

positively with HuHMFG1. Using internal MUC1 detection with CT2 for comparison, the sensitivity & positive predictive value for external MUC1 detection were 95%; 95% for HuHMFG1 and 40%; 93% for NCL-MUC-1.

Conclusion This study suggests MUC1 expression inferred by detection with HuHMFG1 and CT2, binding extra and intracellularly, increases early in progression to OA. The MUC1 epitope bound by NCL-MUC-1 appears later. This may be due to changes in glycosylation during progression. Therapeutic modalities targeting MUC1 may be applicable to the majority of patients with preneoplastic BE and OA.

Disclosure of Interest None Declared

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PTU-160 SECOND GENERATION PHOTOSENSITISER BASED PHOTODYNAMIC THERAPY IS EFFICACIOUS AND PENETRATES TISSUE MORE DEEPLY THAN RADIOFREQUENCY AND CRYO- ABLATIVE THERAPIES, OFFERING POTENTIAL FOR MORE INVASIVE GASTROINTESTINAL CANCERS

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Introduction Photodynamic therapy (PDT) has been used to both treat gastrointestinal (GI) cancers and for palliation. PDT has been limited by poor penetration of the laser light used to activate it. In recent years, PDT has been replaced by other minimally invasive modalities such as radiofrequency- and cryo-ablation due to fewer side effects. However, these are limited to superficial cancers. Activation of 2nd generation photosensitisers (PS) such as Talaporfin by light in the near infrared enables deeper tumour penetration. Talaporfin is undergoing clinical trials in the US with encouraging data from phase 1 studies in oesophageal and biliary cancers. This study aimed to compare the potency of several other PS's activated in the near infrared for GI tumours.

Methods The cytotoxic efficacy of five chlorin based PS's were evaluated against human oesophageal (OE19) and colon (HT29) cancer cell lines using a 670nm cold laser. Equivalent concentrations of PS were compared in the presence or absence of laser "light" activation. Power was set intentionally low at 0.33J/cm² to highlight the efficacy of the PS's. Cell viability was measured with standard MTT assay and the plates read on an Elisa plate reader at 490nm. The concentrations required to kill 50% of cells (IC₅₀) were calculated, and the dose response curves in light and dark compared using linear regression analysis and F tests to show selectivity to those cells exposed to near infrared light.

Results Cell viability counts in all plates were initially corrected for the untreated cell survival controls in the plate itself and then plotted on a log scale to produce dose response curves. This confirmed significantly cytotoxic efficacy in light vs dark for the PS's PPa (p = 0.001, IC₅₀ = 4.82 µM), PS1 (p = 0.03, IC₅₀ = 24.8 µM) and CE6 (p = 0.001, IC₅₀ = 75.8 µM) against OE19 cells, and PPa (p = 0.01, IC₅₀ = 3.8 µM), PS4 (p = 0.02, IC₅₀ = 4.5 µM) and CE6 (p = 0.0004, IC₅₀ = 26.1 µM) against HT29 cells.

Conclusion This study has shown these second generation chlorin-based photosensitisers to be effective against GI tract cancer cell lines. By virtue of being activated in the near infrared, they further offer deeper tissue penetration when compared with Porfimer sodium which is excited at 630 nm. Further quality control to GMP

standards and evaluation in-vivo is required before these PS can be used. However when translated, they may provide more effective PDT in the clinic than current minimally invasive strategies for GI cancers, and offer therapy to more deeply infiltrating tumours.

Disclosure of Interest None Declared.

PTU-161 EXPRESSION OF POLO-LIKE KINASE 1 AND GEMININ IS UP-REGULATED IN THE SQUAMOUS-METAPLASIA-DYSPLASIA-CARCINOMA SEQUENCE AND CORRELATES WITH ANEUPLOIDY

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Introduction Population based studies have shown a small but significant proportion of patients with Barrett's oesophagus (BE) progress to oesophageal adenocarcinoma (OA). Predicting which patients progress is of vital importance for risk stratification into increased surveillance regimes or early therapeutic intervention. We have previously shown the replication licensing factors (RLF) such as polo-like kinase-1 (PLK1) may act as surrogate markers of DNA ploidy abnormalities (DNA-PA) (1) and subsequent risk of progression to OAC. This study aimed to assess whether the RLF's are up-regulated in the metaplasia-dysplasia-carcinoma sequence independently of DNA-PA.

Methods Paraffin embedded oesophageal specimens were selected from 94 patients, and pathology grade (PG) scored as 1 (squamous = Sq; n = 4), 2 (non-dysplastic BE = NDBE; n = 19), 3 (low grade dysplasia = LGD; n = 20), 4 (carcinoma in-situ = HGD/IMC; n = 36) and 5 (invasive OA = IOA; n = 15). Sections were immunostained with the antibodies PLK1-M, PLK1-L and Gem using the automated BOND-MAX system (Leica). Intensity (I) (0 to 3+) and extent (E) (0; < 1% = 1; 1–10% = 2; 10–33% = 3; 33–66% = 4; > 66% = 5) of staining were scored by 2 expert GI pathologists, and mean scores calculated. DNA-PA was assessed using image cytometry (IC). Pearson r coefficient and two-tailed P values were calculated for correlations and significance.

Results A significant correlation with extent (r = 0.87, p = 0.05; r = 0.91, p = 0.03; r = 0.99, p = 0.0008) was seen with all RLFs (PLK1-M; PLK1-L; Gem). Only PLK1-M correlated with intensity (r = 0.92, p = 0.03) and total (I+E) scores (r = 0.91, p = 0.03). Aneuploidy was present in NDBE (6%), LGD (25%), HGD/IMC (61%) and IOA (67%). The proportion of aneuploid cases/group correlated significantly with PG (r = 0.97, p = 0.007) and mean I, E and total scores for PLK1-M (r = 0.97, p = 0.008; r = 0.96, p = 0.008; r = 0.98, p = 0.96).

Conclusion All assessed RLFs were found to be significantly up-regulated in the progression to OA, with geminin scoring highest when evaluated by extent scores. Overall PLK1-M appeared the best antibody, showing additional correlation with its intensity and total staining scores with PG and DNA-PA. We further demonstrated that aneuploidy still correlates with PG as we have previously reported. In future, PLK1-M and aneuploidy may provide the basis of a biomarker panel to help guide screening and therapy for those predicted to be at increased risk of progression to OA.

Disclosure of Interest None Declared

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PTU-162 OESOPHAGEAL MUCOSAL DILATED INTERCELLULAR SPACES (DIS), TRANSEPIHELIAL ELECTRICAL RESISTANCE AND PERCEPTION OF HEARTBURN

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