PTU-181 OPTIMISED RESPONSE PREDICTION IN OESOPHAGOGASTRIC ADENOCARCINOMAS (OGA) WITH COMBINATION OF MOLECULAR BIOMARKERS, SERUM CELL DEATH MARKERS AND FDG-PET

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Introduction Predictive biomarkers (BMs) for OGA would optimise treatment selection and avoid ineffective therapy. Metabolic response (MR) defined as >35% decrease in tumour FDG Standardised Uptake Value (SUV) between day 0 and day 14 after starting chemotherapy has a high negative predictive value (95%) for response, but limited positive predictive value (50%). Combining molecular BMs and serum cell death markers with FDG-PET may optimise response prediction. We used global gene expression profiling (GEP) and cell death ELISAs to identify molecular BMs and serum markers that when combined with FDG-PET would improve predictive accuracy.

Methods 28 patients with locally advanced/metastatic OGA received platinum based chemotherapy (PBC). FDG-PET scans were at day 0 & 14 and GEP (Affymetrix ST1.0 Exon Genechips) on day 0 tumour biopsies. A tissue microarray comprising an independent set of 154 OGA who had surgery +/-neoadjuvant PBC was used with immunohistochemistry (IHC) for qualification of GEP results. Cytokeratin 18 (CK18) M30 (apoptosis) and M65 (apoptosis +necrosis) ELISAs (Pevivia, Sweden) were used to assess cell death from serial serum samples during chemo. Radiological response was assessed after 3/4 cycles of PBC by RECISTv1.1.

Results We identified a gene expression signature (86 genes) that separated FDG-PET MR patients (>35% fall SUV day 0–14) into those that do and do not have a RECIST response. In cross validation this signature correctly predicted response in 14/14 metabolic responders (MRs). Pathway analysis on GEP data identified potential novel mechanisms of response including the Leptin pathway. Leptin mRNA was higher in FDG MRs who did **not** have a RECIST response compared to those that did (p=0.026). In the independent set high Leptin protein by IHC was associated with **lack** of histopathologic response to neoadjuvant PBC (n=64, p=0.007). High Leptin expression also had a therapy independent prognostic effect with longer survival in the absence of histopathologic response or with no neoadjuvant PBC and in low Leptin patients poor survival was mitigated to a degree by neoadjuvant PBC. Serum CK18M30 decreased from day 0–14 in MRs but in metabolic non-responders (MNRs) there was a smaller fall or a rise (p=0.021). Levels in MNRs did not change with subsequent chemo. In MRs levels continued to fall in RECIST responders but increased again in non-responders.

Conclusion Molecular biomarkers (Leptin in particular) and serum cell death markers combine with FDG-PET to optimise response prediction in OGA. Further investigation of this combined molecular, serum and imaging approach is warranted.

Competing interests None declared.

PTU-182 PERCUTANEOUS RADIOLOGICAL GASTROSTOMY IN OESOPHAGEAL CANCER PATIENTS: A FEASIBLE AND SAFE ACCESS FOR NUTRITIONAL SUPPORT DURING MULTIMODAL THERAPY

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Introduction Percutaneous endoscopic gastrostomy is not widely used in malnourished oesophageal cancer (OC) patients because of concerns about feasibility in frequently obstructive tumours, suitability of the stomach as an oesophageal substitute, and potential for metastatic inoculation. A percutaneaous radiological gastrostomy (PRG) could be an optimal alternative.

Methods Experience with PRG among 1205 consecutive patients presenting with OC from 2000 to 2010 in our department was retrospectively reviewed. PRG was proposed for malnourished patients for whom neoadjuvant chemoradiation was scheduled. PRG placement success rate and major (Dindo-Clavien>II) related complications were analysed. A matched cohort analysis was then constructed in patients who underwent oesophagectomy with gastroplasty (n=759) to evaluate the impact of PRG placement on suitability of the gastric pull-up and on postoperative course. From 76 resected patients with PRG (PRG group), 152 randomly selected controls without PRG (no PRG group) were matched 2:1 by gender, age, ASA grade, cTNM stage and neoadjuvant treatment delivery.

Results PRG placement was planned in 269 (22.3%) patients mainly with locally advanced OC (63.8%). PRG placement was feasible in 259 (96.3%) patients. 60-day PRG-related mortality and major morbidity rates were 0% and 3.8% respectively. For resected patients with gastroplasty, the PRG and no PRG groups were comparable regarding perioperative characteristics except for malnutrition more frequent in the PRG group (p<0.001). At the time of operation, PRG takedown and site closure were uncomplicated and the use of the stomach was possible in all 76 patients. Despite higher malnutrition rate at presentation in the PRG group, overall and oesophageal surgery related morbidity rates were similar between the two groups (p>0.432).

Conclusion PRG is feasible, safe and useful in non-selected patients with OC and does not compromise the suitability of the stomach as an oesophageal substitute in patients deemed to be resectable.

Competing interests None declared.

PTU-183 INEFFECTIVENESS OF 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IN THE EVALUATION OF TUMOUR RESPONSE AFTER COMPLETION OF NEOADJUVANT CHEMORADIATION IN OESOPHAGEAL CANCER

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Introduction After primary CRT, a non-invasive evaluation of the tumour response could help in the treatment decision to identify patients who may benefit from surgery. Whether FDG-PET provides clinically relevant information remains questionable. The objective of this prospective trial was to evaluate the role of 18F-Fluorodeoxyglucose-positron emission tomography (FDG-PET) in the assessment of tumour response after the completion of neoadjuvant chemoradiation (CRT) in patients with locally advanced resectable oesophageal cancer.

Methods Operable patients with locally advanced oesophageal cancer (clinically staged T3 N0-1 M0) were enrolled. The complete

treatment plan included neoadjuvant CRT (cisplatin + 5-Fluorouracil/45 Gy) followed 6–8 weeks later by a transthoracic en bloc oesophagectomy. Morphological evaluations combined with FDG-PET results were performed 2 weeks before and 4–6 weeks after the completion of CRT. Intratumoural pre- and post-treatment FDG-standardised uptake values were assessed (SUV1, SUV2, percentage change). These variables were correlated with pathologic and morphologic responses and survival. Investigators were blinded to the FDG-PET results unless metastatic disease was suspected.

Results Out of 60 total patients, 46 underwent the complete treatment plan (median age: 60.1 years; adenocarcinoma: 25 patients; squamous cell cancer: 21 patients). A major pathological response occurred in 19.6% of patients and was associated with a favourable outcome (p=0.057). Neoadjuvant CRT led to a significant reduction in intratumoral FDG-uptake (p<0.001). No significant association was seen between a pathologic response (either complete or major) and the FDG-PET results (p>0.280). The SUV2 value was correlated with a morphological response and the possibility to perform an R0 resection (p<0.018; ROC analysis: SUV2 threshold = 5.5). No significant association was found between metabolic imaging and recurrence or survival.

Conclusion FDG-PET does not effectively correlate with pathologic response and long-term survival in patients with locally advanced oesophageal cancer undergoing neoadjuvant CRT followed by surgery (registered on http://www.e-cancer.fr website, RECF0350, 2002-1936R).

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Competing interests None declared.

PTU-184 DEFINING AND TREATING A POSITIVE CIRCUMFERENTIAL RESECTION MARGIN IN OESOPHAGEAL AND GASTRO-OESOPHAGEAL JUNCTIONAL CANCER

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Introduction A positive circumferential resection margin (CRM) has been implicated with poorer prognosis in oesophageal and gastro-oesophageal junctional (OGJ) cancer. The Royal College of Pathologists (RCP) defines a margin as positive if tumour cells are present within 1 mm. In contrast, the College of American Pathologists (CAP) only defines a margin as positive if tumour cells are observed at the margin. The equivalence of the systems is not clear and the impact of adjuvant treatment has not been assessed.

Aims To compare the prognostic ability of the RCP and CAP systems in a cohort from a single UK centre and to determine if adjuvant radiotherapy offers a survival benefit for CRM positive patients.

Methods Patients with a "T3" adenocarcinoma or squamous cell carcinoma of the oesophagus or OGJ undergoing potentially curative resection between 1994 and 2010 were identified from a prospective database. Resection specimens were reviewed and the CRM was measured to ± 0.1 mm by a consultant pathologist. Univariate, multivariate and propensity score matching analyses (PSMA) were performed.

Results A total of 226 patients were included. Cox regression demonstrated patient sex (p=0.009), tumour differentiation (p=0.015), nodal (N) stage (p<0.001) and CRM group (p=0.045) were independently predictive of prognosis. Patients were grouped into CRM of 0 mm (CAP+ve, n=47), CRM >0 mm but <1 mm (RCPCRM, n=83) and CRM ≥1 mm (CRM-ve, n=96). Median survivals (95% CIs) were significantly different across groups (p=0.019) with CAP+ve = 18 months (13.0 to 23.0), RCPCRM = 28 months (18.6 to 37.3) and CRM-ve = 33 months (25.8 to 40.2). A trend for poorer survival was noted for the CAP+ve vs the RCPCRM group (p=0.073) although there was heterogeneity in N stage across groups. PSMA demonstrated no residual survival difference between CAP+ve and RCPCRM groups when other prognostic variables were controlled. Significant selection bias was observed for patients undergoing adjuvant radiotherapy. PSMA was applied to assess the treatment effect. Patients undergoing adjuvant radiotherapy (n=23) showed significantly improved survival when compared to controls (n=23) matched for sex, pre-operative treatment, N stage, histology and differentiation (p=0.04).

Conclusion The survival difference between CAP+ve and RCPCRM groups could be explained by existing prognostic variables. The CAP and RCP systems therefore appear equivalent in our cohort. In selected patients with a CRM <1 mm, adjuvant radiotherapy may be of benefit and a prospective randomised trial is indicated.

Competing interests None declared.

PTU-185 NOVEL TECHNIQUES FOR ASSESSING OESOPHAGO-PHARYNGEAL REFLUX IN PATIENTS WITH HOARSENESS AND SUSPECTED LARYNGOPHARYNGEAL REFLUX

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Introduction It is suggested that hoarseness along with typical signs on laryngoscopy can be caused by oesophago-pharyngeal reflux, often referred to as LPR. New methods are proposed to assess pharyngeal exposure to gastric contents. They are suggested to measure (1) liquid or mixed gas-liquid acid and non-acid reflux (HMII-pH), (2) aerosolized acid reflux (Dx-pH measuring system, Restech), and (3) presence of pepsin in saliva. We **aimed** to quantify pharyngeal exposure to gastric contents in patients with hoarseness and healthy controls using the above techniques.

Methods 21 patients with hoarseness and a positive laryngoscopy (mean age: 51 range: 23–75) and 10 asymptomatic controls (mean age: 26, range: 21–34) underwent simultaneous HMII-pH monitoring, oropharyngeal pH monitoring and saliva pepsin sampling. The HMII-pH catheter was located with impedance sensors in the oesophageal body, 3–5 cm distal and 0–2 cm proximal to the UOS. The Dx-pH catheter was located posterior to the uvula and pepsin in saliva was measured using an in vitro device utilising two pepsin monoclonal antibodies (PepTest) at five different times during the 24-h period. Patients were studied "off" PPI.

Results Healthy controls had (1) no liquid or mixed gas/liquid reflux in the pharynx, (2) two controls had +ve Dx-pH and (3) two controls had more than one saliva sample +ve for pepsin with the other tests negative. Patients were classified into four groups: (a) all tests +ve (n=2); (b) two tests +ve (MII-pH + pepsin (n=5) or MII-pH + Dx-pH (n=3); (c) all tests negative (n=5) and (d) patients with +ve Dx-pH or pepsin without evidence of HMII detected reflux. These patients were considered negative (n=6). Dx-pH drops were poorly associated with HMII-pH reflux. 11% of Dx-pH drops to pH<4, 15% of pH drops to pH<5 and 10% of pH drops to pH<5.5 coincided with HMII detected liquid or gas reflux in the oesophageal body. The detection of pepsin in saliva occurred in 7/10 patients with acid or non-acid HMII detected reflux. Positive pepsin saliva samples were preceded by more reflux events in the previous 60 min 3 (1–4) than negative samples 0 (0–2) p<0.0001.