

Phase I study of sorafenib in patients with refractory or relapsed acute leukemias

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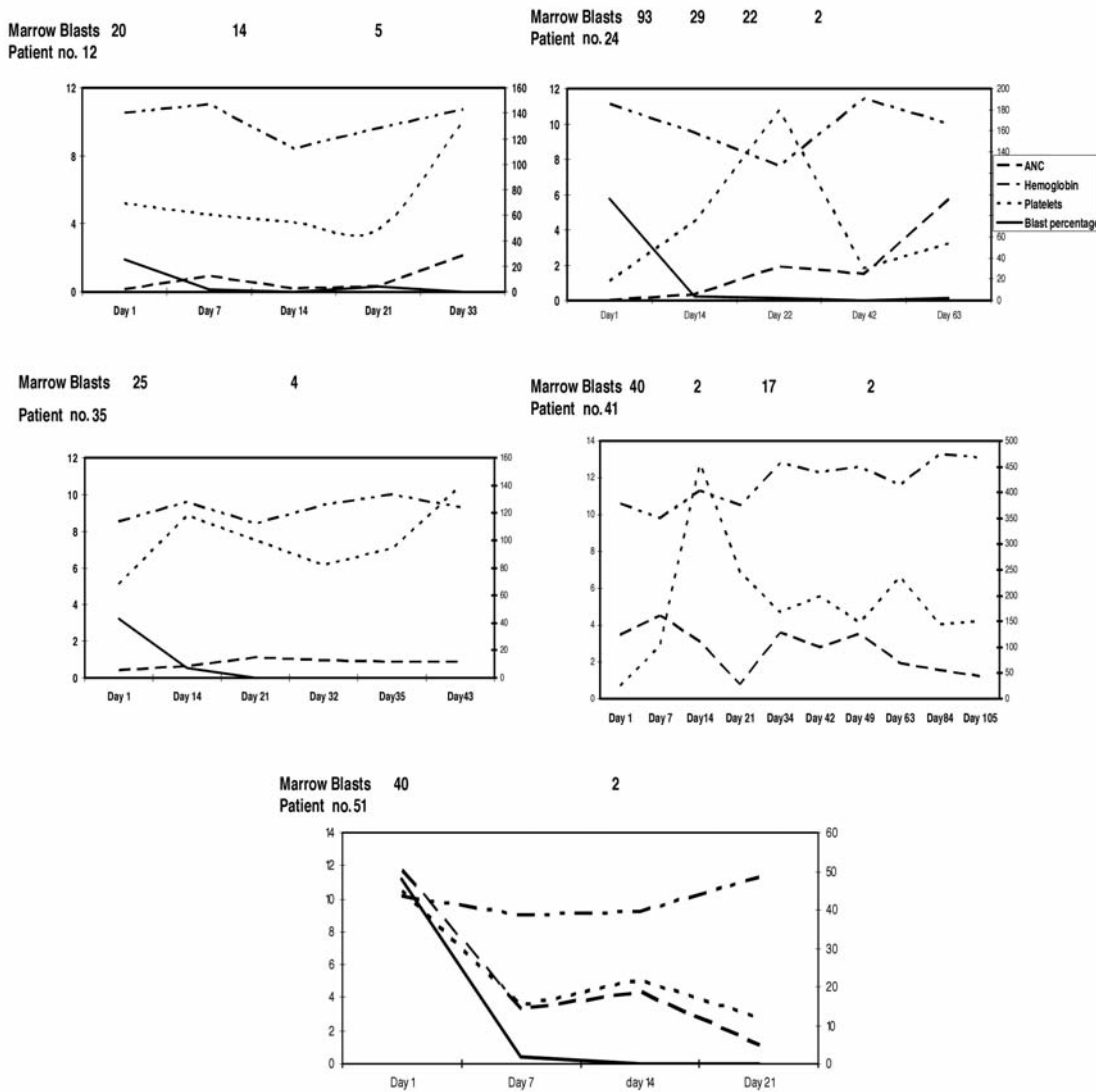


Figure 1. Changes in peripheral blood parameters and bone marrow blast in patients achieving complete remission (CR) or complete remission with incomplete platelet recovery (CRp).

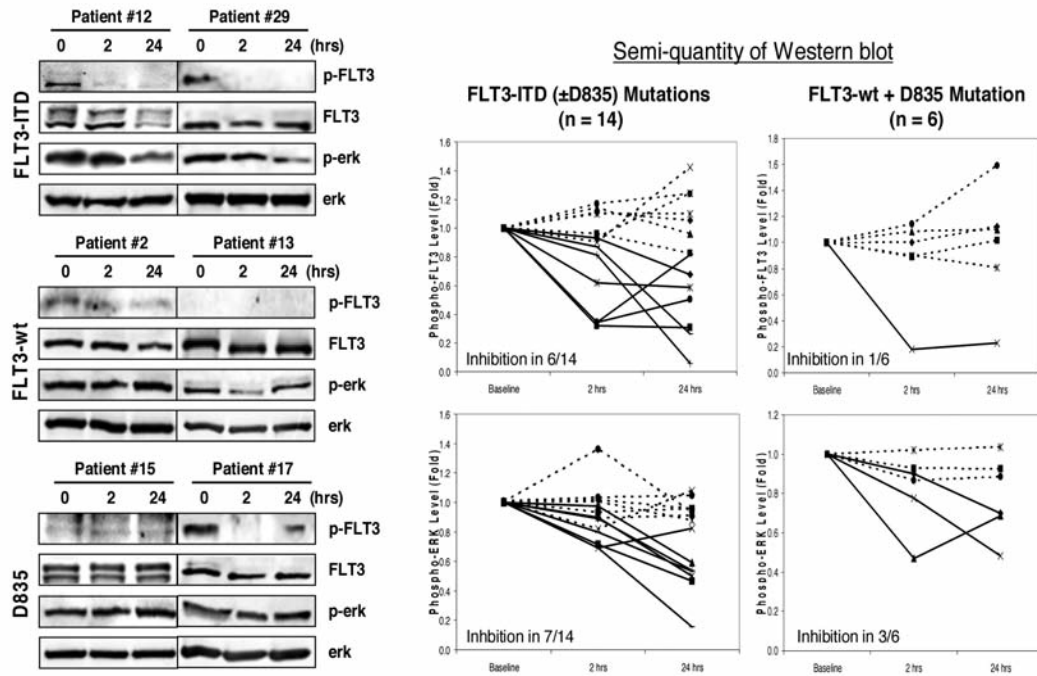


Figure 2. Changes in total and phospho FLT3 and ERK levels in peripheral blood mononuclear cells (PBMC). Lysates of PBMCs were analyzed by Western blot at baseline, two and 24 hours post first dose of sorafenib. The semiquantitative immunoblotting data were generated by Scion Imaging software.

Online Supplementary Table S1. Summary of bone marrow blast responses according to FLT3 status, continued.

FLT Status	Schedule	Dose level	Pat N.	Age	Cytogenetics	N. prior therapies	Bone marrow blast %	
							Pre	Best
D835	A	I	10	70	+8	5	70	NA
	A	III	19	48	Diploid	1	34	16
	B	II	15	57	Diploid	2	46	NA
	B	II	17	80	Diploid	0	14	6
WT-FLT3	B	III	40	49	Diploid	4	96	NA
	A	0	1	68	Diploid	3	45	58
	A	I	13	60	Complex	3	72	NA
	A	II	43	55	t(9;11)	2	86	84
D835	A	II	47	73	-7	2	30	32
	A	II	49	58	Complex	2	52	84
	A	III	28	65	+13, i17	3	55	74
	A	III	32	84	Diploid	4	50	42
	B	0	2	57	t(1;22), del 5q	3	70	NA
	B	0	3	56	+8	4	34	24
	B	II	22	66	Diploid	2	30	NA
	B	III	39	88	-7	3	33	44

Patients with both FLT3-ITD and D835 mutations are listed in FLT3-ITD group; patients with CR/CRps are in bold text.

Online Supplementary Table S2. Summary of bone marrow blast responses according to FLT3 status.

FLT Status	Schedule	Dose level	Pat N.	Age	Cytogenetics	N. prior therapies	Bone marrow blast %		
							Pre	Best	
ITD	A	0	4	50	Diploid	5	81	84	
	A	0	5	61	+15	1	82	NA	
	A	I	7	62	Diploid	3	96	25	
	A	I	12	75	-9	1	20	5	
	A	I	14	81	t(21;21)	1	14	52	
	A	II	18	33	Diploid	2	63	10	
	A	II	21	56	Diploid	2	87	58	
	A	II	33	39	Complex	5	70	NA	
	A	II	34	61	Diploid	2	45	13	
	A	II	35	22	Diploid	3	25	4	
	A	II	36	71	Diploid	3	77	30	
	A	II	44	54	Diploid	3	83	0	
	A	II	45	72	Diploid	3	55	2	
	A	II	46	66	Diploid	4	88	83	
	A	II	48	44	+9q	4	41	38	
	A	II	50	50	Complex	4	12	65	
	A	II	51	21	+8	4	40	2	
	A	III	26	27	inv7, t(9;12)	3	83	39	
	A	III	27	52	Diploid	3	85	0	
	A	III	29	31	Diploid	4	62	NA	
	A	III	30	37	Complex	3	90	51	
	A	III	31	44	Diploid	4	82	86	
	B	0	6	62	62	Diploid	4	93	51
	B	I	8	61	61	Random	2	72	42
	B	I	9	70	70	Diploid	2	60	45
	B	I	11	62	62	Diploid	1	85	82
	B	II	16	63	63	t(1;5)	2	79	65
	B	II	23	21	21	Diploid	1	66	14
	B	II	24	66	66	t(13;17)	3	93	2
	B	II	25	26	26	Complex	3	55	54
	B	III	37	68	68	Diploid	2	55	21
	B	III	38	70	70	Diploid	1	47	65
	B	III	41	73	73	Diploid	2	40	2
B	III	42	60	60	-15q	5	93	NA	