PBI-05204, A SUPERCRITICAL CO2 EXTRACT OF Nerium oleander, INHIBITS THE GROWTH OF HUMAN PANCREATIC CANCER IN PANC-1 ORTHOTOPIC MODEL BY DOWN-REGULATION OF PI3K/MTOR PATHWAYS

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PBI-05204 suppresses proliferation of Pan-cancer tumor and down-regulates phosphorylation of Akt, 4EBP1 and S6 proteins

ABSTRACT
Recent studies have suggested that cardiac glycosides (CGs), such as oleandrin, have an ability in inhibiting cancer cell growth, suppressing those from pancreatic, wound-cell lung cancer, prostate, colonic and breast cancers. However, the efficacies of CGs in many cancers or tumors including the CGs on the growth of human pancreatic cancer remains to be shown. The anticancer effects of the botanical drug PBI-05204, a supercritical CO2 extract of Nerium oleander, was examined in human pancreatic cancer Panc-1 cell line xenografts. In this study, we showed that PBI-05204 markedly inhibited tumor proliferation in the Panc-1 orthotopic model as evidenced by a marked reduction of tumor size in both control and PBI-05204 (40 mg/kg) treated mice (left). Histological examination showed that PBI-05204 inhibited Panc-1 tumor growth by inhibiting the phosphorylation of PI3k/mTOR pathways. The results will be presented at the annual meeting.

Background
Cardiac glycosides are a class of compounds used to treat congestive heart failure and are do by increasing myocardial contractile force. Oleandrin is a cardiac glycoside derived from Nerium oleander used over the years in Russia and China for this purpose. In contrast, preclinical and retrospective patient data suggest that cardiac glycosides (e.g. digoxin, digitoxin, ouabain and oleandrin) affect the growth of various cancers including breast, lung, prostate and leukemia (1). Recent work from our laboratory and others showed that these compounds induced selective cell death in cancer cells but not murine tumor cells or normal human cells. The sensitivity of cancer cells to cell death treatment was likely mediated through the both expression and distribution of Na+,K+-ATPase (2). Compared to its in vitro studies, information on whether oleandrin or oleandrin containing plant extracts have an ability to inhibit tumor growth in the human pancreatic cancer mouse orthotopic model is very limited. In this study, we sought to evaluate the antitumor efficacy of PBI-05204, a supercritical CO2 extract of Nerium oleander, with or without combination of gemcitabine in human pancreatic cancer Panc-1 mouse orthotopic model and relevant pharmacologic mechanisms. Results of our study suggest that PBI-05204 exerts potent antitumor efficacy which is able to inhibit pancreatic cancer, a standard care for pancreatic cancer, in this particular model.

Results

EXPERIMENTAL DESIGN

Diagram 1: Schematic image of Panc-1 tumor was performed prior to and at the end of drug treatment. The tumor size in both control and PBI-05204 (40 mg/kg) groups was similar before the mice were treated with drugs or at time. Importantly, the tumors grew substantially in control mice, while the PBI-05204 treated mice showed no visible tumor after 6 weeks treatment.

Conclusion

- PBI-05204 obtained the development of 85% human pancreatic cancer Panc-1 tumors in this mouse orthotopic model and relevant pharmacologic mechanisms. Results of our study suggest that PBI-05204 exerts potent antitumor efficacy which is able to inhibit pancreatic cancer, a standard care for pancreatic cancer, in this particular model.

Reference: