Introduction Aberration of MLN64 (Metastatic Lymph Node Protein 64), also known as StARD3 (StAR Related Lipid Transfer Domain Containing 3), has been reported in endocrine related cancers including breast and prostate cancers and found to be present in insulinoma cells. The present study evaluated the clinical and prognostic values of MLN64 to clarify its role in human pancreatic cancer.

Methods Human pancreatic cancer cell lines, PANC1 and MIA PaCa-2 were used. The levels of MLN64 gene transcripts were quantitatively evaluated in a cohort of human pancreatic cancer with matched normal tissues. The expression of the transcripts were evaluated against the clinical, pathological and outcome parameters of the patients.

Results Pancreatic cancer tissues had a markedly increased levels of MLN64 (Median (Q1-Q3)): 4.85 (0-61) compared with normal tissues (0.03 (0-7.6)) (p<0.001). It was also revealed that MLN64 in tumours of patients who died of pancreatic cancer during the followup period had a significantly highly levels of MLN64 (7.66 (0-20)), compared with those who survived (0.02 (0-72.5)) (p<0.01), further indicating MLN64 as a significant prognostic factor (HR 8.37, p<0.01). Our data also revealed node positive pancreatic tumours had a significantly higher levels of MLN64 than node negative tumours (p<0.05), although no significant difference was seen between those with distant metastases and those without. Significant correlation was also found between MLN64 and the Her family members, namely Her4 (p<0.001) and Her3 (p<0.05) and that the combining the pattern of expression of MLN64 and Her4 further enhance the power in predicting outcomes of the patients. Using our pancreatic cancer cell models, we have demonstrated that blocking Her family kinases using a pan-Her inhibitor, namely Nerlynx and a key cell migration regulator, phospholipase C-gamma1 (PLCγ1), had a marked impact on cellular migration and adhesion of pancreatic cancer cells, key functions observed with MLN64 in cancer cells.

Conclusions MLN64/StARD3, one of the key regulators of cancer cells, has an aberrant expression in human pancreatic cancer which is linked to the clinical outcome. With its role in cancer cells and discovery of inhibitory means to MLN64/StARD3, the molecule presents a good target for therapeutic considerations in pancreatic cancer.

Methods The human BxPC-3 cell line was used as an in vitro model for pancreatic adenocarcinoma. The target cells were incubated with free hematoporphyrin (free HP) and hematoporphyrin-containing nanoparticles (HPNP) that were formed by self-assembly with a polyglutamate-tyrosine co-polymer, in order to determine the cytotoxicity in the absence of ultrasound. Cells were treated with HPNP combined with ultrasound irradiation for determining the effect of SDT. These effects were examined at normoxic and hypoxic conditions, at pH 6.4 and pH 7.4.

Results The HPNP nanoparticles showed increased toxicity against the target cell line, when compared with free HP. The HPNP toxicity was further enhanced at acidic conditions and this is particularly important for confining the ablation effect within the acidic pancreatic tumour mass. Utilising the nanoparticle carrier, cellular uptake of hematoporphyrin was significantly increased compared to the free HP (p<0.0001), at both acidic and physiological pH. SDT, at varying ultrasound treatment conditions and at both normoxic and hypoxic environment, demonstrated a clear cytotoxic effect against the BxPC-3 cell line (<0.001), while toxicity of ultrasound alone or the nanoparticles alone was minimal.

Conclusion BxPC-3 cells have significant positive response to treatment with SDT. Further preclinical experimentation is currently being carried out in experimental animals to evaluate the effect of SDT in vivo for supporting the clinical translation of this promising therapeutic modality in the treatment of pancreatic cancer.