Supplemental Table 1. Comparison of therapeutic outcomes in FLT3-ITD-positive AML depending on allo-HSCT and AR

(A) Impact on RFS and OS of allo-HSCT and *FLT3*-ITD AR (Figure 3. B)

		allo-HSCT(+)							
		AR<0.5				AR≥0.5			
		MRD (days)	*p*	MST (days)	*p*	MRD (days)	*p*	MST (days)	*p*
allo-HSCT (-)	AR<0.5	NR vs 172	0.012	NR vs 207	<0.001	NR vs 172	0.785	367 vs 207	0.001
	AR≥0.5	NR vs 250	<0.001	NR vs 294	<0.001	NR vs 250	0.784	367 vs 294	0.002

Figures indicate cases with allo-HSCT(+) vs. without allo-HSCT(-)

(B) Impact on RFS and OS of allo-HSCT in CR1 and *FLT3*-ITD AR (Figure 4. A)

		allo-HSCT in CR1							
		AR<0.5				AR≥0.5			
		MRD (days)	*p*	MST (days)	*p*	MRD (days)	*p*	MST (days)	*p*
other cases¶	AR<0.5	NR vs 175	<0.001	NR vs 329	<0.001	NR vs 175	0.003	NR vs 329	0.002
	AR≥0.5	NR vs 124	<0.001	NR vs 334	<0.001	NR vs 124	<0.001	NR vs 334	<0.001

Figures indicate cases with allo-HSCT in CR1 vs. other cases

¶ : cases other than those with allo-HSCT in CR1 (incl. those not receiving allo-HSCT)

(C) Impact on RFS and OS of allo-HSCT in CR1 and *FLT3*-ITD AR with *NPM1* gene mutation (Figure 4. B)

		allo-HSCT in CR1							
		AR<0.5				AR≥0.5			
		MRD (days)	*p*	MST (days)	*p*	MRD (days)	*p*	MST (days)	*p*
other cases§	AR<0.5	NR vs 160	0.013	NR vs 329	0.003	NR vs 160	0.111	NR vs 329	0.038
	AR≥0.5	NR vs 146	<0.001	NR vs 294	<0.001	NR vs 146	0.036	NR vs 294	0.030

Figures indicate cases with allo-HSCT in CR1 vs. other cases

§ : cases other than those with allo-HSCT in CR1 (incl. those not receiving allo-HSCT)

allo-HSCT: allogenic hematopoietic transplantation; CR1: first complete remission; AR: allele ratio; MRD: median remission duration; MST: median survival time; NR: not reached.

Supplemental Table 2. Clinical background of the AML patients with *FLT3*-ITD low-AR (age<70 years)

Supplemental Table 2. Clinical background of the AML patients with *FLT3*-ITD low-AR (age<70 years)

		FLT3-ITD AR < 0.5		
	All (N=37)	allo-HSCT in CR1 (+) (N=15)	allo-HSCT in CR1 (-) (N=22)	*p* value
Age, median years (range)	53 (21-66)	51 (21-65)	54 (27-66)	0.446
Sex				
Male	19	9	10	0.508
Female	18	6	12	
ECOG-PS, 0/1/2/3/4	16/11/1/1/0	9/6/0/0/0	7/5/1/1/0	
WBC, median / μL (range)	59660 (1000-62000)	44600 (2700-620000)	63170 (1000-483000)	0.592
Hb, median g/dL (range)	8.7 (4.1-15.0)	9.7 (5.1-15.0)	8.0 (4.1-14.3)	0.016
Plt, median $\times 10^4$/μL (range)	5.3 (0.6-63.0)	5.2 (1.3-15.2)	5.8 (0.6-63.0)	0.428
LDH, median IU/L (range)	729 (151-5930)	496 (151-1923)	992 (227-5930)	0.046
FAB				
M1	14	7	7	0.493
M2	13	4	9	0.491
M4	7	2	5	0.474
M5	2	1	1	1.000
not determined	1	1	0	0.405
Chromosomal aberrations				
t(8,21)	1	0	1	1.000
inv(16)	1	0	1	1.000
normal	27	11	16	1.000
trisomy 8	0	0	0	1.000
11q23	0	0	0	1.000
complex	0	0	0	1.000
Unknown	5	2	3	1.000
Gene mutation				
FLT3-TKD	0	0	0	1.000
NPM1	23	8	15	0.493
CEBPA(sm)	3	1	2	1.000
CEBPA(dm)	2	2	0	0.158
Induction threrapy				
(IDA/DNR/ACR)+Ara-C	17	14	15	0.108
AVVV, BHAC-DM, CAG	5	0	7	0.028
Others	0	0	0	1.000

AML: acute myeloid reukemia; *FLT3*-ITD: *fms-like kinase 3*-internal tandem duplication; AR: allele ratio

ECOG-PS: Eastern Cooperative Oncology Group Performance Status; FLT3-TKD; fms-like kinase 3-tyrosine kinase domain;

NPM1: *nucleophosmin member1*; CEBPA: CCAAT/ enhancer-binding protein α;

sm: single mutation; dm: double mutation; IDA: idarubicin; DNR: daunorubicin; ACR: aclarubicin;

AraC: cytarabine; AVVV: cytarabine+etoposide+vincristine+vinblastine; BHAC-DM: enocitabine + daunorubicin + 6-mercaptopurine;

CAG: cytarabine+ cytarabine+granulocyte colony-stimurating factor; HU: hydroxyurea; CR1: first complete remission.

Note: some data are missing due to the unavailability of certain follow-up data in a retrospective study.

Supplemental Table 3. Clinical background of the AML patients positive for both *FLT3*-ITD low-AR and *NPM1* mutation (age<70 years)

		FLT3-ITD AR < 0.5 and *NPM1* mutation		
	All (N=19)	allo-HSCT in CR1 (+) (N=8)	allo-HSCT in CR1 (-) (N=11)	*p* value
Age, median years (range)	55 (26-66)	55 (26-64)	55 (27-66)	0.572
Sex				1.000
Male	9	4	5	
Female	10	4	6	
ECOG-PS, 0/1/2/3/4	9/5/1/0/0	5/3/0/0/0	4/2/1/0/0	
WBC, median / μL (range)	66200(1000-470500)	79650 (2700-176000)	49900 (1000-470500)	0.358
Hb, median g/dL (range)	9.0 (4.7-14.3)	9.4 (5.1-12.5)	8.8 (4.7-14.3)	0.533
Plt, median $\times 10^4$/ μL (range)	5.2 (1.1-15.2)	7.1 (1.3-15.2)	4.5 (1.1-10.8)	0.231
LDH, median IU/L (range)	738 (204-3788)	496 (204-805)	769 (227-3788)	0.207
FAB				
M1	10	4	6	1.000
M2	4	1	3	0.603
M4	3	2	1	0.566
M5	2	1	1	1.000
Chromosomal aberrations				
t(8,21)	0	0	0	1.000
inv(16)	0	0	0	1.000
normal	15	6	9	1.000
trisomy 8	0	0	0	1.000
11q23	0	0	0	1.000
complex	0	0	0	1.000
Unknown	3	1	2	1.000
Gene mutation				
FLT3-TKD	0	0	0	1.000
NPM1	19	8	11	1.000
CEBPA(sm)	0	0	0	1.000
CEBPA(dm)	0	0	0	1.000
Induction threrapy				0.103
(IDA/DNR/ACR)+Ara-C	15	8	7	
AVVV, BHAC-DM, CAG	4	0	4	
Others	0	0	0	

AML: acute myeloid reukemia; *FLT3*-ITD: *fms-like kinase 3*-internal tandem duplication; AR: allele ratio

ECOG-PS: Eastern Cooperative Oncology Group Performance Status; FLT3-TKD; fms-like kinase 3-tyrosine kinase domain;

NPM1: *nucleophosmin member1*; CEBPA: CCAAT/ enhancer-binding protein α;

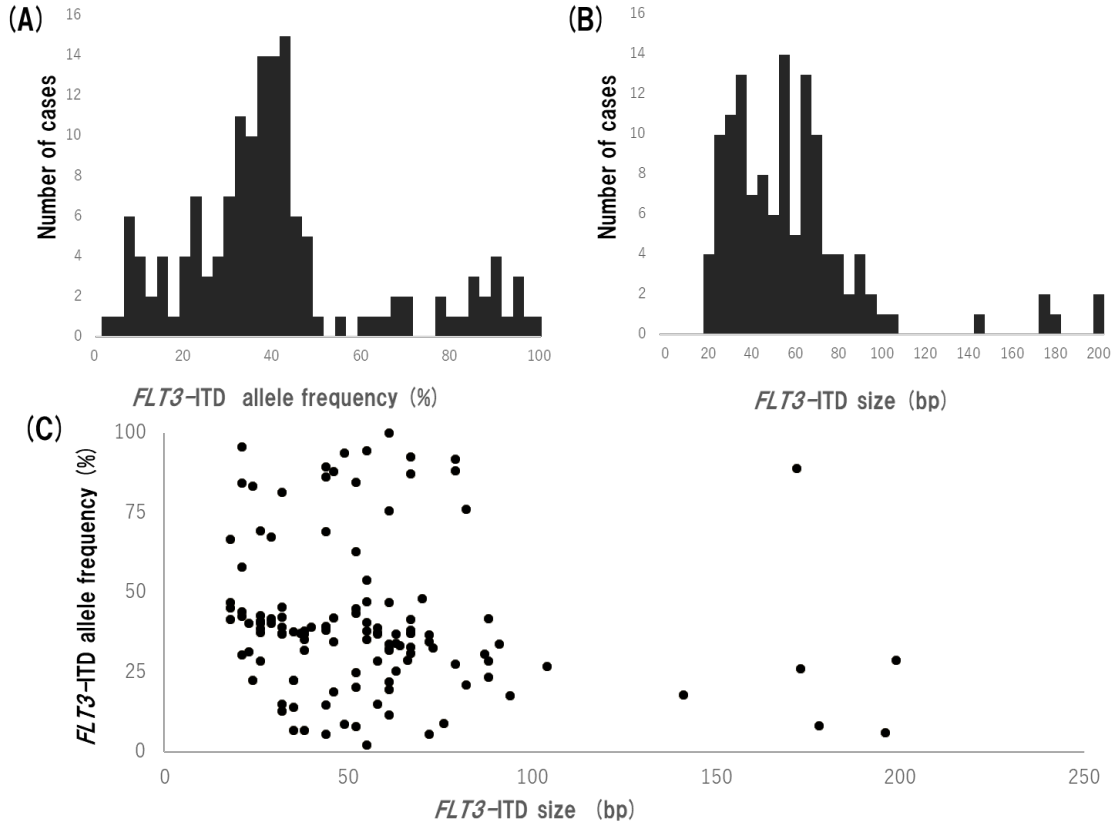
sm: single mutation; dm: double mutation; IDA: idarubicin; DNR: daunorubicin; ACR: aclarubicin;

AraC: cytarabine; AVVV: cytarabine+etoposide+vincristine+vinblastine; BHAC-DM: enocitabine + daunorubicin + 6-mercaptopurine;

CAG: cytarabine+ cytarabine+granulocyte colony-stimurating factor; HU: hydroxyurea; CR1: first complete remission.

Note: some data are missing due to the unavailability of certain follow-up data in a retrospective study.

Supplemental Figure 1. *FLT3*-ITD allele frequency and *FLT3*-ITD size

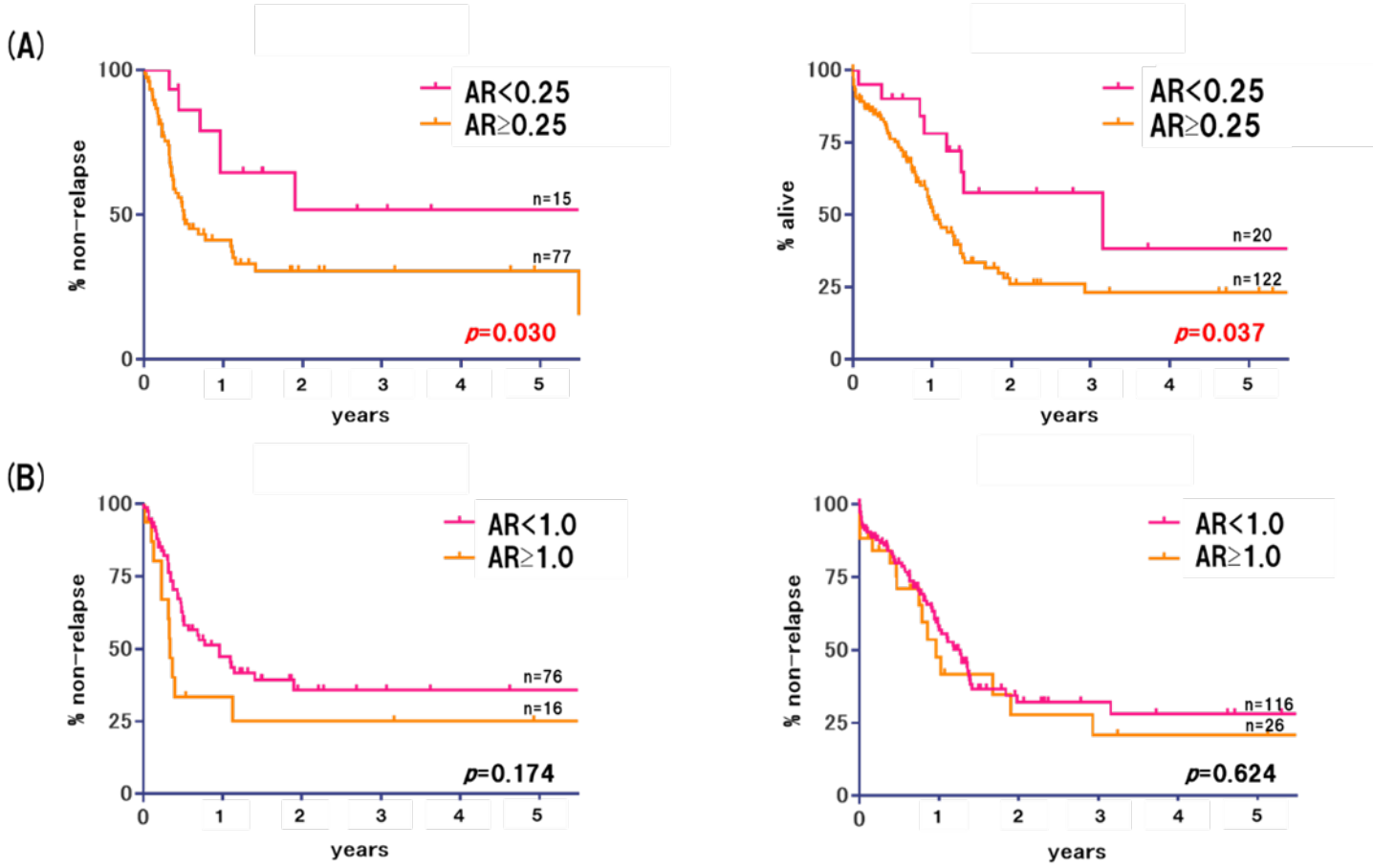


(A) Total *FLT3*-ITD allele frequency in 147 *FLT3*-ITD^{+} patients.

(B) *FLT3*-ITD size in 124cases with a single mutant.

(C) Correlation between *FLT3*-ITD allele frequency and size.

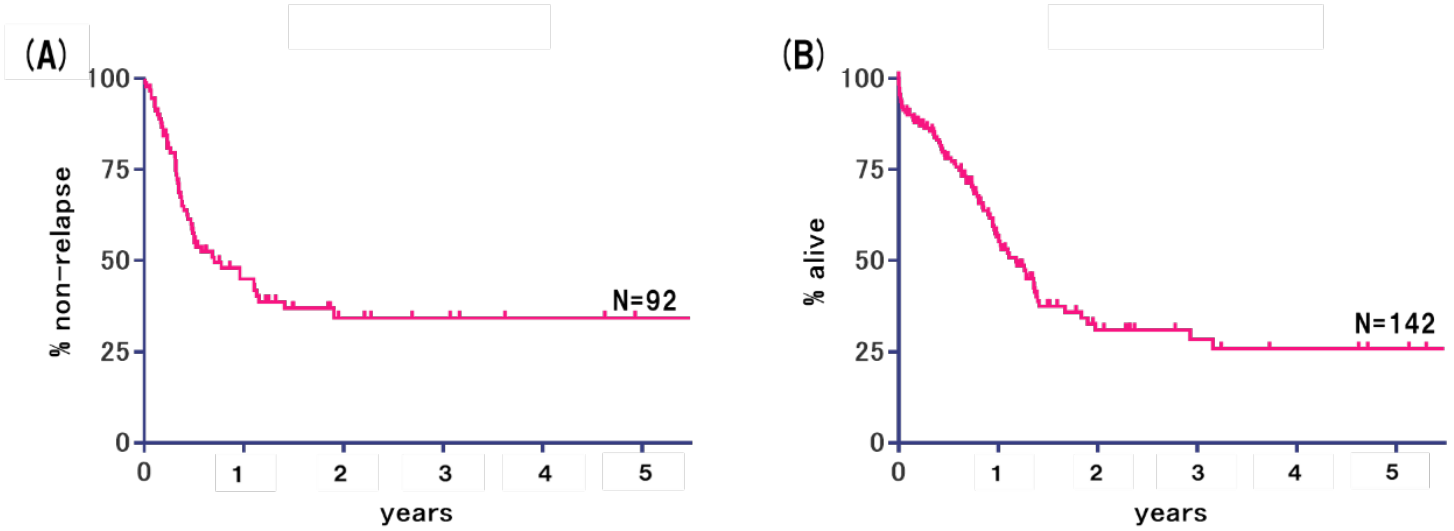
Supplemental Figure 2. Impact on RFS and OS of *FLT3*-ITD AR



(A) RFS(left) and OS(right) of *FLT3*-ITD AR cutoff value set at 0.25

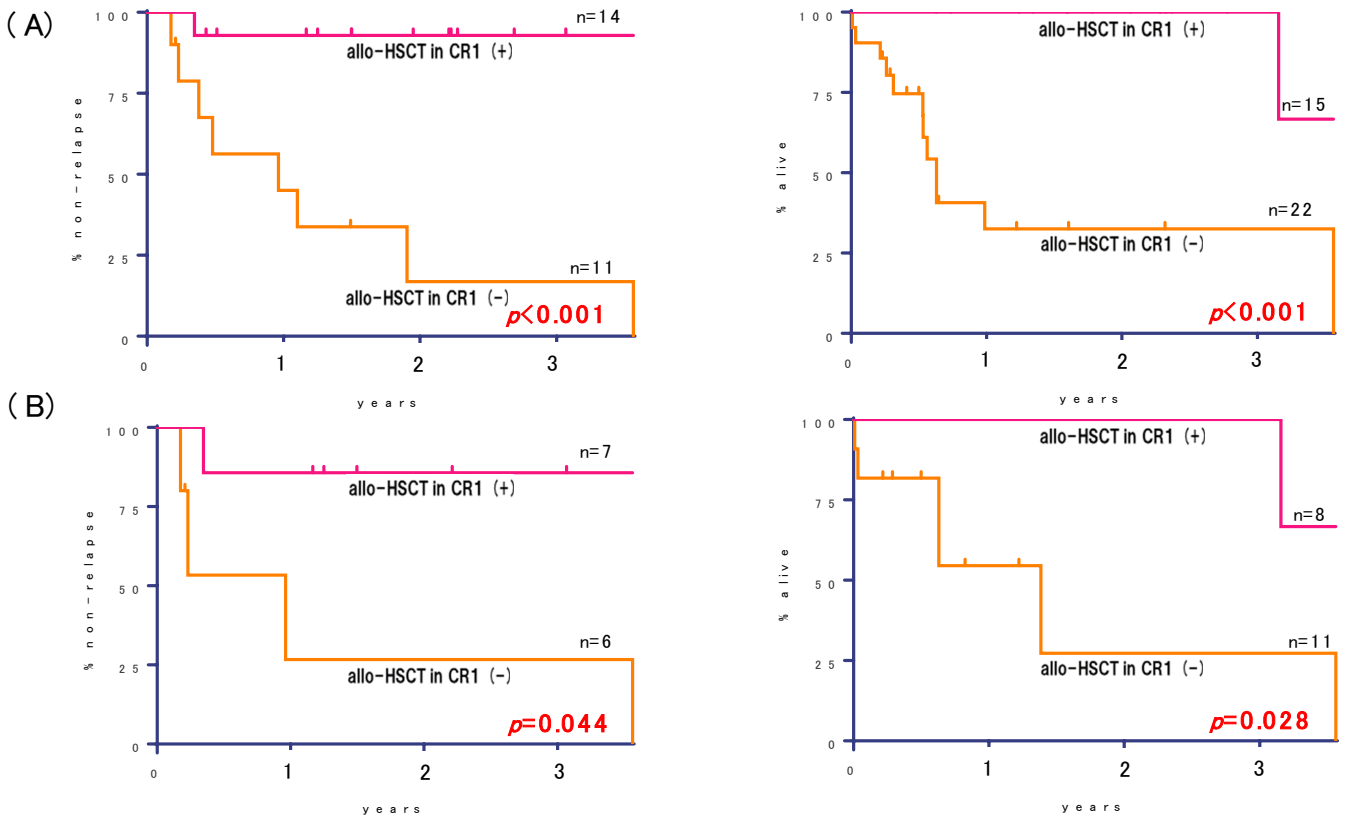
(B) RFS(left) and OS(right) of *FLT3*-ITD AR cutoff value set at 1.00

Supplemental Figure 3. Impact on RFS and OS of *FLT3*-ITD-positive AML patients



(A) RFS (B) OS

Supplemental Figure 4. Prognostic impact of allo-HSCT in CR1 in patients aged below 70 years with low-AR *FLT3-ITD*



(A) RFS (left) and OS (right)

(B) NPM1 mutation-positive cases: RFS (left) and OS (right)