Supplementary Materials

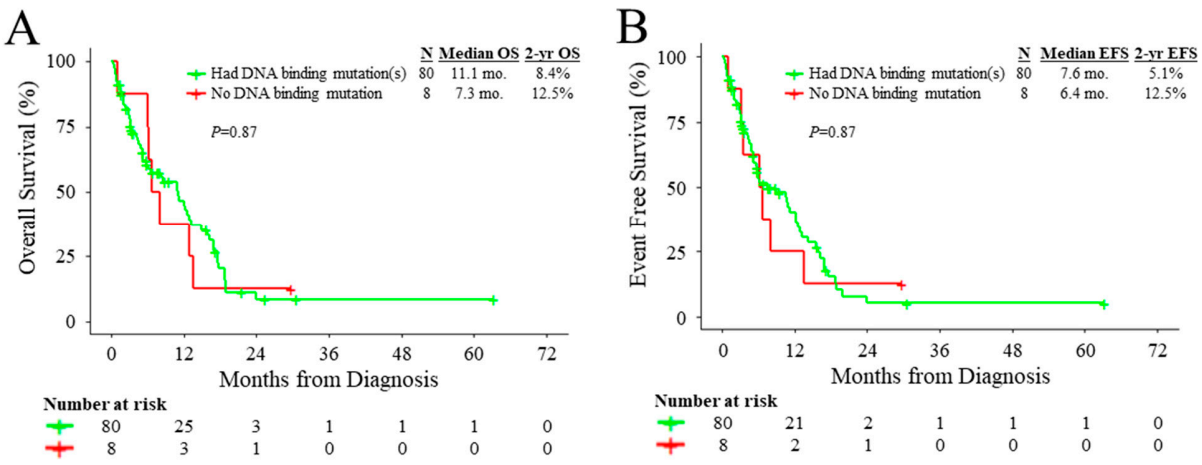
Intensive induction dosage

FLAG-IDA: G-CSF 300 µg daily day 0-5, Idarubicin 10 mg/m^2 daily day 1-3, Fludarabine 30 mg/m^2 daily day 1-5, Cytarabine 2 g/m^2 daily day 1-5

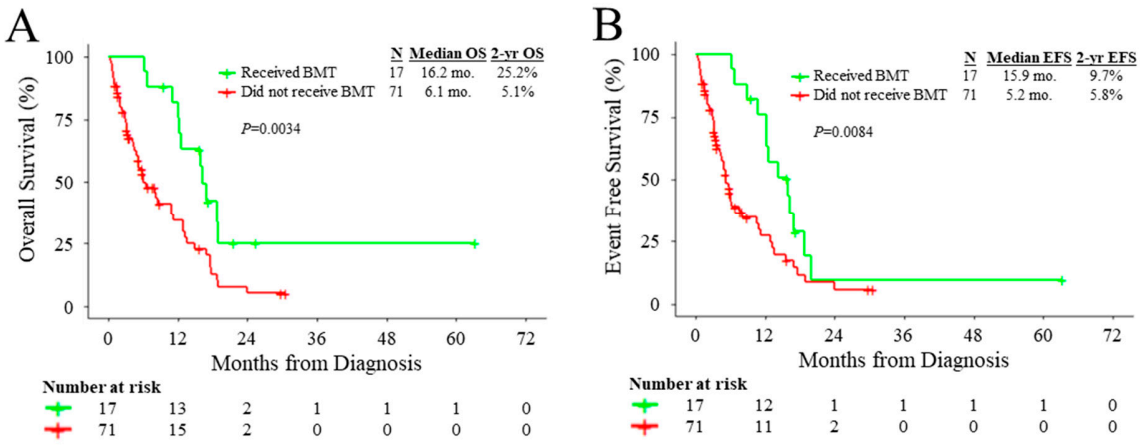
7+3: Daunorubicin 60 mg/m^2 daily day 1-3, Cytarabine 200 mg/m^2 daily day 1-7, Cytarabine dose reduction to 100 mg/m^2 for patients age > 60 years

CPX-351 (Vyxeos): 44 mg/m^2 day 1, 3 and 5

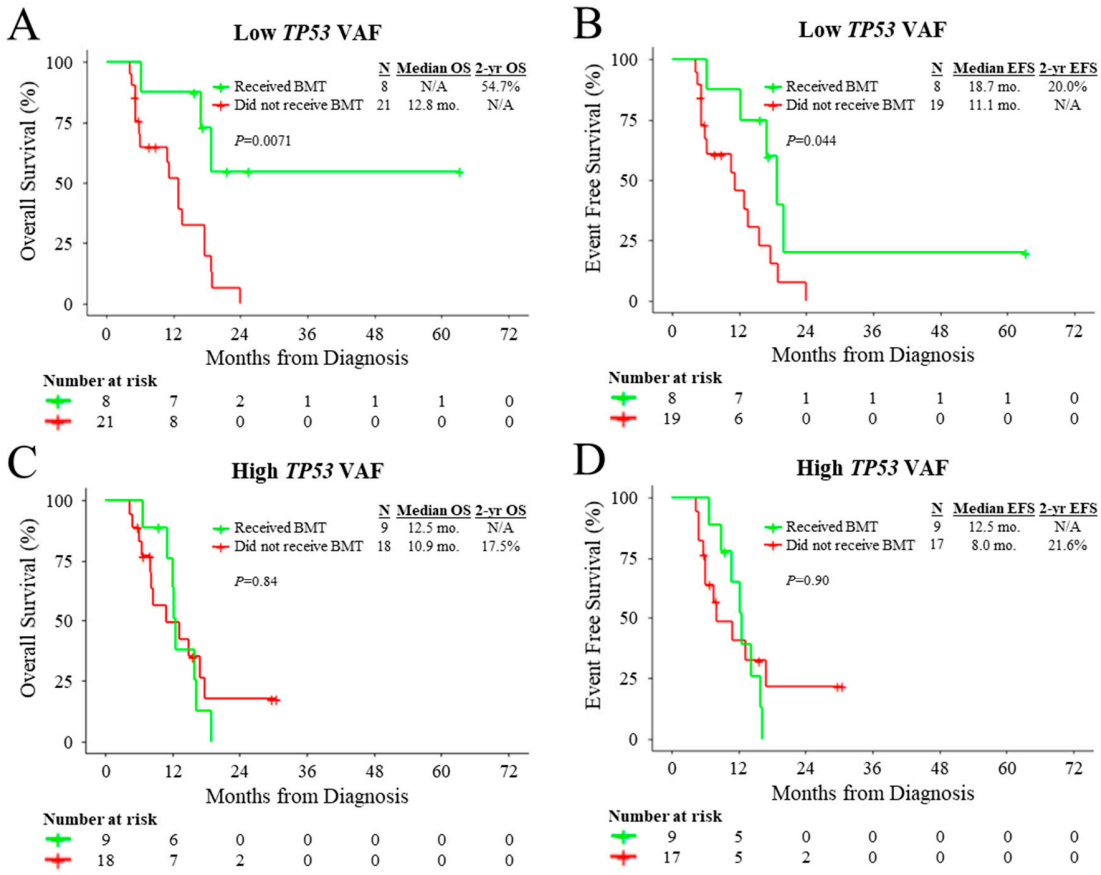
Supplementary Figure S1. (A) OS and (B) EFS of treated *TP53*^{MUT} patients stratified by presence or absence of *TP53* mutation within its DNA binding domain (amino acids 95-288).



Supplementary Figure S2. (A) OS and (B) EFS of all treated *TP53*^{MUT} patients stratified by allo-HCT status.



Supplementary Figure S3. (A-B) Landmark analysis for OS and EFS for patients with low *TP53* VAF (< 45%) stratified by allo-HCT status. (C-D) Landmark analysis for OS and EFS for patients with high *TP53* VAF (≥ 45%) stratified by allo-HCT status.



Supplementary Table S1. Gene panel for targeted sequencing	
Complete coding region coverage (13/41)	**Hotspot coverage (28/41)**
BCOR	*ASXL1*
BCORL1	*BRAF*
CEBPA	*CALR*
CUX1	*CBL*
DNMT3A	*CSF3R*
ETV6	*FBXW7*
EZH2	*FLT3*
IKZF1	*GATA2*
PHF6	*GNAS*
RAD21	*IDH1*
RUNX1	*IDH2*
STAG2	*JAK2*
ZRSR2	*KIT*
	KMT2A
	KRAS
	MPL
	MYD88
	NOTCH1
	NPM1
	NRAS
	PTPN11
	SETBP1
	SF3B1
	SRSF2
	TET2
	TP53
	U2AF1
	WT1

Supplementary Table S2. Exon coverage for hotspot genes	
Gene	**Exon Coverage**
ASXL1	12
BRAF	15
CALR	9
CBL	8, 9
CSF3R	14-17
FBXW7	9-11
FLT3	14, 15, 20
GATA2	2-6
GNAS	8, 9
IDH1	4
IDH2	4
JAK2	12, 14
KIT	2, 8-11, 13, 17
KMT2A	5-8
KRAS	2,3
MPL	10
MYD88	3-5
NOTCH1	26-28, 34
NPM1	12
NRAS	2, 3
PTPN11	3, 13
SETBP1	4
SF3B1	13-16
SRSF2	1
TET2	3-11
TP53	2-11
U2AF1	2, 6
WT1	7, 9

Supplemental Table S3. Summary of additional clinicopathological features	
Clinical feature	
AML subtype (WHO-HAEM4), *n*	
AML with myelodysplasia-related changes	92
Therapy-related AML	13
AML, NOS	3
AML with mutated *NPM1*	2
AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2*, *MECOM*	1
AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*	1
AML with mutated *RUNX1* (provisional entity)	1
Co-mutations, *n* (VAF range)	
DNMT3A	17 (5-44)
IDH1	11 (6-39)
TET2	8 (5-46)
JAK2	5 (7-48)
CEBPA	4 (10-97)
RUNX1	4 (22-54)
ASXL1	4 (19-31)
IDH2	4 (36-44)
BCOR	3 (6-44)
CUX1	3 (7-34)
NPM1	3 (4-30)
NRAS	3 (10-40)
SF3B1	3 (31-42)
SRSF2	3 (39-46)
U2AF1	3 (19-43)
STAG2	2 (18-29)
CALR	2 (15-32)
FLT3	2 (5-13)
KIT	2 (24-49)
KRAS	2 (12-19)
MPL	2 (17-36)
PTPN11	2 (34-34)
BCORL1	1 (39)
ETV6	1 (17)
EZH2	1 (52)
CSF3R	1 (5)
FBXW7	1 (8)
GATA2	1 (6)
GNAS	1 (8)
NOTCH1	1 (51)
WT1	1 (54)
Common cytogenetic abnormalities, *n*	
Complex karyotype	95
-5/del(5q)	69
-7/del(7q)	52
-17/del(17p)/dic(17p)	49