

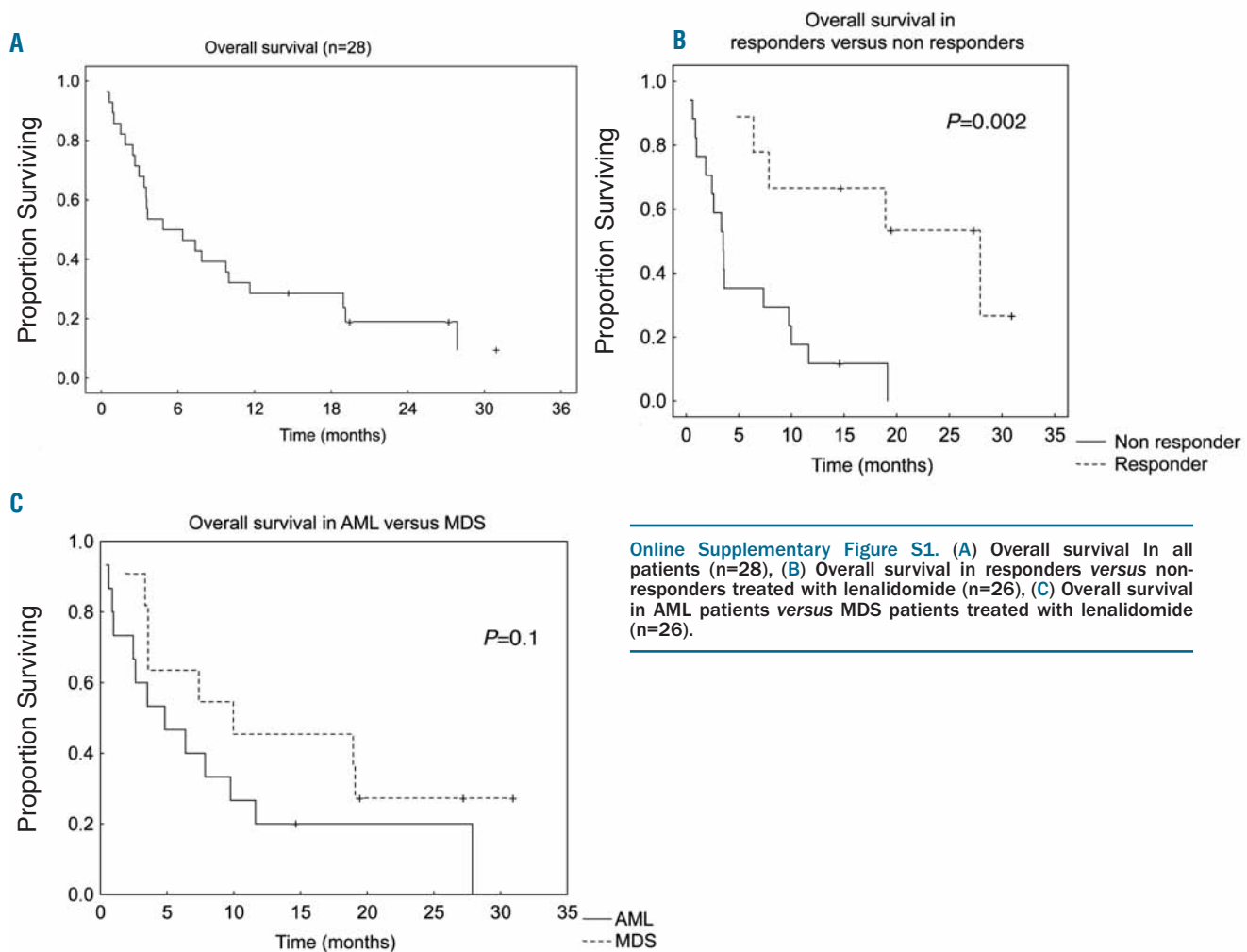
Clinical effect of increasing doses of lenalidomide in high-risk myelodysplastic syndrome and acute myeloid leukemia with chromosome 5 abnormalities

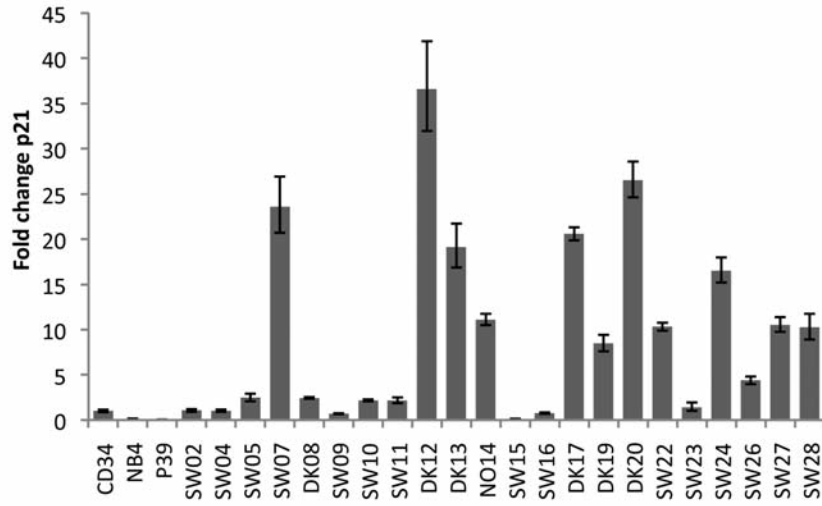
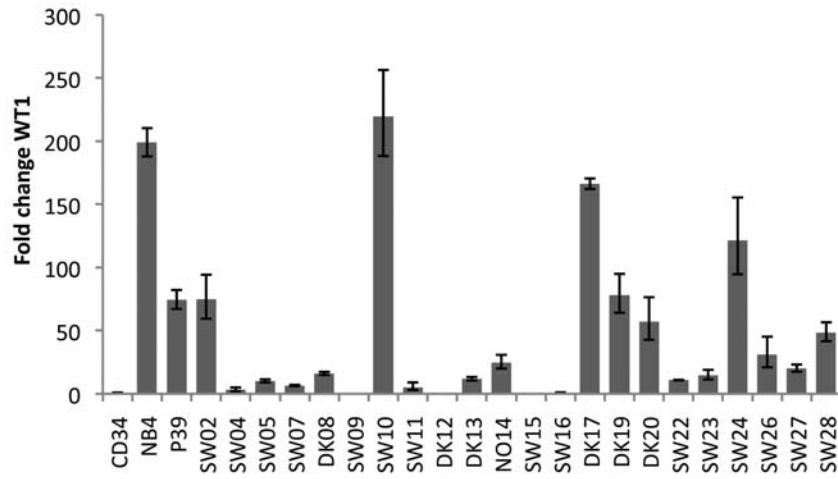
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A**B**

Supplementary Figure 2. Expression of p21 (A) and WT1 (B), as determined by reverse transcriptase quantitative PCR, in CD34⁺ bone marrow cells. Fold change compared to normal CD34⁺ cells from healthy normal donors. NB4: human acute promyelocytic leukemia. P39: human myelomonocytoid cell line.

Online Supplementary Table S1. Characteristics of all 28 patients included in the trial.

N.	Sex	Age	AML/ MDS	Cytogenetics		Response*	Bone marrow blasts %		Bone marrow FISH %		P53** expression %**		P53 mutated		P53 mutation	Effect of P53 mutation ***	WT1**** wk 1	p21**** wk 1
							wk 1	wk 16	wk 1	wk 16	wk 1	wk 16	wk 1	wk 16				
1	F	61	AML	5q-	ND		20	-	77	-	-	-	Yes	-	TAG>TGC	Y234C ms	-	-
2	F	69	AML	5q-	+≥2 abn		75	-	93	-	15	-	Yes	-	CAG>CCG	Q144P ms	74.9	1.05
3	F	63	AML	5q-	isolated	BM CR	20	5	65	90	0	0	-	-			-	-
4	F	71	MDS	-5	+≥2 abn		-	-	88	-	-	-	Yes	-	CAT>GAT	H193D ms	3.2	1.03
5	F	71	AML	5q-	+≥2 abn	Minor	28	21	83	46	0	0	No	No			10.1	2.46
6	F	51	AML	5q-	+≥2 abn		20	-	88	-	1	51	-	-			-	-
7	M	78	MDS	5q-	+≥2 abn		2	-	7	-	-	-	No	No			6.5	23.6
8	M	65	AML	-5	+≥2 abn		49	-	70	-	29	-	Yes	-	ATC>AGC	I254S ms	16.0	2.45
9	F	48	MDS	5q-	+1 abn	Major	9.5	4	81	12	0	0	No	-			0	0.71
10	M	61	AML	5q-	+≥2 abn		60	-	94	-	0	-	Yes	-	c.624del2(AG)	fs(S215X)	220	2.17
11	M	58	MDS	5q-	+≥2 abn		8	-	77	-	0	-	Yes	-	c.574 ins1(A)	fs(D208X)	5.13	2.16
12	M	75	MDS	5q-	+1 abn		11	-	51	-	19	-	Yes	-	TAT>TGT	Y220C ms	0	36.6
13	F	62	MDS	-5	+≥2 abn		7	-	92	-	26	-	Yes	-	CGC>CCC, c.673-2A>G	R283P ms Splice def.	11.9	19.1
14	F	72	AML	5q-	+≥2 abn		84	-	78	-	64	-	Yes	-	CCG>CAG	R248Q ms	24.8	11.1
15	F	78	MDS	-5	+≥2 abn		8	-	76	-	31	-	Yes	-	CAT>AAT	H179N ms	0	0.11
16	F	85	MDS	5q-	+≥2 abn	BM CR [§]	10	3.5	26	69	49	19	Yes	Yes	CGC>CAC	R175H ms	0.7	0.76
17	F	73	AML	5q-	+≥2 abn		20	-	82	-	0	-	No	-			166	20.5
18	F	57	MDS	5q-	+≥2 abn	Major	2	3	55	14	0	-	No	-			-	-
19	F	66	AML	5q-	+1 abn		75	-	45	-	65	-	Yes	-	ATG>ATA c.526ins(C)	M237I ms Fs(E180X)	78.0	8.46
20	F	69	MDS	5q-	+≥2 abn		15	-	80	-	0	-	Yes	-	GGA>GTA	G266V ms	57.2	26.5
21	F	58	MDS	5q-	+≥2 abn	Minor	10	15	60	38	13	29	-	-			-	-
22	M	74	MDS	5q-	+1 abn		5.5	1	93	83	-	49	Yes	-	TCC>TAC	S241Y ms	10.8	10.3
23	F	77	AML	5q-	+≥2 abn	Major	62.5	22	93	32	50	64	Yes	Yes	GAA>GAC	E258D ms ^{§§}	14.7	1.41
24	F	84	MDS	5q-	isolated	Major	15	-	93	6	2	0	No	-			121	16.5
25	M	69	AML	5q-	+1 abn		20	-	57	-	0	-	-	-			-	-
26	F	87	AML	5q-	isolated		70	-	98	-	1	-	No	-			30.8	4.37
27	F	62	MDS	5q-	+1 abn		41	-	91	-	1	-	No	-			20.1	10.5
28	F	70	AML	5q-	+≥2 abn	Major	35	2.5	70	12	1	0	No	No			48.5	10.2

MDS: myelodysplastic syndrome; AML: acute myeloid leukemia; wk: week; abn: abnormality/abnormalities; WT1: Wilms' tumor 1; -: not done; ms: missense mutation; fs: frame shift mutation. *Cytogenetic response (major or minor) assessed by FISH. **p53 protein expression by immunohistochemistry was assessed as 0, no expression, weak (light brown staining) suggestive of activation of normal p53 function, and strong (dark nuclear staining) suggestive of a TP53 mutation. Only the percentage of strong p53 (p53**) staining is given in the Table. ***Effect of the mutation is listed as: the normal amino acid, codon number, the new amino acid. X means stop codon. ****WT1 and p21 mRNA expression was assessed in selected CD34+ bone marrow cells. Fold change compared to normal CD34+ cells. §Bone marrow with fewer blasts but increasing TP53 mutant clone is increasing. §§Conservative amino acid substitution.

Online Supplementary Table 2. Summary of adverse events.

Adverse Events	AML		MDS		Total	
	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4
Infection	7	8	3	5	10	13
Thrombocytopenia	2	3	2	4	4	7
Neutropenia	0	3	3	3	3	6
Skin rash	4	1	1	2	5	3
Abdominal pain	4	1	0	1	4	2
CNS hemorrhage	0	1	0	1	0	2
Thromboembolism	0	0	1	1	1	1
Syncope	0	1	0	1	1	1
Athritis	0	1	0	0	0	1
Bleeding or hematoma	0	1	2	0	2	1
Lesion in oral cavity	1	1	0	0	1	1
Diarrhea	4	0	4	0	8	0
Musculoskeletal pain	4	0	3	0	7	0
Fatigue	3	0	4	0	7	0
Abnormal liver enzymes	1	0	2	0	3	0
Allergic reaction	1	0	1	0	2	0
Dyspnea	2	0	0	0	2	0
Dizziness	1	0	1	0	2	0
Sweating	1	0	1	0	2	0
Edema of lower extremities	2	0	0	0	2	0
Headache	1	0	1	0	2	0
Dry skin	1	0	1	0	2	0
Constipation	0	0	2	0	2	0
Hypothyroidism	0	0	1	0	1	0
Gastritis	1	0	0	0	1	0
Vomiting	1	0	0	0	1	0
Weight loss	1	0	0	0	1	0
Fever	1	0	0	0	1	0
Urinary frequency	1	0	0	0	1	0
Heart palpitations	1	0	0	0	1	0
Hematuria	1	0	0	0	1	0
Dry eyes	0	0	1	0	1	0
Low potassium	1	0	0	0	1	0
Hypocalcemia	0	0	1	0	1	0
Nausea	0	0	1	0	1	0
Fracture of right arm	0	0	1	0	1	0
Atrial fibrillation	1	0	0	0	1	0
Seizure	1	0	0	0	1	0