Figure S1. Synergistic inhibition of low-dose cytarabine and pan-RAF inhibitors in the proliferation of *RAS* mutant cells. Cell proliferation was assessed in HL-60 (*NRAS* Q61L), NB4 (*KRAS* A18D) and KG-1 cells (wild-type *RAS*) after treatment with low dose-cytarabine and the pan-RAF inhibitors (A) LY3009120 or (B) LXH254. Grey and white represent high and low percent proliferation, respectively.

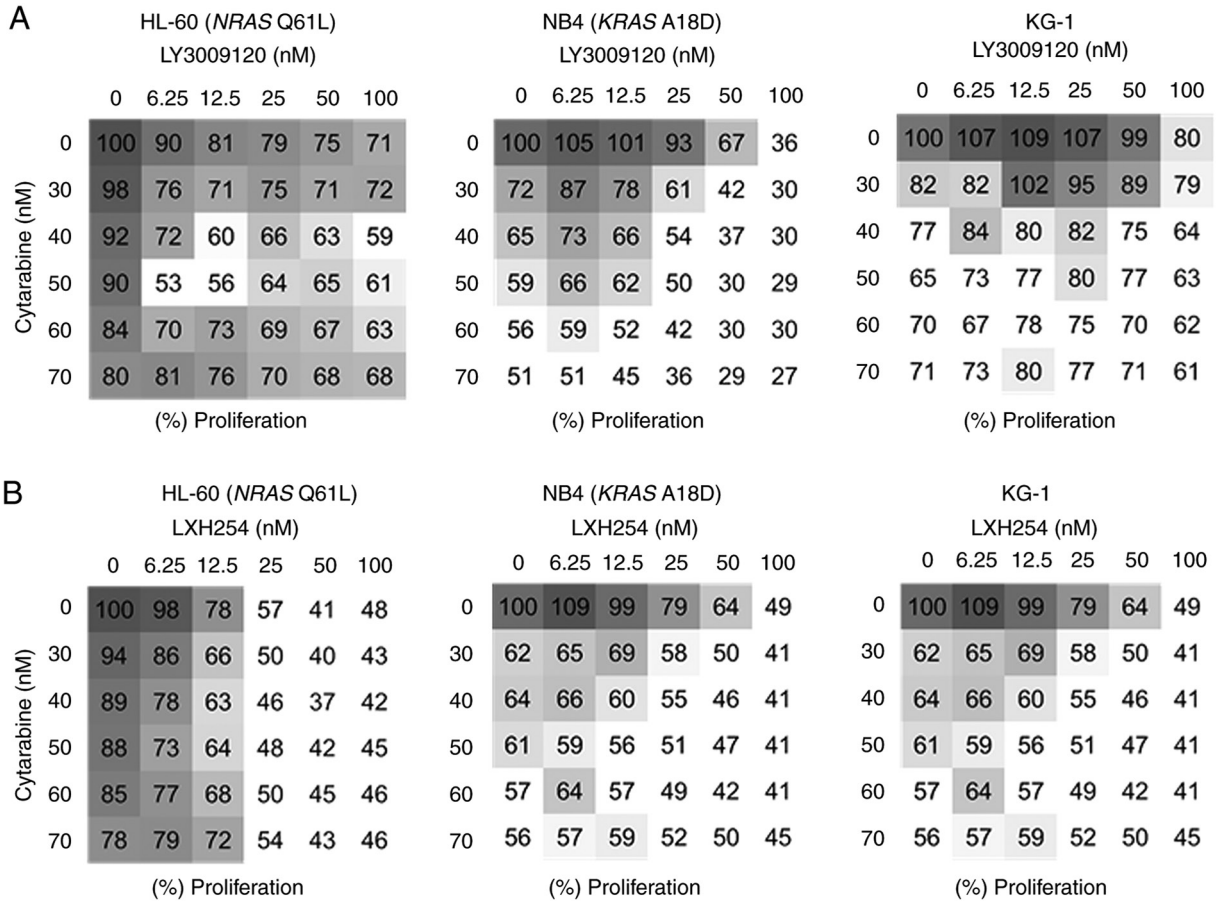

Figure S2. Evaluation of the synergistic effect of azacitidine combined with pan-RAF inhibitors. Cell proliferation was assessed in HL-60 (*NRAS* Q61L), NB4 (*KRAS* A18D) and KG-1 (wild-type *RAS*) cells after treatment with azacitidine and the pan-RAF inhibitors (A) LY3009120 or (B) LXH254. Black and grey represent high and low percent proliferation, respectively.

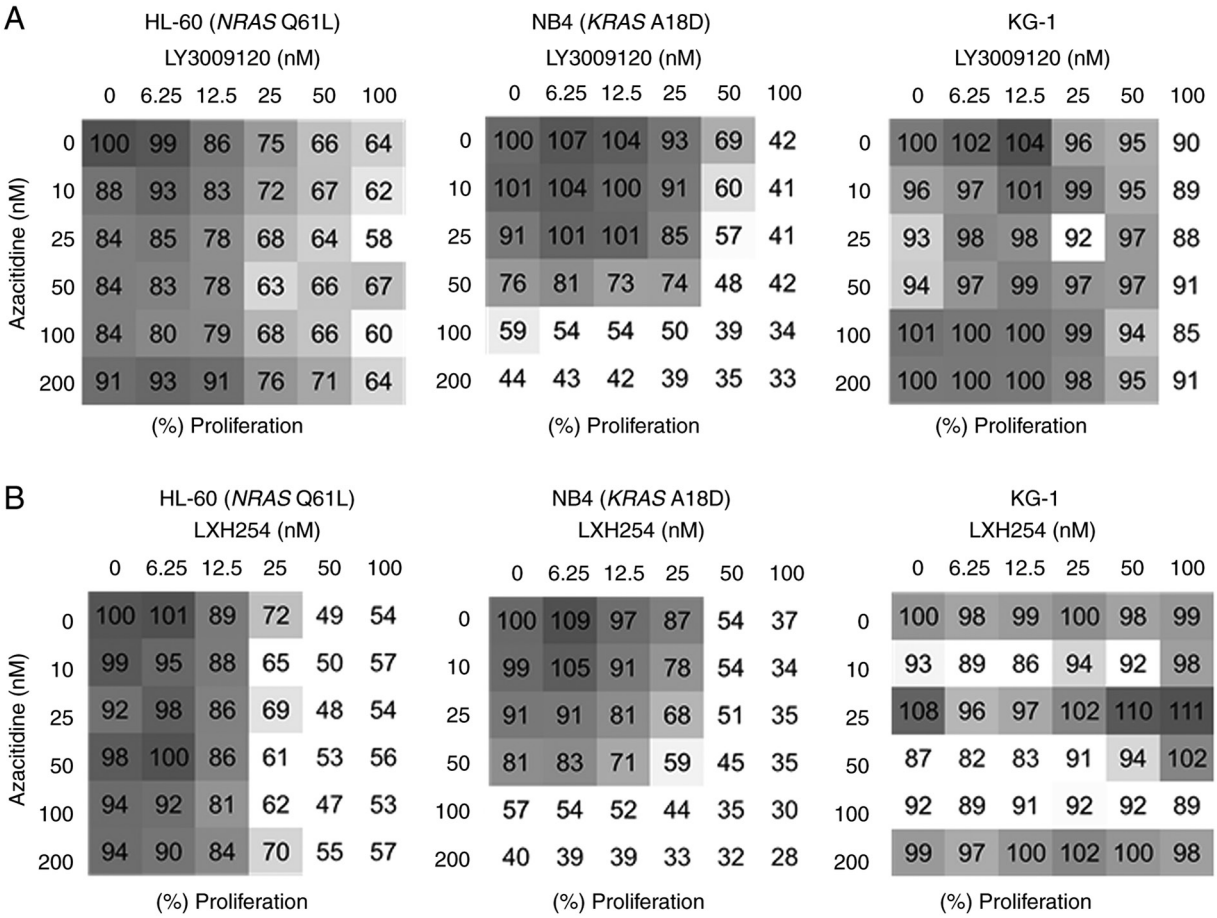

Figure S3. No induction of autophagy in *RAS* mutant acute myeloid leukemia cells following treatment with low-dose cytarabine combined with LY3009120. The HL-60 cell line was treated with 50 nM cytarabine, 6 nM LY3009120 or 50 nM cytarabine + 6 nM LY3009120. The NB4 cell line was treated with 50 nM cytarabine, 50 nM LY3009120 or 50 nM cytarabine + 50 nM LY3009120. Western blotting was performed using antibodies against LC-3, Beclin1 and p62.

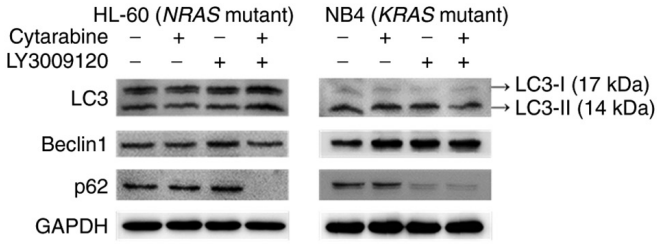

Figure S4. Data on the induction of apoptosis in primary cells of *NRAS* mutant AML following treatment with low-dose cytarabine combined with LY3009120. Cells were treated with inhibitors at the indicated concentrations for 72 h to ensure apoptosis. The apoptotic cells were analyzed by Annexin V and PI staining. AML, acute myeloid leukemia; BM, bone marrow.

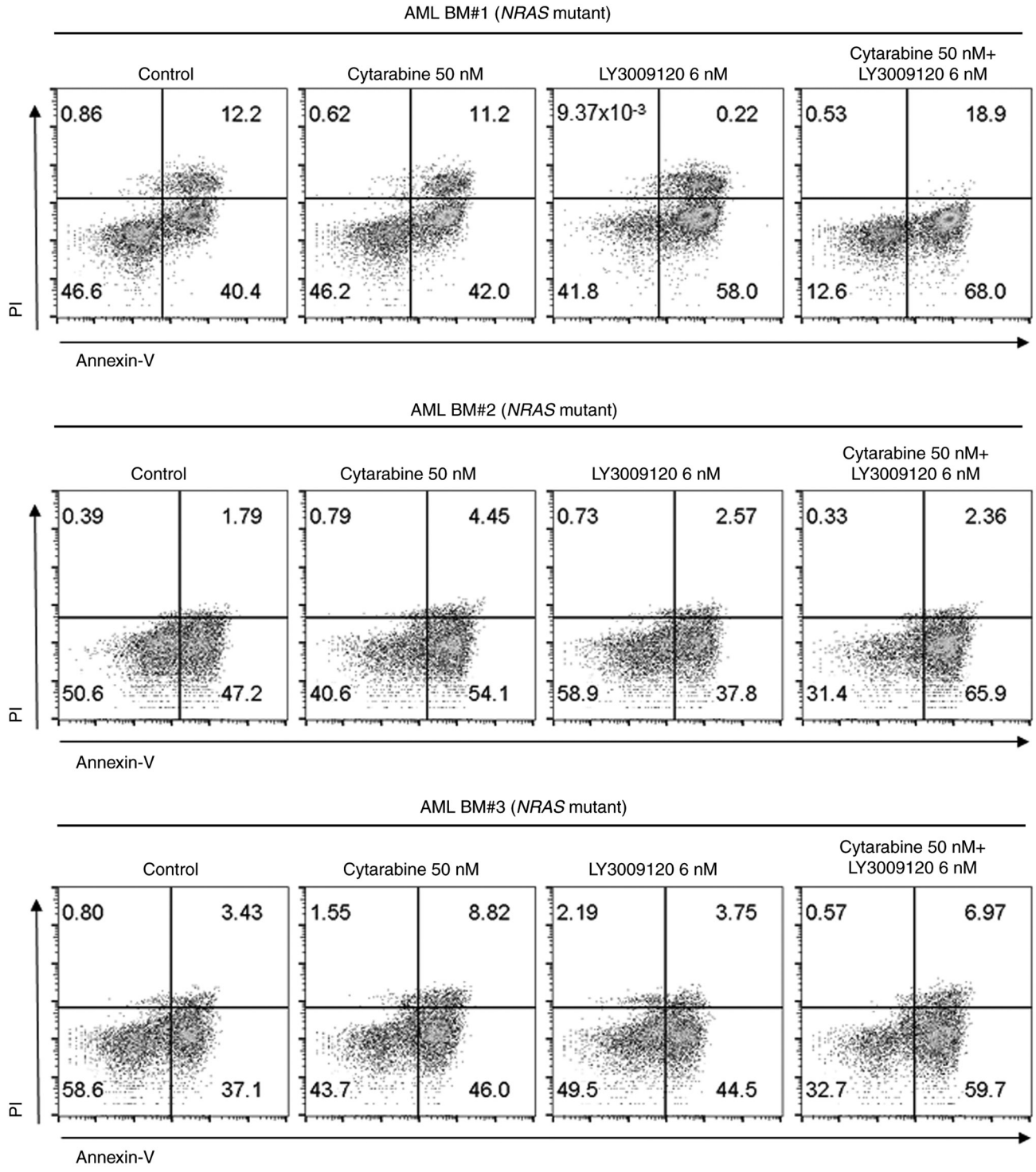

Figure S5. Data on the induction of apoptosis in primary cells of *KRAS* mutant AML following treatment with low-dose cytarabine combined with LY3009120. Cells were treated with inhibitors at the indicated concentrations for 72 h to ensure apoptosis. The apoptotic cells were analyzed by Annexin V and PI staining. AML, acute myeloid leukemia; BM, bone marrow.

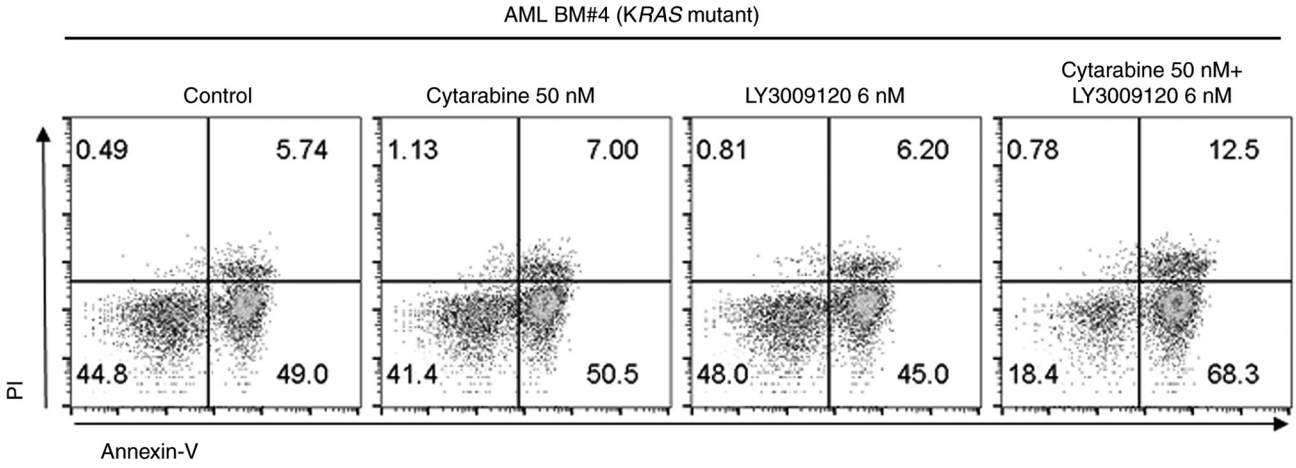

Table SI. Measurement of IC_{50} values following treatment with cytarabine and MAPK inhibitors in AML cells with wild type (KG-1) or mutated RAS (HL-60 and NB4).

	IC_{50}, μM					
Cell line	Cytarabine	Azacitidine	LY3009120	LXH254	Dabrafenib	Trametinib
HL-60	1.73	0.55	0.26	0.96	3.36	N/A
NB4	0.26	4.19	0.09	0.17	1.80	0.00
KG-1	1.44	9.99	0.44	4.89	21.28	0.00

AML cell lines were cultured under standard conditions in the presence of DMSO or each drug. After 72 h, using WST-8 solution, the IC_{50} was calculated as the concentration of drug required to inhibit 50% proliferation compared with control cells cultured in the absence of drug. AML, acute myeloid leukemia; N/A, measurement not possible due to the value being too low.

Table SII. Clinical information of patients with primary AML.

Sample ID	Sex	Age, years	BM blast, %	Cellularity, %	WBC count, $1x10^3/\mu l$	Hb, g/dl	Platelet count, $1x10^3/\mu l$	RAS mutation
AML BM #1	F	50	9.8	51-60	1.81	10.1	229	*NRAS*
AML BM #2	F	78	50.5	41-50	74.26	8.1	46	*NRAS*
AML BM #3	F	69	84.0	70-80	11.41	9.9	23	*NRAS*
AML BM #4	M	22	92.6	>95	2.01	11.3	152	*KRAS*

BM mononuclear cells from patients with AML isolated by the Ficoll gradient method were used. AML, acute myeloid leukemia; F, female patient; M, male patient; BM, bone marrow; WBC, white blood count; Hb, hemoglobin.