that gene transcripts of determinants of gemcitabine activity could be used to tailor PDAC chemotherapy [2]. **Objective** Therefore, the aim of present study was to evaluate modulation of expression of two pivotal genes (hENT1 and dCK) involved in gemcitabine activity. **Methods** Preclinical studies were performed in PL45 and MIA PaCa-2 cells and primary cell cultures obtained from PDAC patients who underwent resection at Pisa University-Hospital (PPTCC78 and PPTCC109). Cells were treated with ukrain at IC_{50}s for 48 h. PCR amplification data were normalized to the GAPDH housekeeping, and gene expression was quantified using standard curve and ΔΔCT method, in which the amount of target, normalized to the control and relative to the calibrator (untreated control cells) was calculated as $2^{(-\Delta\Delta Ct)}$. **Results** Ukrain positively modulates hENT1 expression all PDAC cultures ($P<0.001$). The $2^{(-\Delta\Delta Ct)}$ analysis revealed a 2.8-fold mean increase ($P=0.001$) with respect to controls. In PL45 and MIA PaCa-2 cells ukrain positively affects dCK expression as well. **Conclusion** To date a few options are available for PDAC treatment. Most gemcitabine-based regimens resulted in a limited disease control, and studies attempting to widen the therapeutic armamentarium against PDAC are warranted. Based on previous clinical data the ukrain-gemcitabine combination appears a promising regimen and our results provide the experimental basis for further testing of the ukrain-gemcitabine schedule in PDAC patients.

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Different Uptake of Ukrain Can Explain the Selective Effect Against Pancreatic Adenocarcinoma Cell Cultures *in Vitro*

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Context Current therapy for PDAC is surgery followed by adjuvant chemotherapy for early-stage and palliative chemotherapy for advanced disease. Gemcitabine is the standard drug in both adjuvant and palliative treatment. The new drug ukrain in combination with gemcitabine significantly increased the median survival of advanced PDAC patients with respect to gemcitabine alone (10.4 *vs*. 5.2 months; $P<0.001$). Furthermore, preclinical studies showed that ukrain had selective cytotoxic effects in cancer cell lines derived from different tumor types, but not in normal cell lines. **Objective** To evaluate the cytotoxic effects of ukrain in 2 primary pancreatic cancer cell lines (PPTCCs), fibroblasts derived from PDAC specimens (F-PDAC) and an immortalized epithelial ductal pancreatic cell line (HPNE). **Methods** Cytotoxicity was assessed by the CellTiter 96 kit (Promega) based on the cellular metabolism of the tetrazolium compound XTT, which is reduced by living cells to yield a soluble formazan product in the presence of the electron coupling agent phenazine methosulfate, while the modulation of ukrain uptake in the medium was studied using the fluorescence property of ukrain with the AlphaDigiDoc software by UV light excitation (ULA-DC test). **Results** Cytotoxic effects of ukrain in PPTCCs were significantly higher than those observed in F-PDAC and HPNE cells (20% *vs*. 80% alive cells, at 10 μM ukrain concentration). Furthermore, the ULA-DC test revealed that PPTCCs cells consumed more drug than F-PDAC and HPNE cells (paired Student's test, $n=4$, $P<0.001$). **Conclusion** These data demonstrated the selective effect of ukrain in PPTCCs, which may be related to a different transport system or higher metabolism of the drug in PDAC, and warrant further investigations in order to support the possible role of ukrain in PDAC treatment.