

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 In recent years, PDT has been replaced by other minimally invasive modalities such as radiofrequency- and cryo-ablation due to fewer side effects.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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Introduction It is proposed that the presence of oesophageal mucosa dilated intercellular spaces (DIS) underlies heartburn in patients with NERD. However, 20% of asymptomatic subjects display DIS in distal oesophageal biopsies. Furthermore, oesophageal experimental acidification in healthy volunteers provokes DIS, but often without heartburn despite ongoing acid perfusion. These observations suggest that mucosal impairment above and beyond DIS may be relevant in heartburn perception. Functional mucosal integrity in response to acid challenge can be tested in oesophageal mucosal biopsies “in vitro” by measuring changes in transepithelial electrical resistance (TER).

We aimed to further assess the relationship between presence of DIS, changes in functional oesophageal mucosal integrity (TER) and heartburn perception.

Methods We took distal oesophageal biopsies from patients with and without heartburn. Histological examination for epithelial intercellular space diameter (ISD) was done using light microscopy by taking 50 random measurements at several levels from the basal epithelial layers for each biopsy. DIS was declared at above the 95% CI for normal values as previously published ($> 0.72 \mu\text{m}$).

We identified 11 subjects with DIS (4 with predominant daily troublesome heartburn, 7 with predominant dyspepsia and no heartburn). Biopsies were placed in mini-Ussing chambers, and baseline TER was measured. The luminal aspect of the biopsy was then exposed for 30min to an acidic solution (pH2 + 1 mg/ml pepsin + 1 mM taurodeoxycholate). During exposures, % changes in TER relative to baseline were analysed.

Results

The mean ISD in all subjects was $0.94 \mu\text{m}$ (range $0.74\text{--}1.18 \mu\text{m}$). There was no significant difference in ISD (0.95 vs. $0.91 \mu\text{m}$) or baseline TER (144 vs. $165 \Omega\cdot\text{cm}^2$) between predominant heartburn and predominant dyspepsia groups.

Despite the pre-existing DIS in all subjects, 30 minutes acid exposure was able to induce a further reduction in TER (-23.0% change from baseline, $p < 0.01$).

The reduction in TER was greater in subjects with predominant reflux vs. those with predominant dyspepsia ($-40.4 \pm 10.3\%$ vs. $-11.2 \pm 3.7\%$, $p = 0.01$).

Conclusion In subjects with pre-existing DIS with and without heartburn, trans-epithelial electrical resistance can be further impaired with in vitro acid exposure, suggesting that the mechanism for acid-induced mucosal integrity impairment is not limited to DIS. Furthermore, acid-induced functional integrity impairment was greater in patients with heartburn. This difference in mucosal behaviour in the presence of acid suggests that other mechanisms beyond DIS might be needed to further stimulate afferent nerves in heartburn generation.

Disclosure of Interest None Declared

PTU-163 PROXIMAL OESOPHAGEAL FUNCTIONAL MUCOSAL INTEGRITY DURING DISTAL OESOPHAGEAL ACIDIFICATION IN PATIENTS WITH NERD AND FH

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Introduction Although macroscopically normal, the oesophageal mucosa in patients with non-erosive reflux disease (NERD) displays epithelial dilated intercellular spaces (DIS). Such loss of barrier integrity is thought to be important in disease pathogenesis. Patients with NERD have DIS in both the distal and proximal oesophagus. Patients with functional heartburn (FH) do not have DIS. In healthy volunteers acid perfusion of the distal oesophagus induces DIS not only in the exposed distal, but also the unexposed proximal oesophagus. It is unknown what impact distal acid perfusion has in the proximal oesophageal mucosa in symptomatic

patients. Oesophageal impedance measurements can be an “in vivo” surrogate marker of functional mucosal integrity.

We aimed to assess with impedance the proximal oesophageal mucosal integrity during distal acid perfusion in symptomatic patients with NERD (+ve DIS) and FH (-ve DIS).

Methods We studied 22 patients (mean age 48, range 20–75) with typical reflux symptoms and negative endoscopy. 24-hour MII-pH monitoring identified 11 patients with NERD and 11 with FH. A pH-impedance catheter was inserted transnasally such that the proximal impedance segment was 15cm above the LOS. A 10 minute perfusion (10ml/min) of a neutral (pH7), then acidic (pH1) solution was performed in the distal oesophagus (10 cm from LOS) whilst simultaneously measuring proximal impedance. The absence of proximal fluid contamination was suggested by a lack of impedance drop during the neutral perfusion. Baseline impedance, and percentage change from baseline during the perfusion was calculated.

Results Distal perfusion of neutral solution caused no fall in proximal impedance (mean impedance $107 \pm 2.8\%$ of baseline). Distal perfusion of acidic solution caused a significant reduction in proximal impedance (mean impedance $80.3 \pm 5.3\%$ of baseline, $p < 0.01$). The drop of proximal impedance started at a mean of 175 seconds after commencement of acid perfusion. Proximal impedance did increase to a mean of 90% of baseline until 30 minutes after cessation of the acid perfusion. There was no significant difference in baseline proximal impedance ($3165 \pm 216\Omega$ vs. $3116 \pm 232\Omega$) or acid-induced change in proximal impedance ($79.4 \pm 8.1\%$ vs. $81.2 \pm 7.1\%$ of baseline) between FH and NERD patients respectively.

Conclusion In keeping with morphological studies of healthy volunteers, distal oesophageal acidification modifies mucosal functional integrity of the proximal, unexposed oesophagus. This appears to occur regardless of the presence of pre-existing proximal DIS, suggesting that mechanisms of functional mucosal integrity as measured by impedance are beyond DIS formation.

Disclosure of Interest None Declared.

PTU-164 COST EFFECTIVENESS OF AN ER DOMINANT APPROACH IN THE MANAGEMENT OF HIGH GRADE INTRAEPITHELIAL NEOPLASIA AND MUCOSAL CANCER IN BARRETT'S OESOPHAGUS

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Introduction Endoscopic resection (ER) is an established effective treatment for high grade intraepithelial neoplasia (HGIN) and intramucosal cancer (IMC) arising in Barrett's oesophagus. ER can lead to recurrence so it is suggested that all patients should undergo radiofrequency ablation (RFA) after ER as a complimentary treatment strategy. However no comparative study to support this concept has been performed. We aimed to compare the cost-effectiveness of an EMR-dominant approach vs an EMR-RFA approach for the treatment of HGIN and IMC in Barrett's oesophagus.

Methods All ER procedures between 2005 and 2012 were recorded in a prospective database which was analysed. Demographic data, histology, procedure success, long-term outcome and complications were assessed. Costs were calculated using NHS HRG codes plus equipment costs for ER and RFA.

Results 92 patients were treated for dysplastic Barrett's oesophagus or early Barrett's cancer by ER. The mean age at first procedure was 69 years and 87% of the patients were male. 21 of 92 patients had advanced histological features on the initial ER specimen and were referred for surgical or oncological treatment. Of the remaining 71 cases, 63 have follow-up data with a mean duration of 4.3 years. 59 of 63 cases (94%) had successful eradication of HGIN/IMC by ER. The remaining 4 patients were referred for surgery for advanced disease (3) or extensive bulky disease not amenable to ER