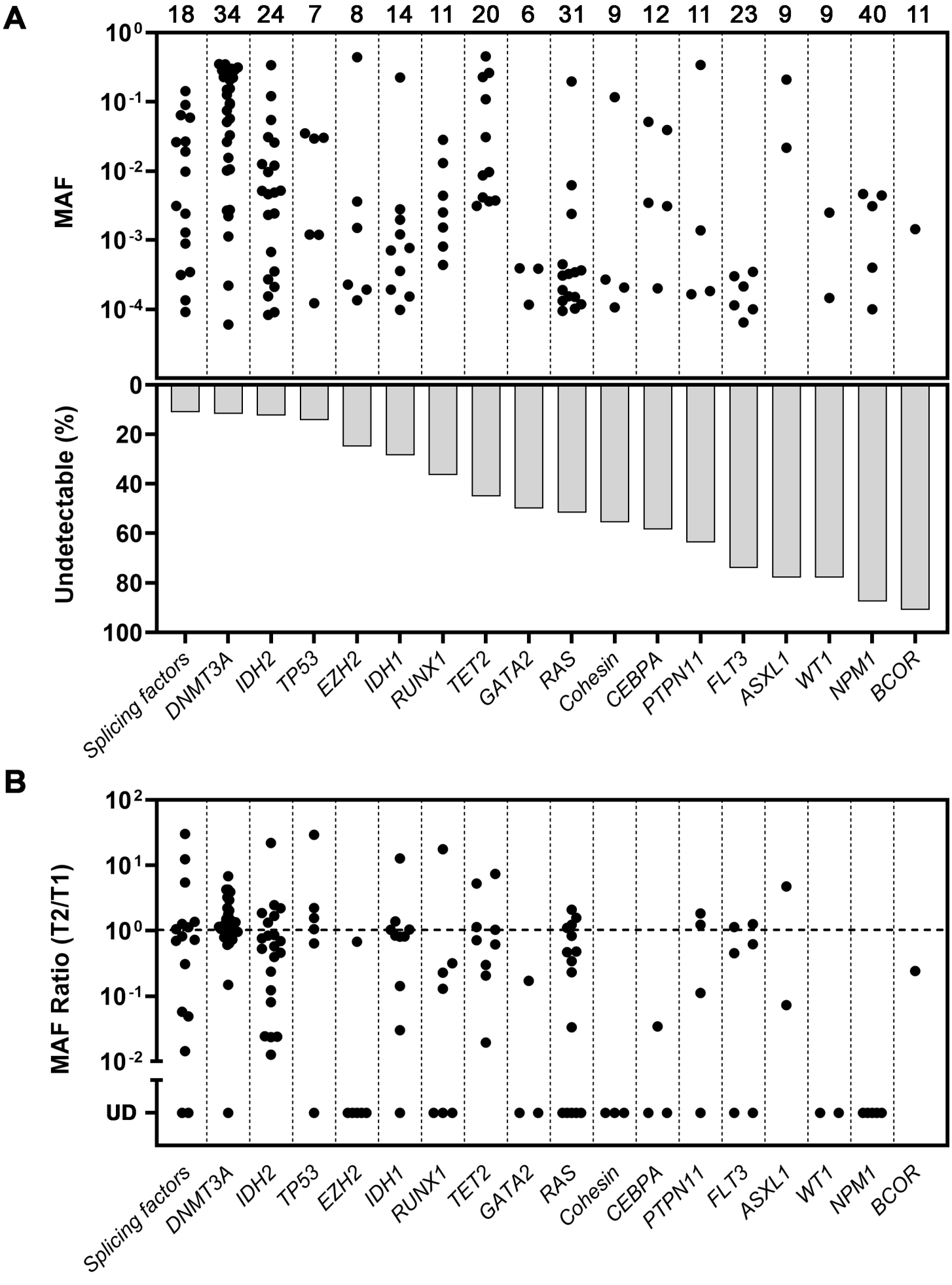
SUPPLEMENTAL LEGENDS

Supplemental Figure 1: Persistence and stability of mutations during remission. (**A**) Top panel shows the mutant allele frequencies (MAFs) of mutations that were detectable at time point 1 (T1) of remission. Bottom panel shows the percentage of mutations that were undetectable at T1. The number on top of each column indicates the number of unique mutations in the indicated gene or gene group. (**B**) For mutations that were detectable at T1, panel shows the ratio of MAF at time point 2 (T2) to T1. Mutations that were undetectable at T2 are shown as UD (undetectable).

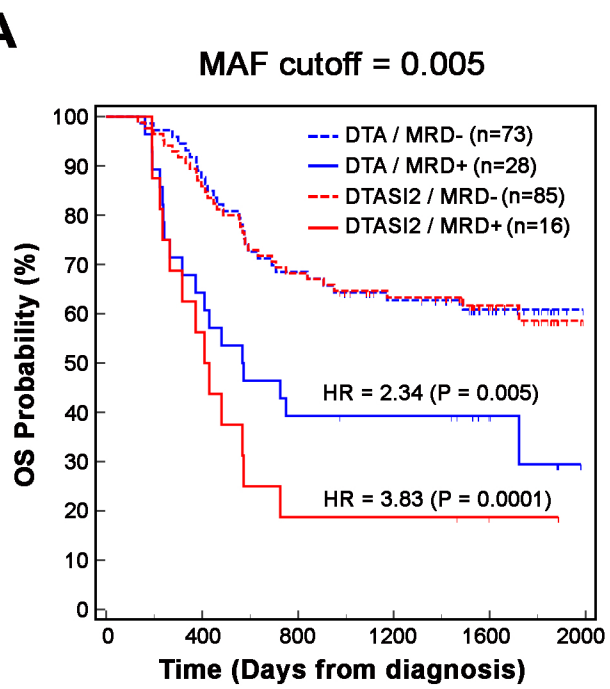
Supplemental Figure 2: Exclusion of mutations in splicing factor genes and *IDH2* in addition to *DTA* mutations improves the prognostic power of molecular MRD assessment. (**A**) Kaplan-Meier plots for overall survival (OS), relapse-free survival (RFS), and cumulative incidence of relapse (CIR) of patients classified as MRD-positive (MRD+) or MRD-negative (MRD-) and based on whether *DTA* or *DTAIS2* mutations were excluded from MRD determination. A MAF cutoff of > 0.005 was used to define MRD positivity. (**B**) Kaplan-Meier plots for OS, RFS, and CIR of patients classified as MRD+ or MRD- with no mutations excluded. A MAF cutoff of > 0.005 was used to define MRD positivity. (**C**) Kaplan-Meier plots for OS, RFS, and CIR of patients classified as MRD+ or MRD- with no mutations excluded. A MAF cutoff of > 0.01 was used to define MRD positivity.

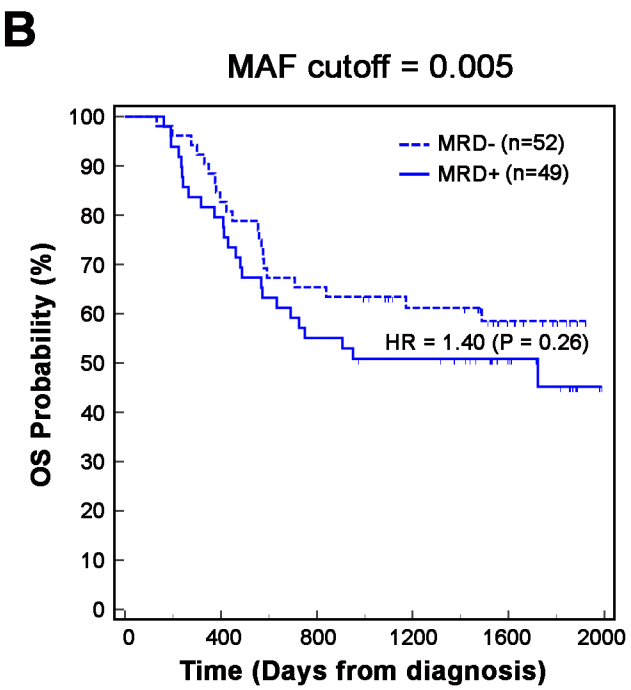
Supplemental Table 1: Clinical characteristics of the study cohort.

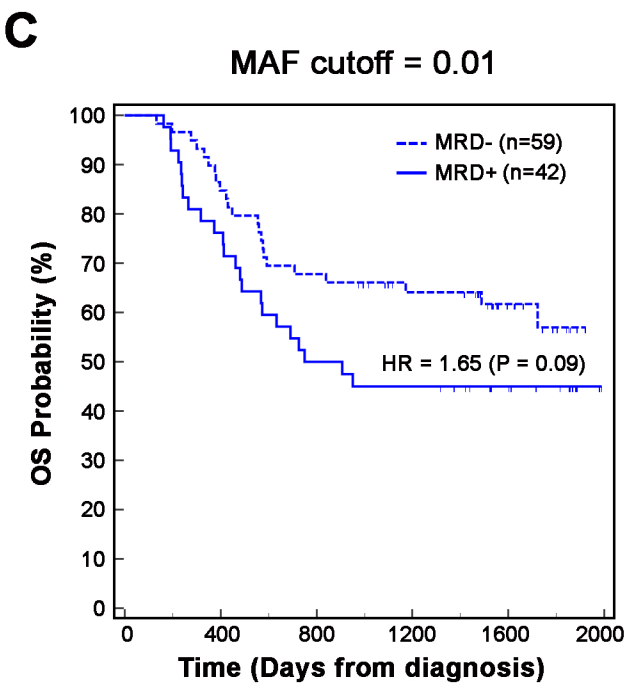
Supplemental Figure 1

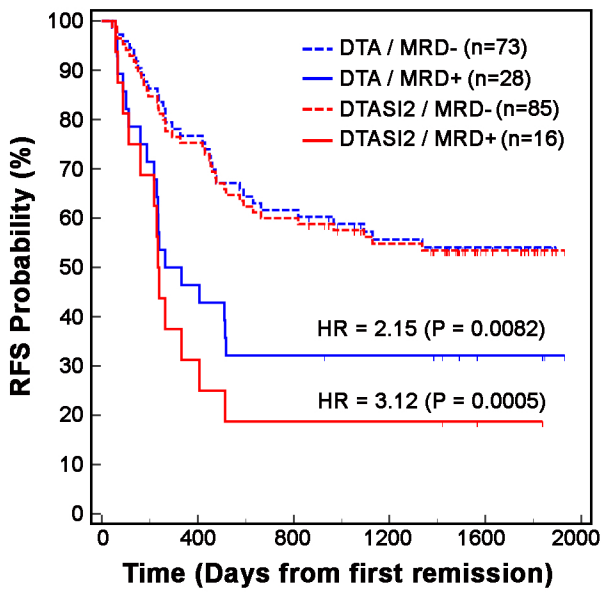


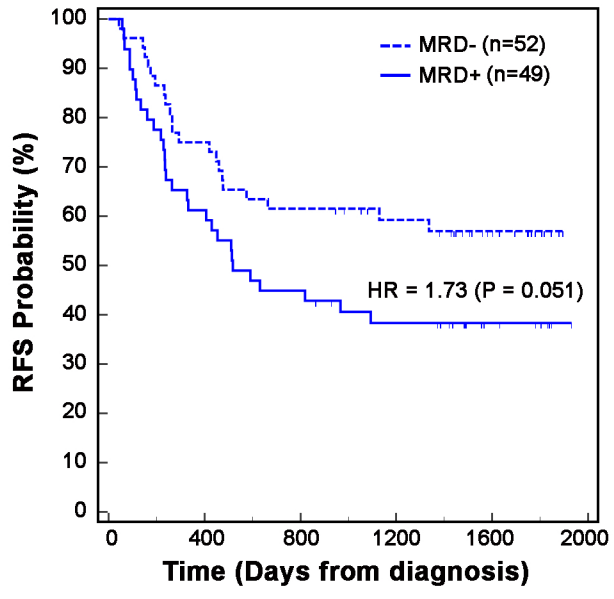
Supplemental Figure 2

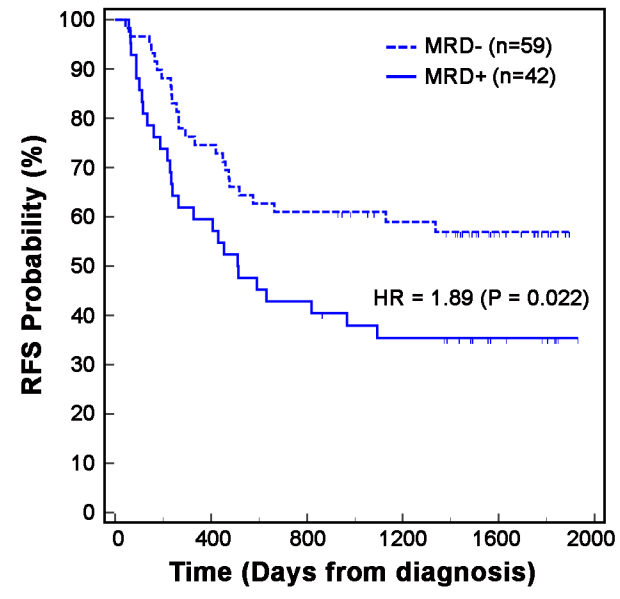


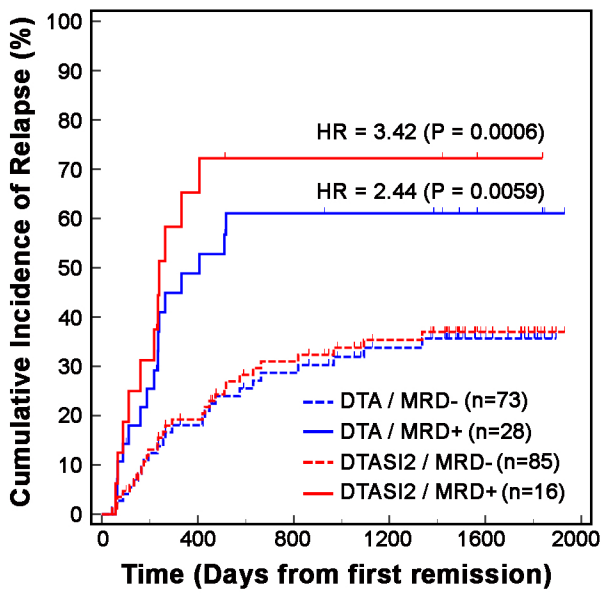


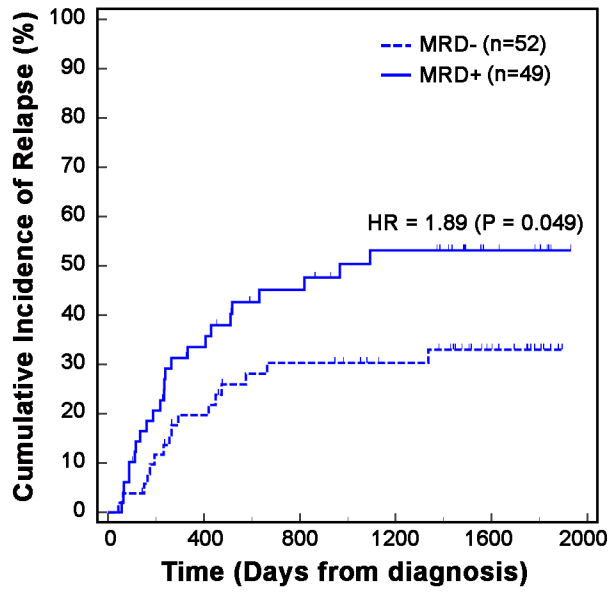


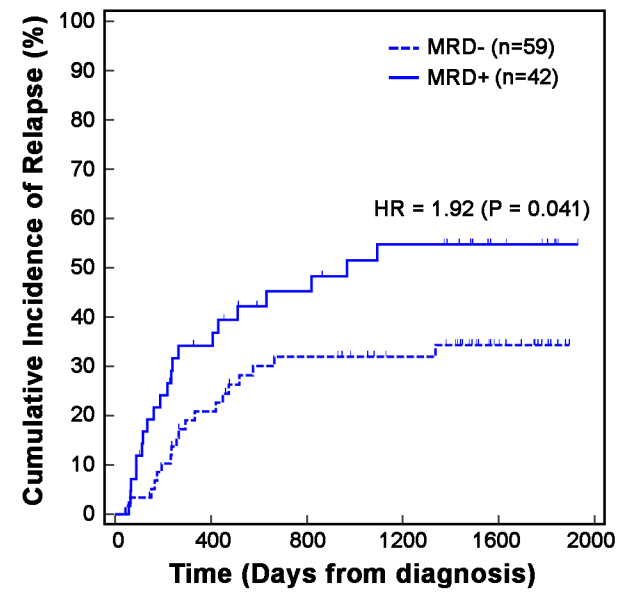












Supplemental Table 1: Clinical characteristics of the study cohort.

Characteristics	N = 114
Age at diagnosis (years), median (range)	60.5 (18 – 82)
Sex, N (%)	
Male	69 (60.5)
Female	45 (39.5)
AML classification, N (%)	
De novo	96 (84.2)
Secondary	18 (15.8)
AML with MRC, N (%)	
No	87 (76.3)
Yes	27 (23.7)
2017 ELN risk group, N (%)	
Favorable	50 (43.9)
Intermediate	24 (21.1)
Adverse	33 (28.9)
Unknown*	7 (6.1)
Chemotherapy regimen, N (%)	
3+7	81 (71.1)
FLAG-IDA[#]	33 (28.9)
CBC values at time of diagnosis, median (range)	
Blasts, x 10^9/L	1.46 (0 – 361.5)
WBC count, x 10^9/L	7.6 (0.4 – 377.8)
ANC, x 10^9/L	1.13 (0 – 57.2)
Hemoglobin, g/L	92 (61 – 157)
Platelets, x 10^9/L	64.5 (4 - 1052)
Patients with mutation(s) in gene, N (%)	
NPM1	40 (35.1)
DNMT3A	29 (25.4)
RAS genes	25 (21.9)
IDH2	24 (21.1)
FLT3	21 (18.4)
Splicing factor genes	18 (15.8)
IDH1	14 (12.3)
TET2	14 (12.3)
PTPN11	11 (9.6)
BCOR	10 (8.8)
CEBPA	9 (7.9)
ASXL1	9 (7.9)
RUNX1	8 (7.0)
Cohesin complex genes	8 (7.0)
WT1	7 (6.1)
TP53	6 (5.3)
EZH2	6 (5.3)
GATA2	6 (5.3)

Abbreviations: MRC, myelodysplasia-related changes; ELN, European Leukemia Network; CBC, complete blood count; WBC, white blood cell; ANC, absolute neutrophil count.

* Unknown due to cytogenetics failure.

Includes patients who required a second cycle of chemotherapy to achieve CR