**Conclusion** YF476 is a promising new medical treatment for type I gastric neuroendocrine tumours. It appears to be well tolerated with no observed toxicity. Further trials of YF476 involving more prolonged treatment regimes are therefore warranted in this condition.

**Competing interests** A Moore grant/research support from: Trio Medicines Ltd., L Ball: None declared, M Boyce: None declared, A Varro: None declared, D Pritchard: None declared.

## OC-098 HOW COMMONLY IS GASTRIC CANCER MISSED AT ENDOSCOPY: A UK PRIMARY CARE BASED STUDY

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**Introduction** Meta-analysis of published single hospital series including 1977 subjects suggests that 14% of gastric cancer (GC) subjects have had an upper gastrointestinal endoscopy (OGD) up to 3 years previously that failed to diagnose their GC (50% in the 12 months before diagnosis and 50% 1–3 years before diagnosis).
**Methods** All patients with GC in the THIN general practice database covering 5 million UK subjects were examined. A nested case-control study was performed with cases subjects who underwent OGD 1–5 years prior to their OGD that diagnosed GC and controls subjects who did not undergo OGD 1–5 years prior to their diagnostic OGD.
**Results** 5473 GC were available for analysis (3402 males (62%), mean age 71 years), with follow-up of 46 779 subject years. 169 (3.1%, 98 males (58%), mean age 71 years) had an OGD which failed to diagnose GC between 1 and 5 years prior to diagnosis of GC, out of whom 128 (2.3%) had OGD between 1 and 3 years before and 41 (0.7%) had an OGD between 3 and 5 years before diagnosis. There were 56 primary care consultations with symptoms pertaining to oesophago-gastric cancer between 1 and 5 years prior to diagnosis of GC (dyspepsia (n) 51, anaemia 9, weight loss 12, dysphagia 3), of which all underwent OGD. No subject who had an OGD that did not diagnose cancer was on proton pump inhibitor (PPI) therapy in the year prior to OGD and 49 (0.9%) of subjects were on PPI therapy in the year prior to being diagnosed with GC. Logistic regression analysis of subjects who had an OGD that failed to diagnose cancer and those that did not, failed to identify any specific predictive factors (age 1.0 (0.99–1.01), p=0.99), sex 0.84 (0.61–1.14), p=0.26), related to an OGD that failed to diagnose GC.
**Conclusion** Missing GC at OGD is, reassuringly, less than half as common as previous much smaller studies in secondary care have suggested. PPI therapy does not contribute to missing GC at OGD. Advances in endoscopy and selection bias in previous studies may account for these differences.

**Competing interests** None declared.

## OC-099 INCREASED AT RISK SCREENING AND RECOGNITION OF ATYPICAL PRESENTATION DOES NOT FULLY EXPLAIN THE 6.5-FOLD INCREASE IN PAEDIATRIC COELIAC DISEASE (CD) INCIDENCE IN THE LAST 20 YEARS IN SE SCOTLAND

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**Introduction** Current diagnostic practice for paediatric CD in the UK includes increased screening of family members and at- risk groups for example, diabetes mellitus.
**Aims** To identify all incident cases of CD in SE Scotland over the 20-year period of 1990–2009 to assess trends in incidence, symptomatology, age at diagnosis and the impact of active screening of at-risk groups. Utility of routine laboratory tests at diagnosis was also evaluated (2005–2009 diagnoses only).
**Methods** A retrospective review of case notes, pathology databases, endoscopy and patient records was performed for all children diagnosed with CD <16 years from 1990 to 2009 on duodenal biopsy in SE Scotland (at-risk population group of 233 000 aged <16 years). Data were age-sex standardised and analysed in 5-year epochs, with Poisson regression models used to calculate changes in incidence over time.
**Results** 266 biopsy positive children were diagnosed from 1990 to 2009 with an increase in incidence from 1.8 (95% CI 1.1 to 2.7) to 11.7 (95% CI 9.8 to 13.9) per 100 000 children aged <16 years during the 1990–1994 and 2005–2009 epochs respectively (p=0.001). The median age (IQR) at diagnosis also increased significantly from 29 (16–53) months to 90 (53–132) between these epochs (p<0.0001), and non-classical presentation (children with a mono-symptomatic presentation and those with extra-intestinal symptoms for example, fatigue, pallor, irritability) increased significantly from 5% to 21% respectively (p=0.008). Additionally, 7% of children were diagnosed through targeted screening in 1990–1994 compared to 23% in 2005–2009 (p=0.002). When cases identified via active screening or with non-classical symptoms were removed, a significant rise from 1.51 (95% CI 0.91 to 2.38) in 1990–1994 to 6.59 (95% CI 5.17 to 8.28) in 2005–2009 (p=0.006) remained. Routine blood investigations demonstrated that over 25% were anaemic and over 50% were iron deficient at presentation in 2005–2009.
**Conclusion** The incidence of paediatric CD has increased 6.5-fold over the last 20 years in SE Scotland. Children are older at diagnosis, presenting with fewer classical and more varied symptoms, and with iron deficiency anaemia the commonest laboratory abnormality. We show that both increased screening of at-risk groups and a lower threshold for serological screening (as a result of greater clinician awareness of the condition's heterogeneic nature) do not fully explain the overall rise in incidence.

**Competing interests** None declared.

## OC-100 THE CLONAL ORIGINS OF GASTRIC ADENOCARCINOMA

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**Introduction** We have previously shown that entire fields of dysplasia in the human stomach are derived from a single mutated, metaplastic gland.[1] This suggests that intestinal metaplasia (IM) can be considered a field defect among which dysplasia can arise and this would indicate that adenocarcinomas derived from such dysplasia would also be clonal. Recent work published by our laboratory has indicated that familial adenomatous polyposis–associated colorectal adenomas as well as some sporadic lesions[2] and dysplasia within Barrett's oesophagus[3] are polyclonal. There is therefore a need to ascertain the clonality of gastric adenocarcinomas (GA).

**Methods** Here we screened a large cohort of GA patients for mutations in genes accounting for nearly 90% of reported mutations in GA in order assess mutation frequencies. The screening was then followed by laser capture microdissection PCR sequencing and loss of heterozygosity (LOH) analysis of the mutated specimens in order to assess clonality of GA from dysplasia and IM.

**Results** From the 51 patients cohort we have found 18 patients (35.3%) presenting mutations, but only one out of the 51 patients (1.9%) presented two independent mutations in a single cancer. We found 3 mutations in APC (6.3%), one in CDKN2A (2.2%), 13 in TP53 (27.7%), one in CTNNB1 (2.2%) and one in K-RAS (2.4%), but none in PIK3CA or PTEN. Our mutation frequencies are comparable to previous reports, however we observed that most functional mutations occurred as a single event despite screening multiple genes. Analysis of the multiple laser capture microdissected areas revealed multiple genotypes within the same cancer in three out of the five patients. Moreover, current LOH data shows LOH of chromosome 17 in IM and throughout the cancers in all different genotypes, suggesting that chromosome 17 LOH might have been the first hit mutation followed by mutations in TP53, and in one patient a subsequent CTNNB1 mutation.

**Conclusion** This suggests that cancer progression may have been initiated by LOH in intestinal metaplasia and that GA cells might become genetically diverse as the cells evolve in the tumour. Therefore, IM is likely to represent a field defect for gastric cancer.

**Competing interests** None declared.

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## OC-101 PREDICTIVE FACTORS FOR POSTOPERATIVE MORTALITY AFTER RESECTION OF JUNCTIONAL AND GASTRIC ADENOCARCINOMAS

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**Introduction** Postoperative mortality (POM) within 30 days of oesophago-gastric resection remains significant and should be minimised to provide maximal chance of long-term survival. This study identifies factors predictive of 30-day POM in a large national multicentre cohort.

**Methods** A retrospective analysis was performed of 2670 patients (mean age 64±13 years) who underwent resection of junctional or gastric adenocarcinomas from 1997 to 2010 in 19 French centres. Ordinal data were compared using either the $\chi^2$ test or Mann–Whitney U test, as appropriate. A stepwise logistic regression model was built to identify by multivariate analysis variables independently predictive of 30-day POM.

**Results** This study included 1893 men and 777 females, with a mean patient age of 64.2±13 years. 774 patients (29.0%) had a junctional, Siewert I or Siewert II type tumour and 1896 patients (71.0%) had either a Siewert type III or gastric adenocarcinoma. The majority of patients (2045, 76.6%) underwent gastrectomy, 625 (23.4%) oesophagectomy and proximal gastrectomy and 209 (7.8%) total oesophagogastrectomy. Resection was R0 in 2224 patients (83.3%). Neoadjuvant treatment was given to 665 patients (24.5%). A total of 114 patients died within 30 days of surgery (4.3%). POM rates increased during three study periods (1997–2000, 3.3%; 2001–2005, 3.6%; 2006–2010, 5.6%; p=0.021). The POM rate was significantly higher in patients who experienced grade III and IV toxicity during neoadjuvant chemotherapy when compared to those who did not (8.7% vs 2.6% respectively, p=0.007). Patients ≥60 years old and American Society of Anaesthesiology grade III or IV correlated with POM (p=0.002 and p=0.000, respectively). Variables indicating advanced disease consistently predicted POM (metastases at diagnosis, p=0.005; disease requiring extended resection, p=0.005; surgery with palliative intent, p 8 resections/annum (OR 0.389, 95% CI 0.157 to 0.965, p=0.042) and no grade III or IV toxicity during neoadjuvant treatment (OR 0.286, 95% CI 0.107 to 0.762, p=0.012) were protective factors.

**Conclusion** This large national cohort study confirms patients with advanced disease are at higher risk of POM and centralisation of oesophago-gastric cancer resection is warranted. The novel finding that poor tolerance of neoadjuvant therapy increases the POM rate has significant implications for decision making in this subgroup of patients (Clinical Trial.gov identifier NCT01249859).

**Competing interests** None declared.

# Pathology free papers

## OC-102 COELIAC DISEASE, ANTI-INFLAMMATORY DRUGS OR *HELICOBACTER PYLORI* ARE THE MOST COMMON IDENTIFIABLE CAUSES OF LYMPHOCYTIC DUODENOSIS

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**Introduction** Lymphocytic duodenosis (LD) is found in 2% of duodenal biopsies. LD is defined by normal villous architecture and intraepithelial lymphocytes (IELs) >25 per 100 enterocytes. This is more commonly recognised as modified Marsh grade 1 on histopathology reports. Such patients should not be diagnosed with coeliac disease, solely by histology, as previous retrospective studies have suggested other associations with LD.

**Aims** To prospectively study the aetiology of LD.

**Methods** One hundred and sixty five patients with LD were rigorously investigated for coeliac disease and other known associations of LD, by means of revisiting the patient's history and recent investigations, followed by a combination of gluten challenge, HLA typing, repeat coeliac serology & duodenal biopsies, and exclusion of infection/inflammatory bowel disease.

**Results** 127 female: 38 male, age range 17–83 years, median age 46 years. Coeliac disease was present in 21% of patients with LD. In the absence of a positive coeliac diagnosis, LD was most commonly associated with anti-inflammatory drugs (17%), *H pylori* (16%), gastrointestinal infections (7%), immune dysregulation (6%), inflammatory bowel disease (3%), and IgA deficiency (1%). Overall, there were 49 (30%) cases where no cause was found and the IEL count normalised in 35/49 (71%). Irritable bowel syndrome (IBS) was a clinical diagnosis in 30 of these 49 patients. All patients with coeliac disease were HLA DQ2 or DQ8 positive, compared to 55% of non-coeliacs (p value <0.0001). Patients with coeliac disease were significantly associated with positive endomysial and/or raised tissue transglutaminase antibodies (p<0.0001). There was no statistical difference in age, gender or baseline bloods (haematology/biochemistry/inflammatory markers) between the coeliac and non-coeliac group (p>0.05).

**Conclusion** This is the largest cohort of patients systematically investigated for a cause of their LD. A cause can be identified in up to 70% of cases, with coeliac disease, anti-inflammatory drugs and *H*