Clinical characteristics and therapeutic determinants of *RUNX1::RUNX1T1* differ from those of *CBFB::MYH11* acute myeloid leukemia

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Received: December 30, 2024.
Accepted: April 22, 2025.
Early view: April 30, 2025.

https://doi.org/10.3324/haematol.2024.287293

Figure S1. The gene mutation profiles for patients with *RUNX1::RUNX1T1* (A) and *CBFB::MYH11* (B). The red squares represent gene mutations, gray represents the wild type, and black indicates that this gene was not tested. Patients without any gene mutations were removed from the oncoplot.

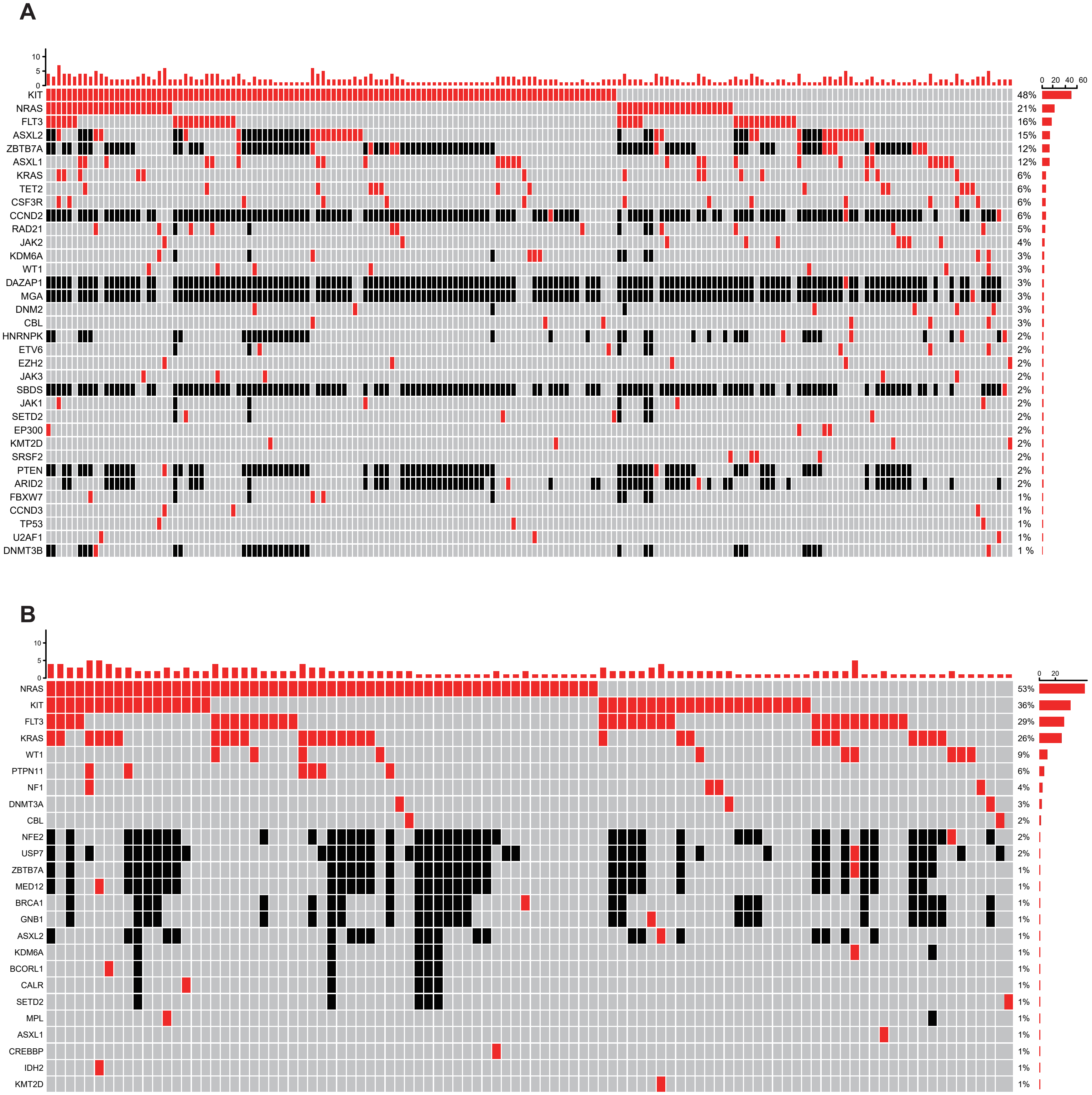


Figure S2. Outcomes of patients with *RUNX1::RUNX1T1* stratified by gene mutations. A and B are patients with or without KIT mutation; C and D are NRAS mutation; E and F are TET2 mutation. A, C and E represent overall survival (OS), while B, D and F represent relapse-free survival (RFS).

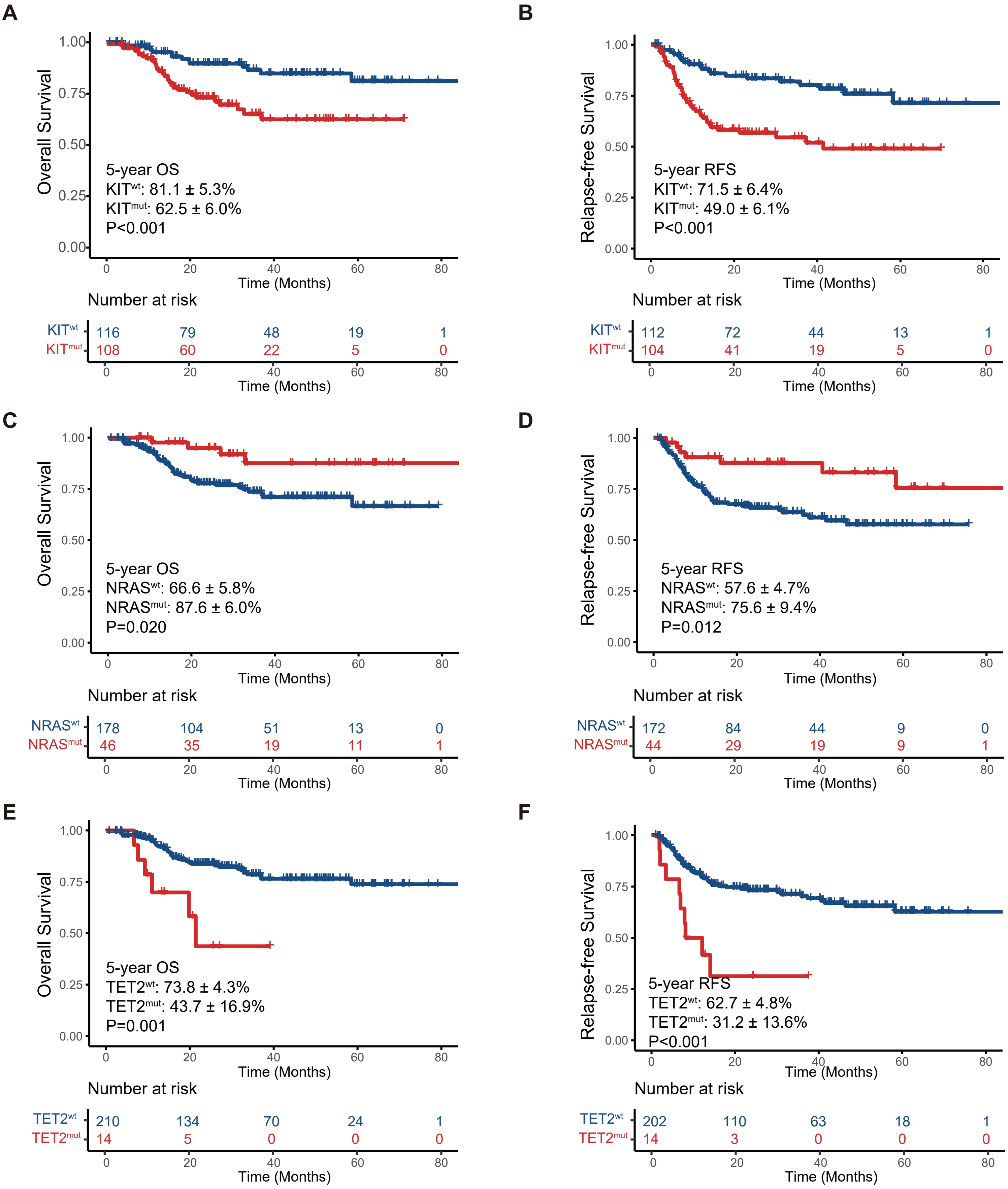


Figure S3. Outcomes of patients with *RUNX1::RUNX1T1* with different cytogenetic abnomalities. A and C are overall survival (OS). B and D are relapse-free survival (RFS). The blue and red line represent patients without or with specific cytogenetic abnomality.

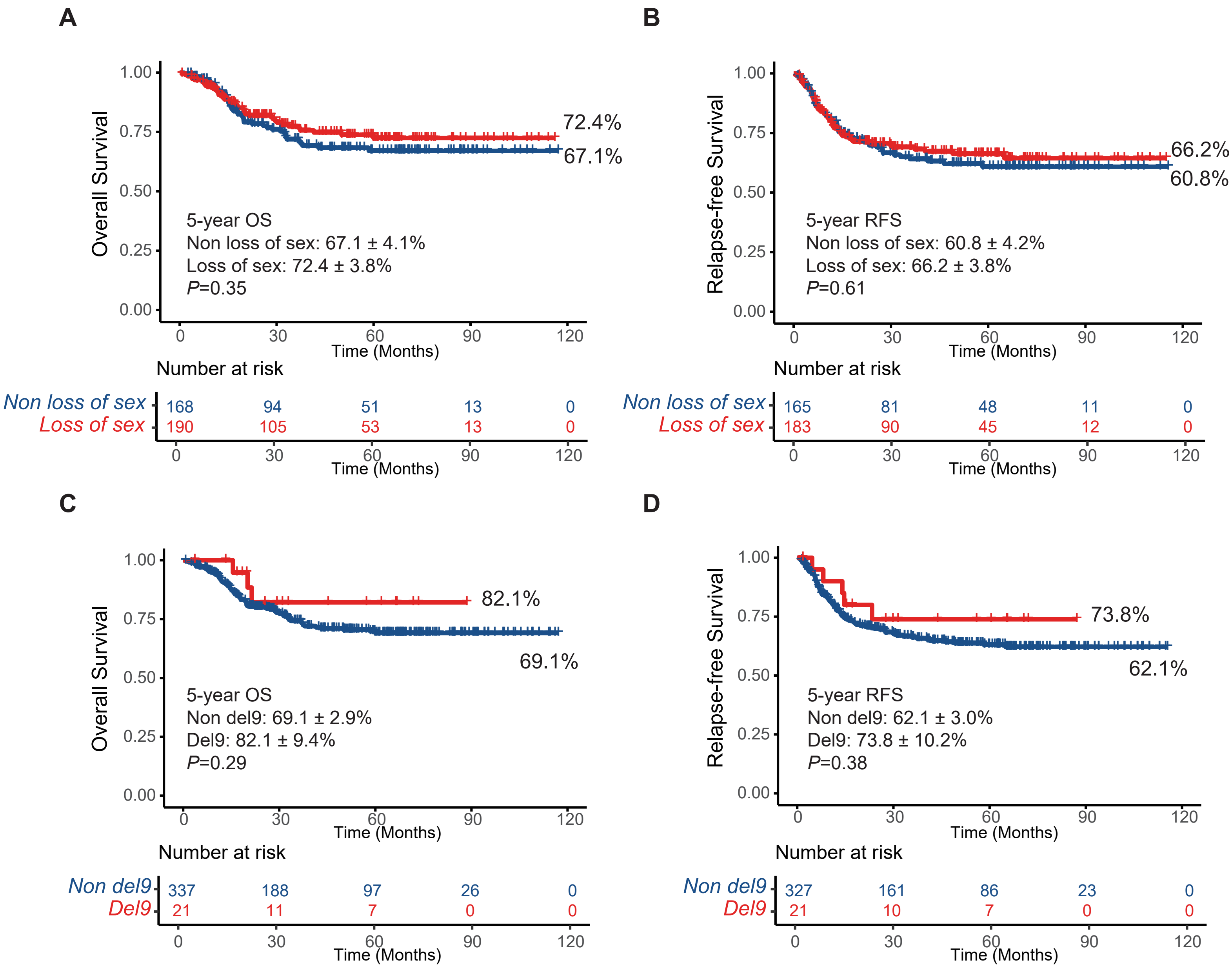


Figure S4. Outcomes of patients with *CBFB::MYH11* with different cytogenetic abnomalities. A and C are overall survival (OS). B and D are relapse-free survival (RFS). The blue and red line represent patients without or with specific cytogenetic abnomality.

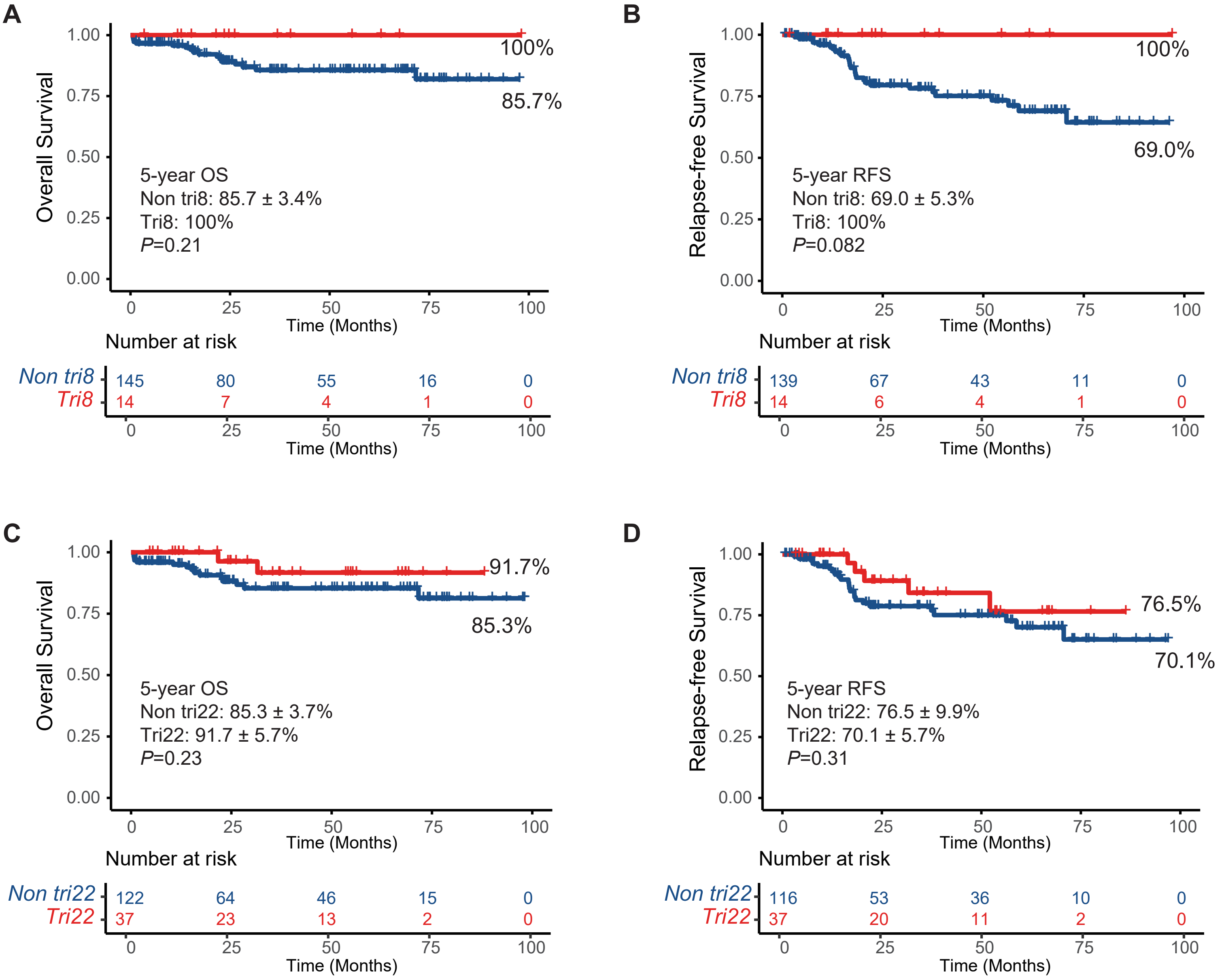


Figure S5. Outcomes of patients diagnosed as core binding factor acute myeloid leukemia (CBF-AML) censored for hematopoietic stem cell transplantation (HSCT). A is overall survival (OS); B is relapse-free survival (RFS). The blue line represents patients with *RUNX1::RUNX1T1*, while red line represents patients with *CBFB::MYH11.*

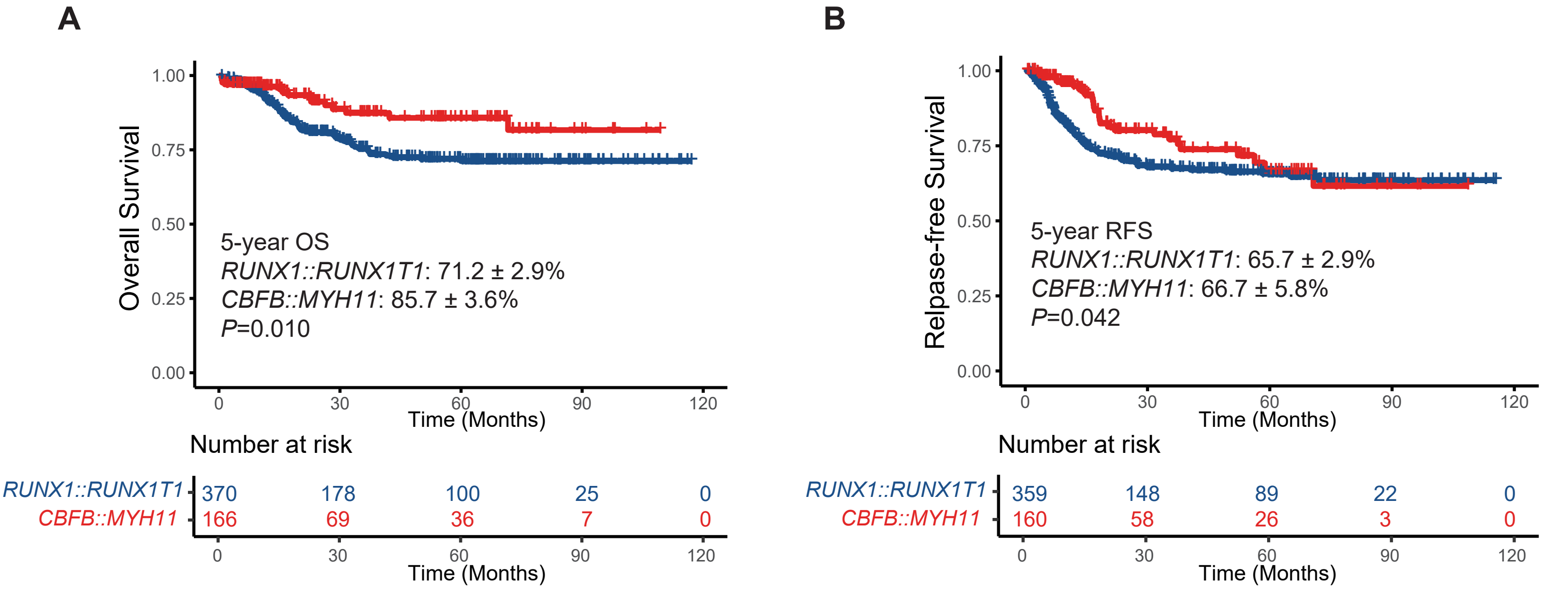


Figure S6. Outcomes of patients with *RUNX1::RUNX1T1* in different clinical trials (A-B: DA regimen; C-D: HAD regimen). A and C are overall survival (OS). B and D are relapse-free survival (RFS). The blue line represents patients receiving intermediate-dose (ID) induction, while the red line represents patients receiving standard-dose (SD) induction.

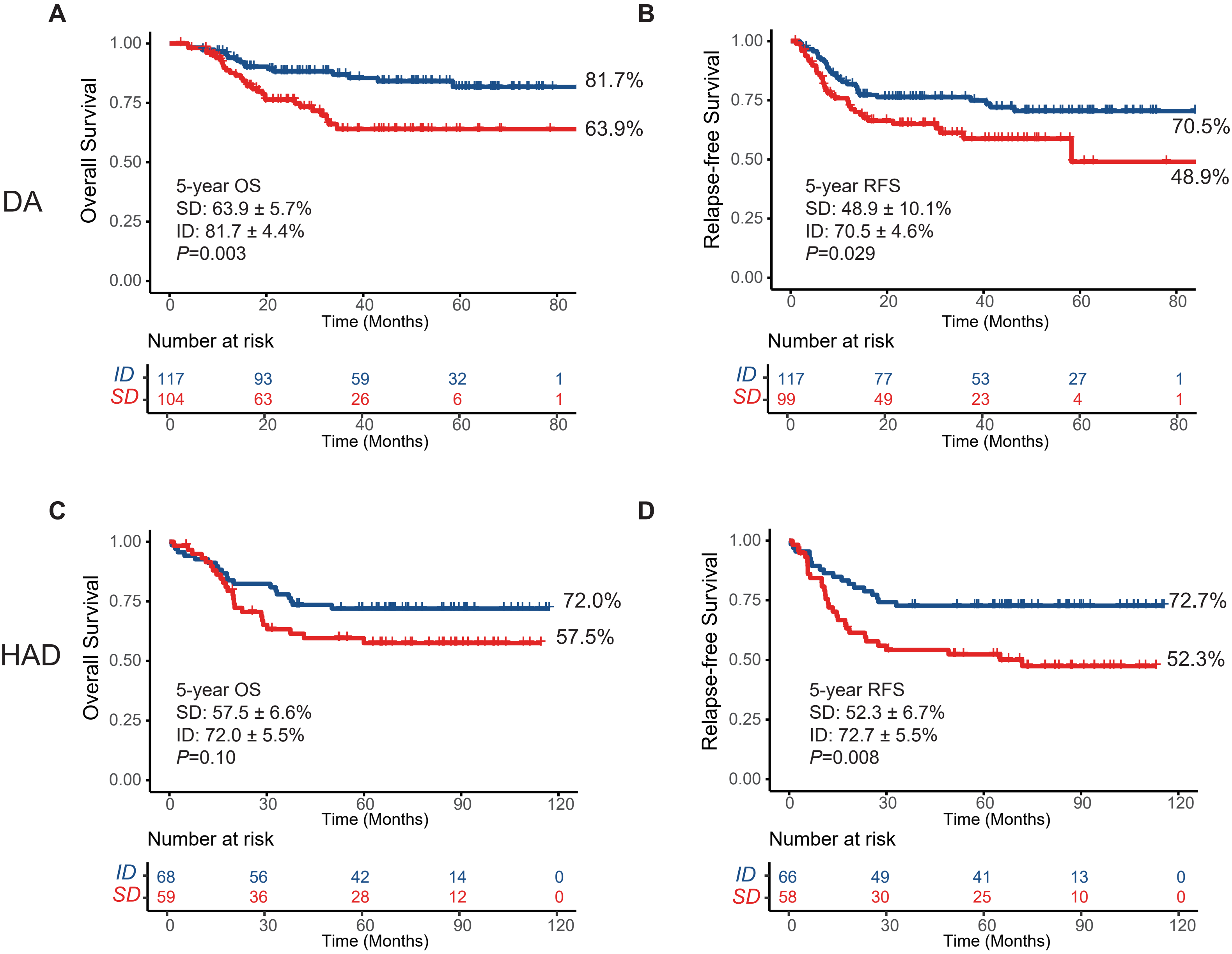


Figure S7. Outcomes of patients with *CBFB::MYH11* in different clinical trials (A-B: DA regimen; C-D: HAD regimen). A and C are overall survvial (OS). B and D are relapse-free survival (RFS). The blue line represents patients receiving intermediate-dose (ID) induction, while the red line represents patients receiving standard-dose (SD) induction.

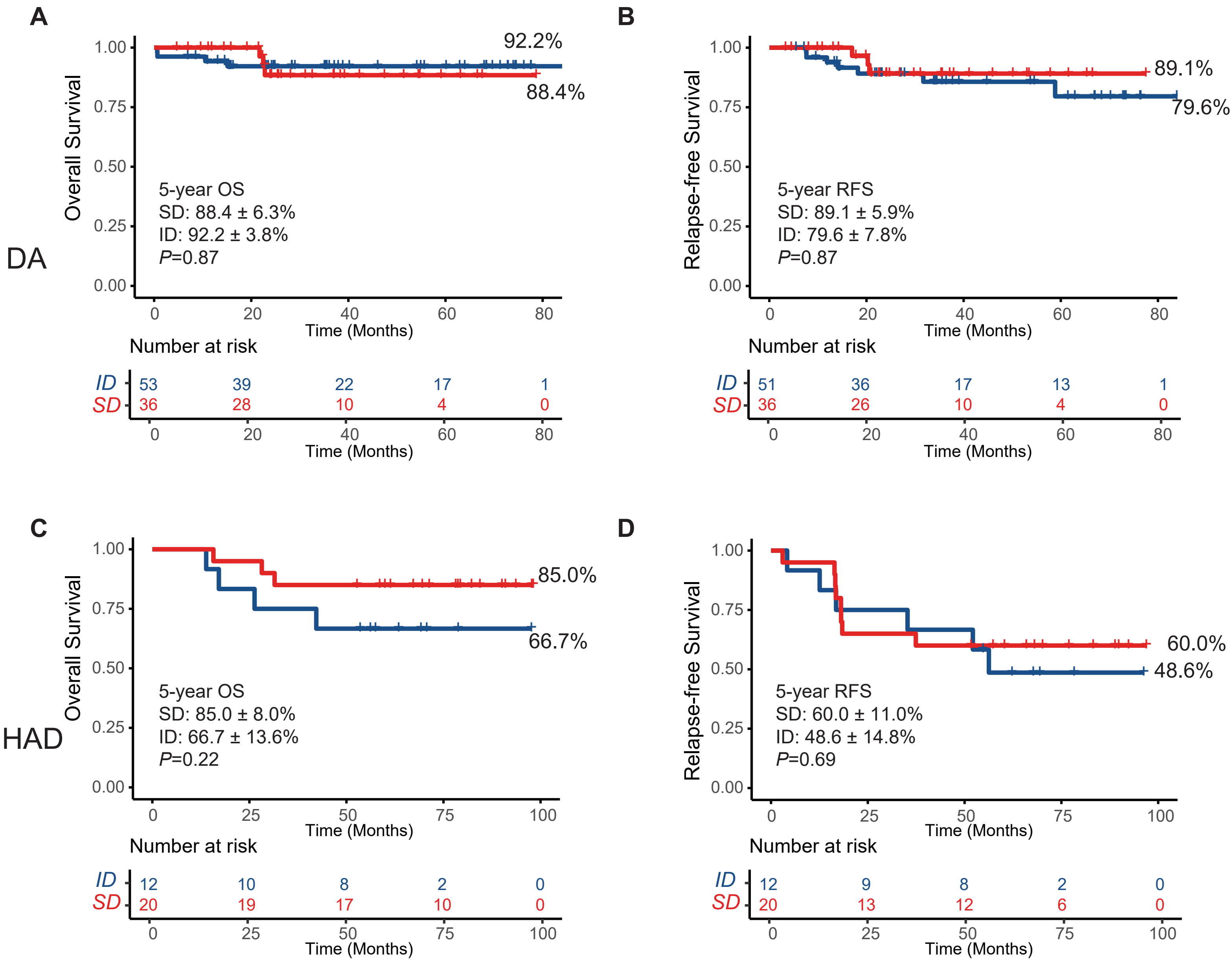


Figure S8. Outcomes of patients diagnosed as AML with *CBFB::MYH11* stratified by different levels of measurable residual disease (MRD). A is the cumulative incidence of relapse (CIR), B is overall survival (OS), and C is relapse-free survival (RFS). The red line represents patients with MRD reduction <2log, while the blue line represents patients with MRD reduction >2log.

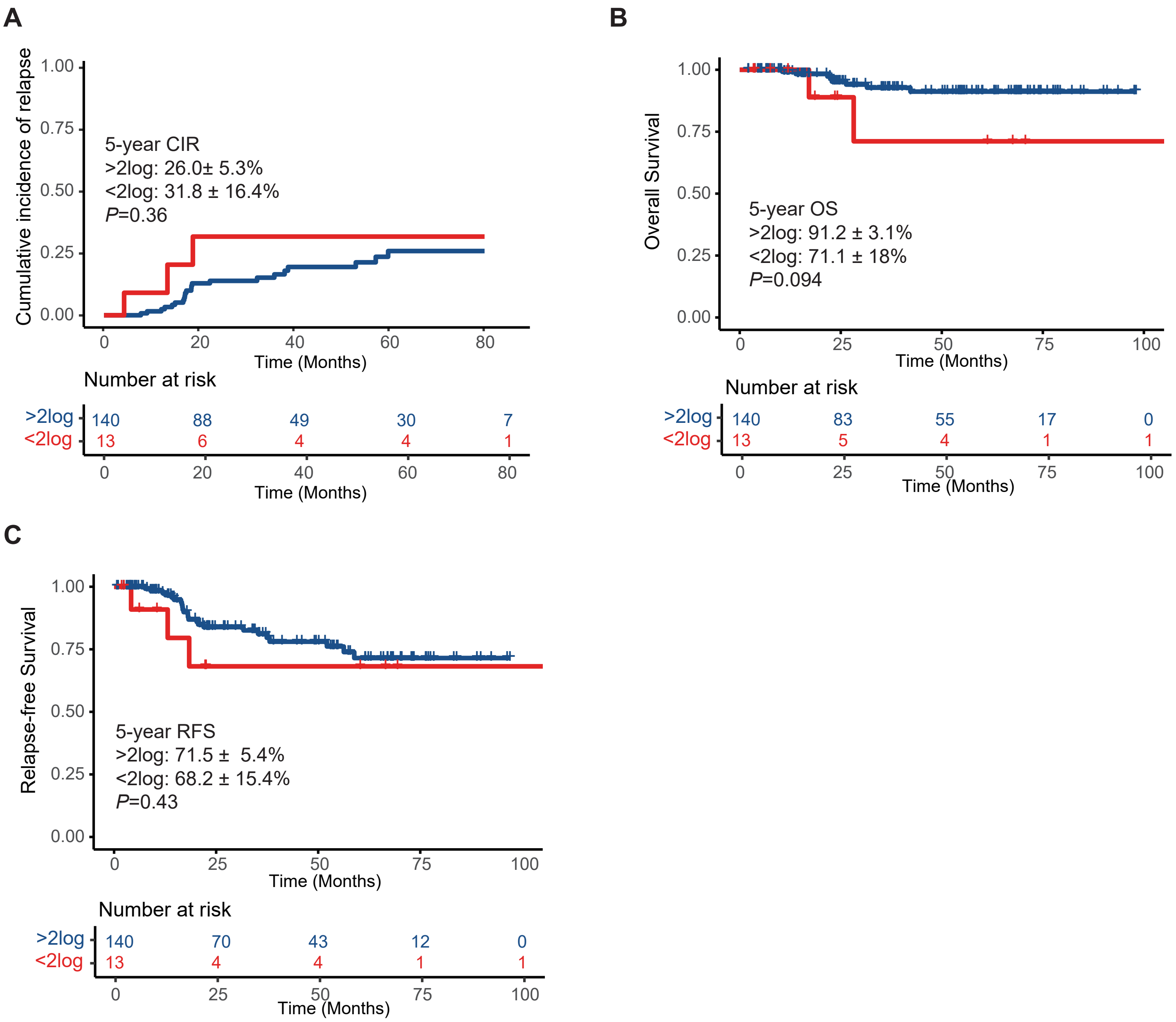


Figure S9. Outcomes of patients with *RUNX1::RUNX1T1* and *CBFB::MYH11* with or without hematopoietic stem cell transplantation (HSCT) by landmark analysis. A is overall survival (OS) and B is relapse-free survival (RFS). The sky blue line represents *CBFB::MYH11* patients with HSCT, the red line represents *CBFB::MYH11* patients without HSCT, the green line represents *RUNX1::RUNX1T1* patients with HSCT, and the blue line represents *RUNX1::RUNX1T1* without HSCT.

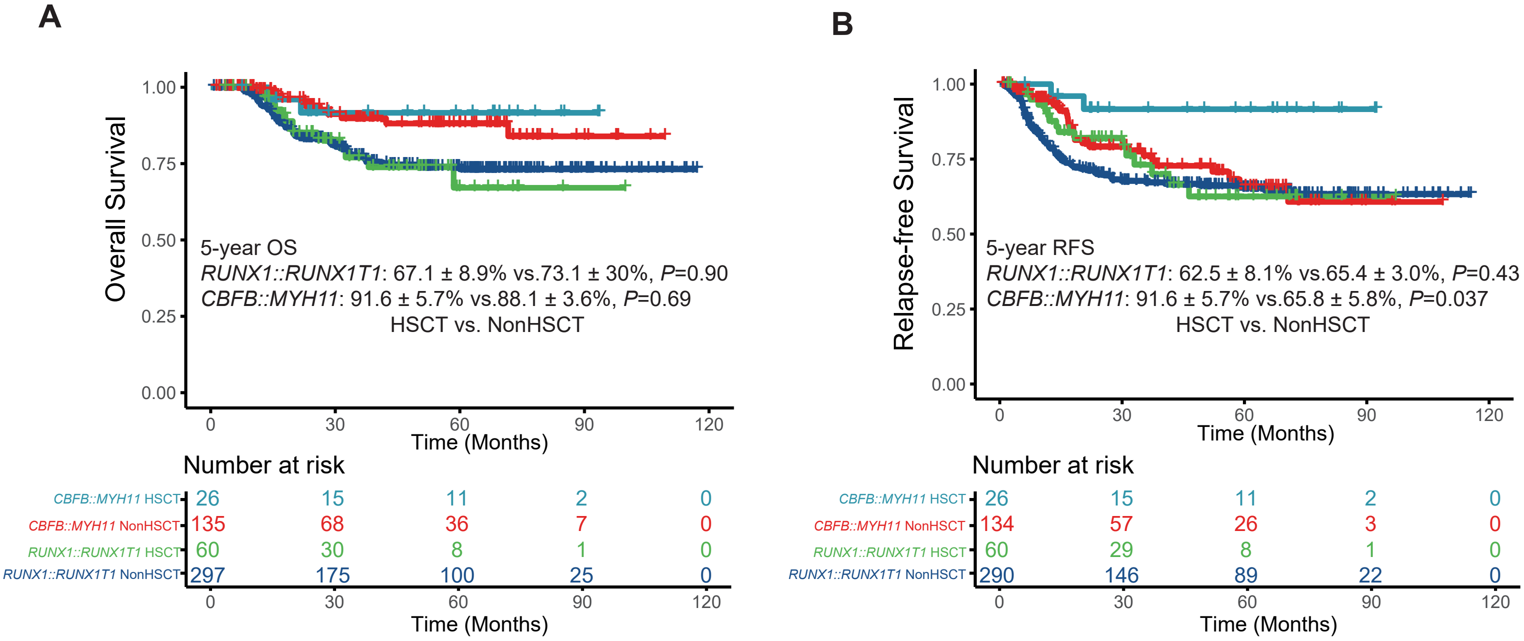


Figure S10. Outcomes of patients with *CBFB::MYH11* (A and B) and *RUNX1::RUNX1T1* (C and D) receiving hematopoietic stem cell transplantation (HSCT) or censored for HSCT. A and C are overall survival (OS). B and D are relapse-free survival (RFS). The blue line represents patients censored for HSCT, while the red line represents patients undergoing HSCT.

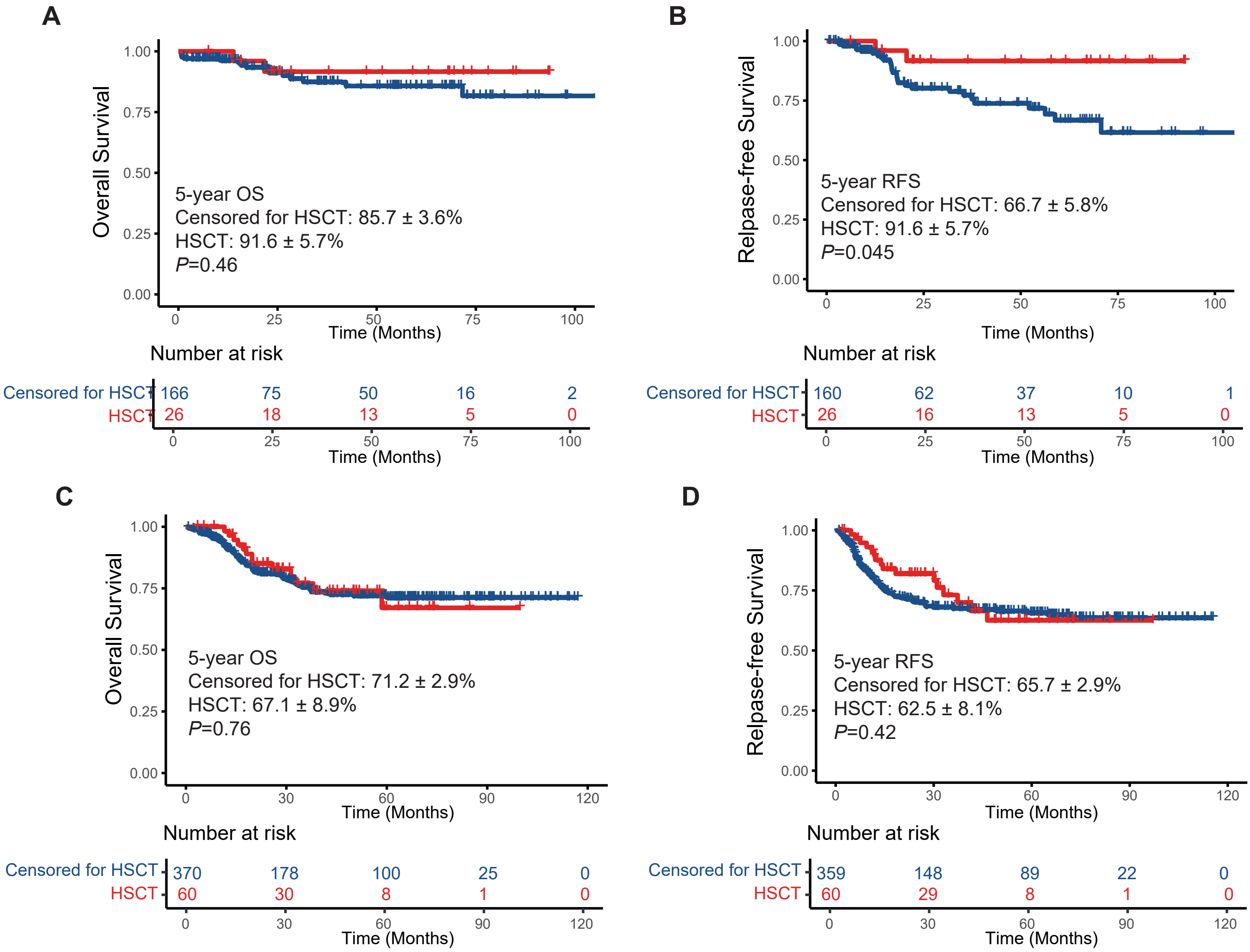
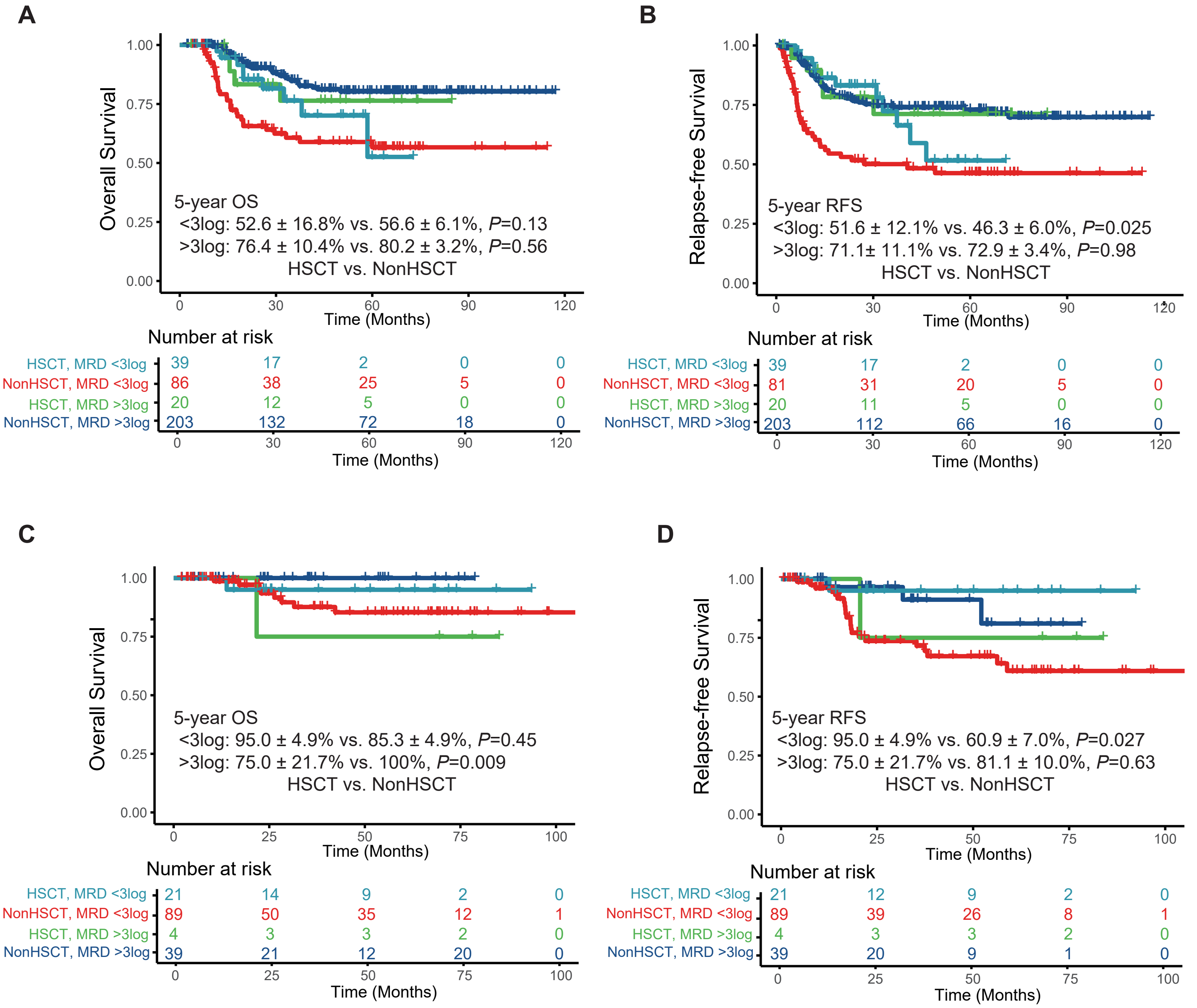


Figure S11. Outcomes of patients with *RUNX1::RUNX1T1* (A and B) and *CBFB::MYH11* (C and D) with or without hematopoietic stem cell transplantation (HSCT) in different measurable residual disease (MRD) status. A and C are overall survival (OS). B and D are relapse-free survival (RFS). The sky blue and red line represent MRD <3log patients with or without HSCT; the green line and blue line represent MRD >3log patients with or without HSCT.



A

5-year OS
<3log: 52.6 ± 16.8% vs. 56.6 ± 6.1%, *P*=0.13
>3log: 76.4 ± 10.4% vs. 80.2 ± 3.2%, *P*=0.56
HSCT vs. NonHSCT

Number at risk

	0	30	60	90	120
HSCT, MRD <3log	39	17	2	0	0
NonHSCT, MRD <3log	86	38	25	5	0
HSCT, MRD >3log	20	12	5	0	0
NonHSCT, MRD >3log	203	132	72	18	0

Time (Months)

B

5-year RFS
<3log: 51.6 ± 12.1% vs. 46.3 ± 6.0%, *P*=0.025
>3log: 71.1± 11.1% vs. 72.9 ± 3.4%, *P*=0.98
HSCT vs. NonHSCT

Number at risk

	0	30	60	90	120
HSCT, MRD <3log	39	17	2	0	0
NonHSCT, MRD <3log	81	31	20	5	0
HSCT, MRD >3log	20	11	5	0	0
NonHSCT, MRD >3log	203	112	66	16	0

Time (Months)

C

5-year OS
<3log: 95.0 ± 4.9% vs. 85.3 ± 4.9%, *P*=0.45
>3log: 75.0 ± 21.7% vs. 100%, *P*=0.009
HSCT vs. NonHSCT

Number at risk

	0	25	50	75	100
HSCT, MRD <3log	21	14	9	2	0
NonHSCT, MRD <3log	89	50	35	12	1
HSCT, MRD >3log	4	3	3	2	0
NonHSCT, MRD >3log	39	21	12	20	0

Time (Months)

D

5-year RFS
<3log: 95.0 ± 4.9% vs. 60.9 ± 7.0%, *P*=0.027
>3log: 75.0 ± 21.7% vs. 81.1 ± 10.0%, *P*=0.63
HSCT vs. NonHSCT

Number at risk

	0	25	50	75	100
HSCT, MRD <3log	21	12	9	2	0
NonHSCT, MRD <3log	89	39	26	8	1
HSCT, MRD >3log	4	3	3	2	0
NonHSCT, MRD >3log	39	20	9	1	0

Time (Months)

Figure S12. Outcomes of *RUNX1::RUNX1T1* patients with or without hematopoietic stem cell transplantation (HSCT) receiving intermediate-dose induction regimens in different measurable residual disease (MRD) level (MRD <2log: A-B; MRD >2log: C-D). The red line represents patients undergoing HSCT, while the blue line represents patients without HSCT. A and C are overall survival (OS), while B and D are relapse-free survival (RFS).

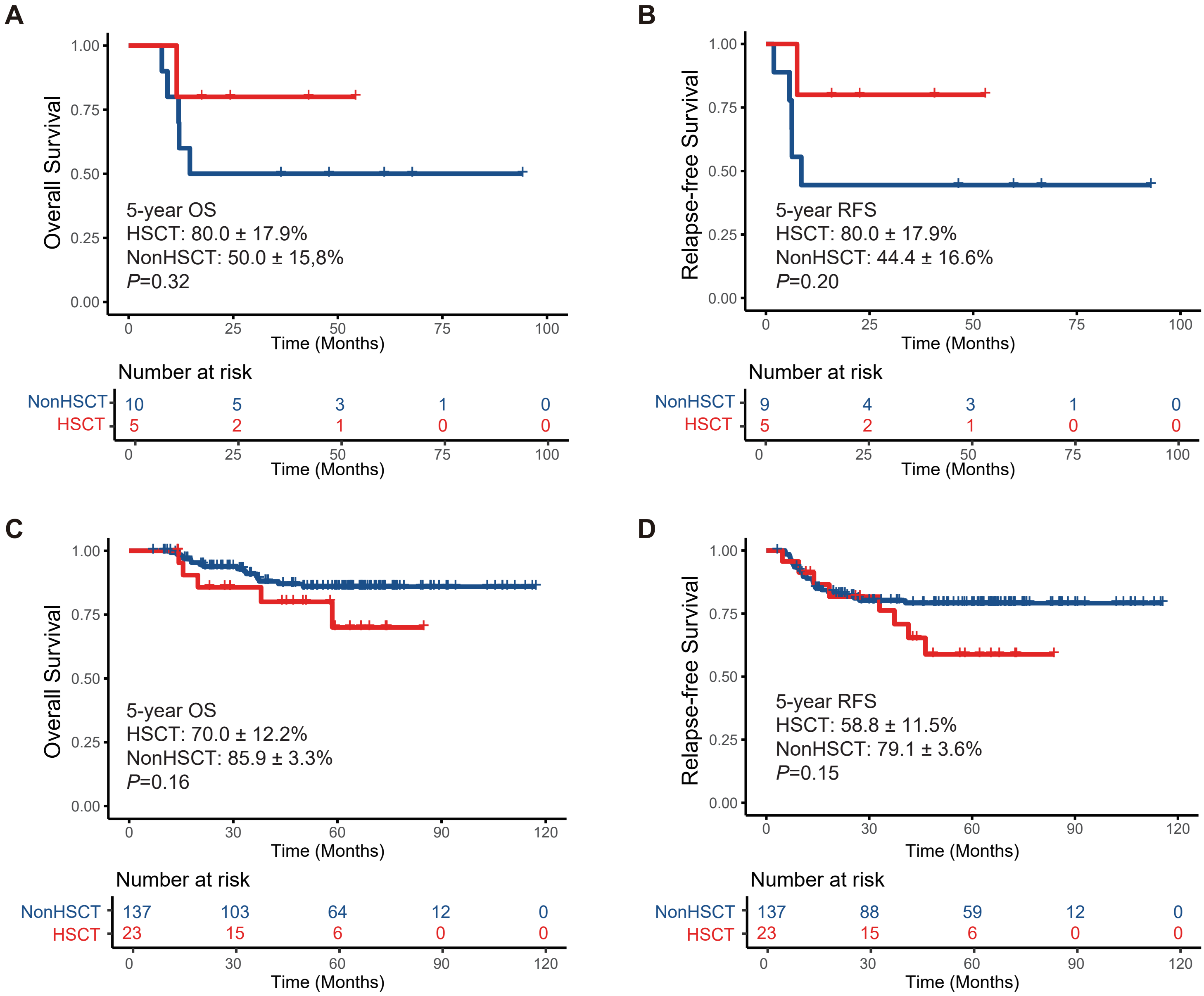


Figure S13. Outcomes of patients with *RUNX1::RUNX1T1* stratified by *KIT* mutations. A and B represent the absence or presence of *KIT* mutation in exon 17, while C and D represent mutation in exon 8. Red: with mutation; blue: without mutation. A, C: overall survival (OS); B, D: relapse-free survival (RFS).

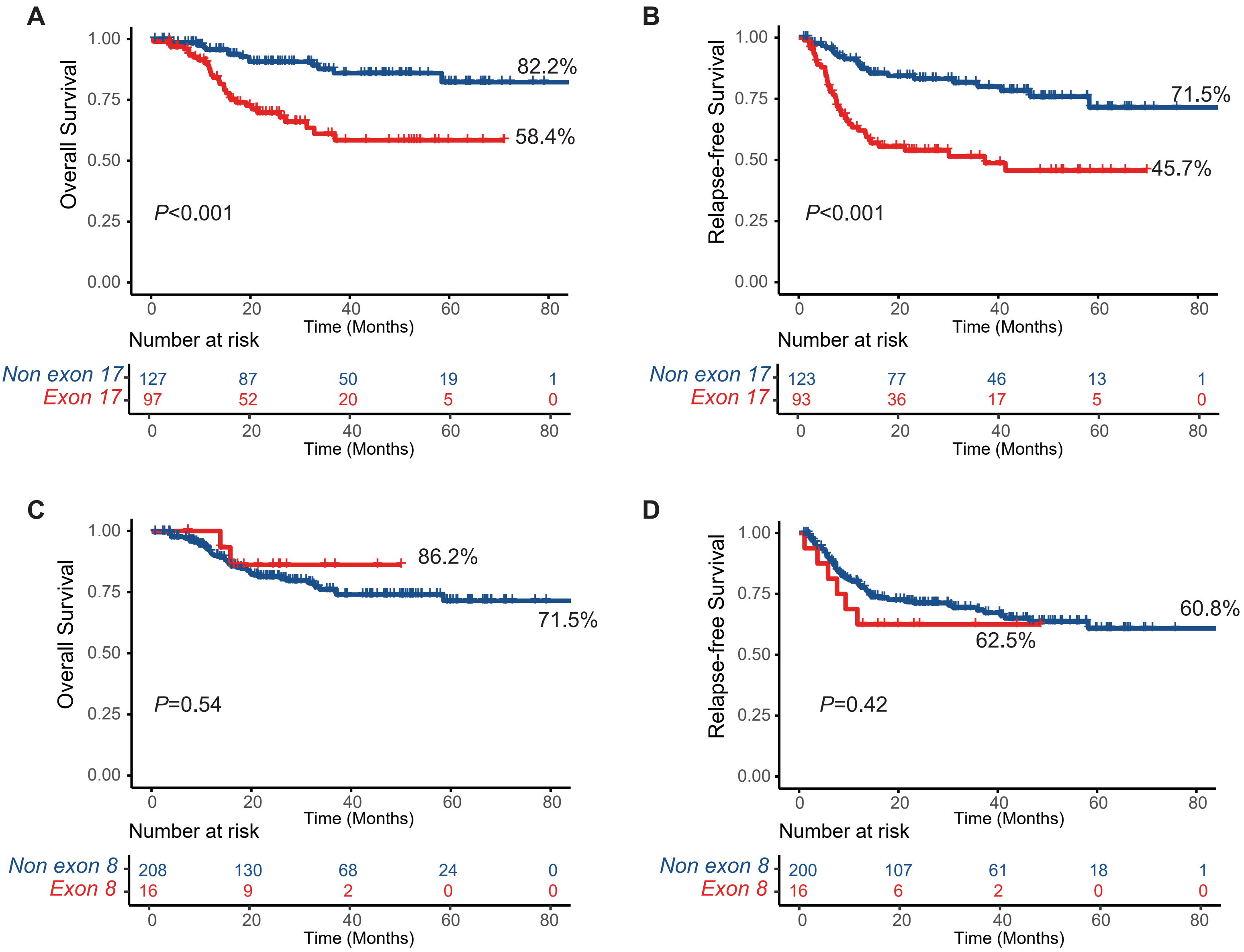


Figure S14. Outcomes of patients with *RUNX1::RUNX1T1* stratified by *KIT* mutations sites. A and B represent the absence or presence of *KIT* mutation in exon 17 D816 site; C and D represent mutation in exon 17 N822 site; C and D represent mutation in exon 8 D419 site. Red: with mutation; blue: without mutation. A, C, E: overall survival (OS); B, D, F: relapse-free survival (RFS).

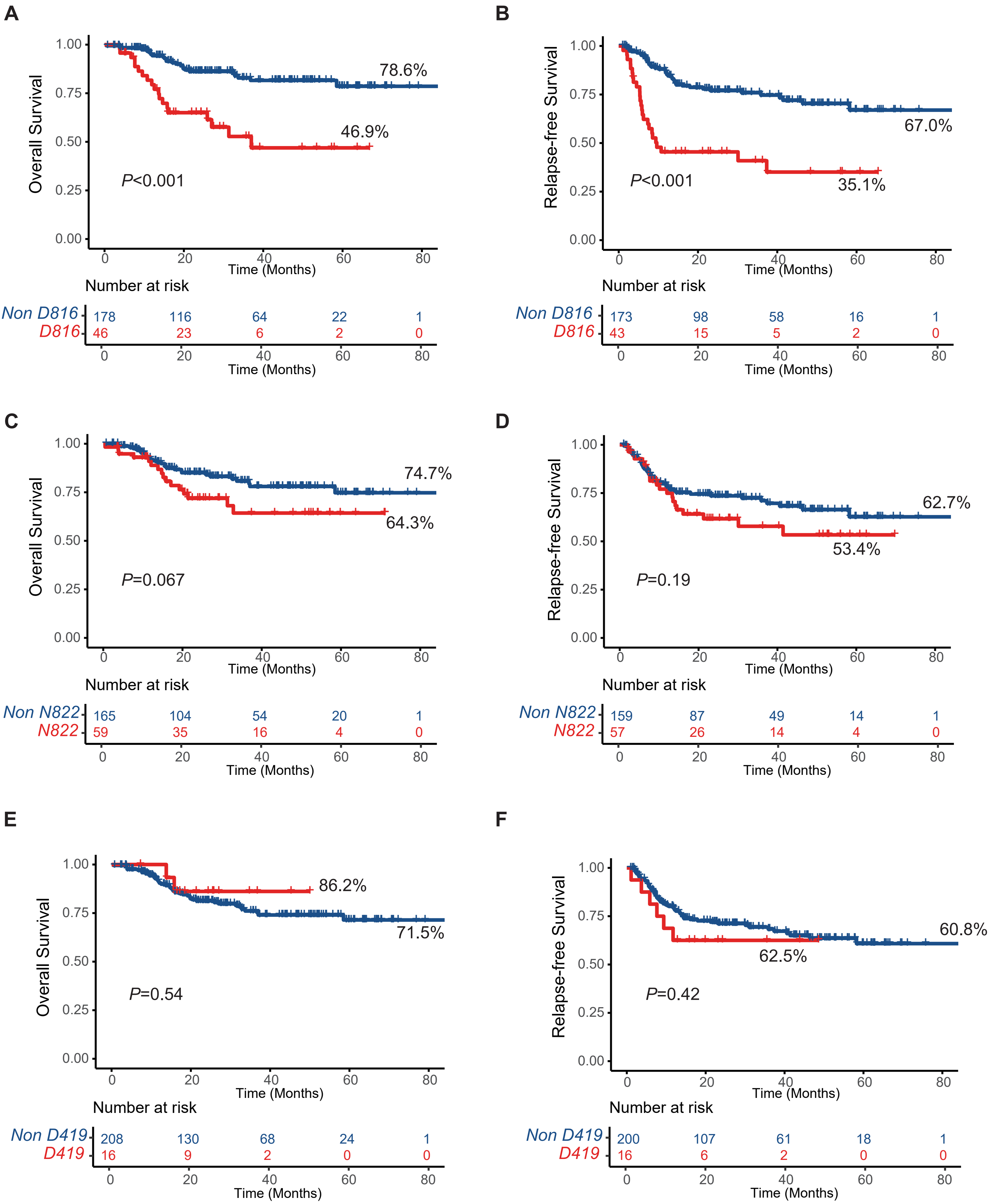


Table S1. Univariate Cox regression analysis results for genes with sample size more than ten patients in *RUNX1::RUNX1T1* or *CBFB::MYH11* group.

		OS		RFS	
		HR (95% CI)	*P*	HR (95% CI)	*P*
RUNX1::RUNX1T1	ASXL1	1.494 (0.629-3.548)	0.362	1.045 (0.451-2.424)	0.918
	ASXL2	0.762 (0.23-2.521)	0.656	0.244 (0.059-1.008)	0.051
	CSF3R	0.442 (0.061-3.214)	0.42	0.59 (0.144-2.413)	0.463
	FLT3	1.53 (0.755-3.1)	0.238	1.659 (0.93-2.957)	0.086
	KIT	2.813 (1.484-5.334)	0.002	2.858 (1.694-4.823)	<0.001
	KRAS	0 (0-Inf)	0.995	0.207 (0.029-1.491)	0.118
	NRAS	0.313 (0.112-0.876)	0.027	0.377 (0.172-0.828)	0.015
	RAD21	0.507 (0.07-3.692)	0.503	0.349 (0.048-2.514)	0.296
	TET2	3.798 (1.587-9.089)	0.003	3.573 (1.751-7.29)	<0.001
	ZBTB7A	0.436 (0.058-3.293)	0.421	0 (0-Inf)	0.997
CBFB::MYH11	FLT3	1.116 (0.288-4.318)	0.874	0.302 (0.038-2.388)	0.256
	KIT	0.395 (0.084-1.865)	0.241	0.674 (0.174-2.615)	0.569
	KRAS	1.077 (0.278-4.175)	0.914	0.261 (0.033-2.06)	0.203
	NRAS	1.254 (0.354-4.451)	0.726	0.327 (0.085-1.267)	0.106
	WT1	3.66 (0.764-17.535)	0.105	0 (0-Inf)	0.998

Abbreviation: CBF-AML, core binding factor acute myelogenous leukemia; OS, overall survival; RFS, relapse-free survival; HR, hazard ratio.