

Significance of combination therapy of zoledronic acid and gemcitabine on pancreatic cancer

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Significance of combination therapy of zoledronic acid and gemcitabine on pancreatic cancer

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In the present study, we examined the cytotoxic effects of combination therapy with zoledronic acid (ZOL) and gemcitabine (GEM) on pancreatic cancer cells in vitro and in vivo. Four human pancreatic cancer cell lines were treated with ZOL, GEM or a combination of both, and the effects of the respective drug regimens on cell proliferation, invasion and matrix metalloproteinase (MMP) expression were examined. A pancreatic cancer cell line was also intrasplenically or orthotopically implanted into athymic mice and the effects of these drugs on tumor metastasis and growth in vivo were evaluated by histological and immunohistochemical analyses. Combination treatment with low doses of ZOL and GEM efficiently inhibited the proliferation ($P < 0.001$) and invasion ($P < 0.001$) of pancreatic cancer cells in vitro. Western blotting assay revealed that MMP-2 and MMP-9 expression levels were decreased after ZOL treatment. In vivo, combined treatment significantly inhibited tumor growth ($P < 0.05$) and the development of liver metastasis ($P < 0.05$). These data revealed that ZOL and GEM, when used in combination, have significant antitumor, anti-metastatic and anti-angiogenic effects on pancreatic cancer cells. The present study is the first to report the significance of the combination treatment of ZOL and GEM in pancreatic cancer using an in vivo model. These data are promising for the future application of this drug regimen in patients with pancreatic cancer.