

Influence of bisphosphonates or recombinant human parathyroid hormone on *in vitro* sensitivity of acute lymphoblastic leukemia cells to chemotherapy

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Supplementary Material

Influence of bisphosphonates or recombinant human parathyroid hormone on *in vitro* chemotherapy sensitivity of acute lymphoblastic leukemia cells

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Table S1. Median combination index (CI) values for the effects of the bone-modifying agents (zoledronic acid, pamidronic acid, and recombinant human parathyroid hormone (rhPTH) with a concentration up to five-fold peak plasma concentration) on the chemotherapeutic agent-induced cytotoxicity of vincristine, daunorubicin, dexamethasone, 6-mercaptopurine and PEG-asparaginase.

N = total of evaluable leukemia cell lines. Ranges of CI values: 0.90-1.10= (near) additive (\pm), 0.30-0.70 = synergism (+++), 0.70-0.85 = moderate synergism (++), 0.85–0.90 = slight synergism (+), 1.10-1.20 = slight antagonism (-), 1.20-1.45 = moderate antagonism (--), and 1.45-3.30 = antagonism (---).

	Zoledronic acid (5fold)		Pamidronic acid (5fold)		rhPTH (15fold)	
	Median (range)	Effect	Median (range)	Effect	Median (range)	Effect
Vincristine (n=9)	1.192 (0.849-2.291)	-	1.926 (0.625-3.584)	-	2.719 (0.706-6.294)	---
Daunorubicin (n=9)	1.074 (1.017-1.312)	\pm	1.014 (0.983-1.224)	\pm	1.047 (1.013-1.446)	\pm
Dexamethasone (n=4)	1.153 (1.051-1.535)	-	1.343 (1.003-1.682)	--	0.9610 (0.666-1.022)	\pm
6-Mercaptopurine (n=8)	1.082 (0.937-1.191)	\pm	0.9194 (0.804-1.027)	\pm	0.9764 (0.812-1.054)	\pm
PEG-Asparaginase (n=9)	1.092 (0.784-2.167)	\pm	1.007 (0.959-1.313)	\pm	1.039 (0.863-1.384)	\pm

Table S2. Median combination index (CI) values for the effects of the bone-modifying agents (zoledronic acid and pamidronic acid with an one-, three-, or five-fold psychological peak plasma concentration) on the chemotherapeutic agent-induced cytotoxicity of dexamethasone and prednisone.

N = total of evaluable leukemia cell lines. Ranges of CI values: 0.90-1.10 = (near) additive (\pm), 0.30-0.70 = synergism (+++), 0.70-0.85 = moderate synergism (++), 0.85-0.90 = slight synergism (+), 1.10-1.20 = slight antagonism (-), 1.20-1.45 = moderate antagonism (--), and 1.45-3.30 = antagonism (---).

	Zoledronic acid (1fold)		Zoledronic acid (3fold)		Zoledronic acid (5fold)	
	Median (<i>range</i>)	Effect	Median (<i>range</i>)	Effect	Median (<i>range</i>)	Effect
Dexamethasone (n=4)	1.057 (0.806-1.221)	\pm	1.044 (0.877-1.812)	\pm	1.150 (1.058-1.515)	-
Prednisone (n=4)	1.024 (0.831-1.110)	\pm	1.061 (0.824-1.239)	\pm	1.061 (0.949-1.305)	\pm
	Pamidronic acid (1fold)		Pamidronic acid (3fold)		Pamidronic acid (5fold)	
	Median (<i>range</i>)	Effect	Median (<i>range</i>)	Effect	Median (<i>range</i>)	Effect
Dexamethasone (n=4)	0.9202 (0.606-1.082)	\pm	0.9778 (0.865-2.454)	\pm	1.336 (1.019-1.961)	--
Prednisone (n=4)	0.9883 (0.759-1.045)	\pm	1.020 (0.687-1.100)	\pm	0.9989 (0.948-1.272)	\pm

Figure S1. Scatterplots (A-C) visualizing the combination index (CI) values per individual leukemia cell line and the median CI (and range) for all leukemia cell lines combined.

A Scatterplot for the combined treatment of zoledronic acid and vincristine. **B** Scatterplot for the combined treatment of pamidronic acid and vincristine. **C** Scatterplot for the combined treatment of recombinant human parathyroid hormone and vincristine. Each dot on the scatterplot represents the CI value per individual T-ALL or B-precursor cell line. Data are presented as the mean CI of three independent experiments. The median and range for all leukemia cell lines combined is presented in red.

