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14th Annual Meeting of the UK and Ireland Neuroendocrine Tumour Society 2016

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Speaker Abstracts
What's new in NETs? ENETS guidelines update (new recommendations applied to interactive cases), UK epidemiology and genetics

Mohid Khan
Cardiff.

With the ENETS guidelines update, there are a number of key issues tackled with this common subtype of NET. Terminology is clarified. Whether one uses neuroendocrine tumour, or neoplasm, as mentioned in the guidelines, the terms ‘midgut’ or ‘hindgut’ are thought not to be as helpful as indicating the primary anatomical site e.g. jejuno-ileal, rectal, colonic, caecal, appendiceal, etc.

Grading with Ki-67 proliferation index, assessed from histology, is considered to be mandatory for prognostication. Ideally a 68Gallium-labelled octreotide PET-CT scan should be obtained after diagnosis with CT or MR imaging and if not available, somatostatin receptor scintigraphy SPECT/CT. CgA and urinary 5-HIAA should be performed on diagnosis and on follow up.

Palliative resection in the presence of liver metastases is discussed in the updated guidelines. Resection should be considered in symptomatic patients with pending obstruction on imaging and overall outcome is better in asymptomatic patients although the direct causal relationship has not been proven.

Annual transhphoracic echocardiography should be performed annually for patients with carcinoid syndrome and carcinoid heart disease. Nt-proBNP and cardiac MRI are considered to be useful for assessing these patients. Closure of any PFO is debated but it is suggested in these guidelines acknowledging there is limited data for this approach.

Management of distant disease (liver metastases) is discussed in a separate guideline but includes somatostatin analogues, interferon, surgical resection (including de-bulking >90% or resection of <90% burden for symptoms), PRRT, with Everolimus now also an alternative option.

DoI: 10.1530/endoabs.46.NETS1

Bronchial NETs
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Manchester.

The incidence and prevalence of well-differentiated Bronchial NETs has been increasing globally in recent years. This may be due to better diagnostic/detection techniques and a greater awareness of these conditions. Despite this, these cancers are still uncommon and therefore most clinicians will not manage many of these patients. As a consequence, gaining experience in treating these cancers can become challenging. In the absence of a move to centralise their care, guidelines can play an invaluable role in helping clinicians manage these patients and standardise the diagnostic and treatment pathways nationally and internationally. The added benefit of national/global adherence to a single set of guidelines is that useful real world data can be extracted on effectiveness of various aspects of the guidelines where practice is uncertain due to brevity of data. The aim of this talk is to discuss the main parts of the most recently published ENETS Bronchial NETS Guidelines using case studies to highlight strengths and weaknesses in the guidelines and to update on recent developments in this field.

DoI: 10.1530/endoabs.46.NETS3

Genomics England with the consent of participants and the support of the public is creating a lasting legacy for patients, the NHS and the UK economy, through the sequencing of 100,000 genomes, 50,000 genomes from cancer, two per patient (tumour and a paired blood sample) and 50,000 from rare disease, three genomes per patient (affected person plus two blood relatives). The main project started sample collection in March 2015, aiming to collect samples by the end of 2017 through its network of 13 Genomic Medicine Centres in England and now extending to include Scotland, Wales and Northern Ireland. It can also link a whole lifetime of medical records to this data, to understand more about the impact of cancer or rare disease. Its four main aims are to create an ethical and transparent programme based on consent; to bring benefit to patients and set up a genomic medicine service for the NHS; to enable scientific discovery and medical insights; and to kick start the development of a UK genomics industry. There are opportunities for individuals with NETs and families with NETs to be recruited within both arms of the programme. Current cancer patients with small bowel and pancreatic NETs are eligible in the cancer programme, with tumour and normal sample collection, to be sequenced in parallel. Patients with NETs—primarily paragangliomas and pheochromocytomas, may be eligible in the rare diseases programme under inherited cancers, provided they meet eligibility criteria in the multiple endocrine tumour category. There is also an opportunity to nominate further rare diseases or tumour types for consideration, for more NET patients to benefit from the project.

DoI: 10.1530/endoabs.46.NETS5

Management of Phaeochromocytoma/Paraganglioma NETs

Abstract unavailable.
NETS9

Abstract unavailable.

Open clinical session

NETS9

UK survey on the use of long-acting somatostatin analogues in neuroendocrine tumours

Mike Tadman
Oxford.

Background and aims
Long-acting somatostatin analogues (SAs) are an established treatment for functional symptoms of neuroendocrine tumours (NETs) and also for their known anti-tumour effect. Discussion with colleagues highlighted variations in their use in practice, surrounding test-dosing and treatment doses of SAs.

Methods
In 2016 an electronic survey of SA use was undertaken to illuminate actual practice in the UK. Questions focused on test-dosing, treatment doses of SAs, monitoring tests whilst on treatment and rationale for choice of SA, both to manage ‘functional NET symptoms’ and also non-functional NETs (use as anti-tumour therapy).

Results
In total, 21 different hospitals across the UK responded to the survey. Findings highlighted wide variation in practice in a number of key areas; the use of test dosing prior to establishing SAs; a range of different SA treatment doses, and variation in monitoring tests whilst on treatment. Practice variation existed both in managing functional symptoms, but also when used as anti-tumour therapy. Despite a wide range of test dosing regimes, there were very few recorded drug reactions and it was extremely rare not to establish patients on an SA after test dosing.

Conclusions
This survey highlights wide variation in practice in terms of test dosing, drug dosing and monitoring tests. It raises a number of practice questions: should detailed guidance exist; are all these practices justified and what are the cost/resource implications. Future projects include a possible multicentre audit of test-dosing and monitoring of patients on SAs. Consideration could also be given to a European wide survey of SA use.

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NETS10

An exploration of psychological symptoms in patients with vasoactive hormone-secreting neuroendocrine tumours (carcinoid syndrome)

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Psychological symptoms including aggression, confusion, irritation, anxiety and depression have been observed clinically in patients with carcinoid syndrome. It has been suggested that vasoactive-hormone secretion is involved in provoking psychological symptoms. The objective of this qualitative study is to explore the presence and experience of specific psychological symptoms in carcinoid syndrome. Nine patients with carcinoid syndrome and psychological issues currently or within past year were recruited from two NET specialist centres. They participated in qualitative interviews focusing on their previous and current experiences of physical and psychological symptoms. Patients experienced various psychological symptoms including anxiety, agitation and irritability and occasional low mood, mood swings and mild aggressive tendency. The unpredictable nature of physical distress from physical symptoms resulted in psychological symptoms. Although many patients had anxiety from cancer-related issues, there was a link between anxiety and flushing in a minority. Patients with positive outlook maintained good mood and were better at coping but no evidence to suggest it affected anxiety-related flushing, agitation or irritability. Cancer-related issues, impacts of physical symptoms, external issues and vasoactive-hormones are all implicated in producing psychological symptoms in carcinoid syndrome. By identifying issues and contributing factors, patients at risk can be monitored and psychological support provided.

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Translational Science Session

NETS11

Abstract unavailable.

NETS12

Abstract unavailable.

International Speaker & Trials update

NETS13

Abstract unavailable.

NETS14

Abstract unavailable.
Oral Communications
OC1

Netazepide, a gastrin/CCK2 receptor antagonist, can eradicate gastric neuroendocrine tumours in patients with autoimmune chronic atrophic gastritis
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Introduction
In a two-centre, 12-week, open trial in 16 patients with autoimmune chronic atrophic gastritis, hypergastrinemia, multiple type 1 gastric neuroendocrine tumours (NETs), and raised circulating CgA, the gastrin/CCK2 receptor antagonist (CCK2RA), netazepide, reduced the tumour number and size, and normalised CgA.

Aim(s)
To treat those patients with netazepide for longer, and to identify new biomarkers.

Materials and methods
After a mean 14 months off netazepide, 13 patients took it for another 52 weeks. Assessments were: gastroscopy; gene transcript expression in corpus biopsies; and blood CgA, miR-222 and gastrin.

Results
While off treatment, the number and size of the tumours, and CgA all increased again. Netazepide for 52 weeks eradicated all tumours in 5 patients, left one patient with only one tumour, and reduced further the number and size of the tumours in the others, and normalised CgA (P<0.01). Gastrin was unaffected. Netazepide was safe and well tolerated. Netazepide reduced mRNA abundances of overexpressed CgA, histidine decarboxylase, pappalyisin 2 (PAPP2), glycoprotein hormones alpha polypeptide, and miR-222 in biopsies, and miR-222 in blood (P<0.05). miR-222 targets the tumour suppressor and oncogene p27kip1.

Conclusions
A CCK2RA is a potential medical and targeted treatment for gastric NETs that are gastrin driven, and an alternative to endoscopic resection or surgery. Treatment

DOI: 10.1530/endoabs.46.OC1

OC2

Tumour size is not a reliable criterion for management of patients with Non-secreting pancreatic neuroendocrine tumours: results of a large, multi-centre, operative cohort
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Background
Small pancreatic neuroendocrine tumours (PNETs) present a management dilemma because of their uncertain natural history. Some clinicians believe that lesions <2 cm are indolent and can be managed with surveillance. By contrast, the most recent WHO classification system regards all PNETs as potentially malignant.

Aim
To assess the malignant behaviour of small PNETs in a large, retrospective, multicentre patient cohort.

Methods
Patients were retrospectively identified from 5 hospitals using inclusion criteria of non-functional, non-familial, resected PNETs of all stages and grades. Logistic regression for clinical, biochemical and pathological variables, and cox regression for survival data, were performed using SPSSv22.

Results
216 patients with a resected PNET were identified. 64 (30%) had tumours ≤ 2 cm. Surgical procedures included 80 Whipple’s resections, 124 distal pancreaticectomies, 7 enucleations and 2 total pancreatectomies. Malignancy was defined as any of local, vascular or lymphatic invasion or distant metastasis. Overall, malignancy was confirmed in 134 (62%) patients; 22 (34%) tumours ≤ 2 cm were malignant, compared to 112 (74%) > 2 cm. (Figure 1) Tumours ≤ 2 cm were staged as stage I:38, II:5, III:11 IV:10. The smallest primary with nodal metastasis was 6 mm and with liver metastasis, 10 mm. Prediction of malignancy was not possible in tumours ≤ 2 cm as logistic regression revealed no association between malignancy and diameter, symptomatic presentation, Ki67 or CgA.

The median survival of this entire cohort was 202 months. 3-year survival did not differ across the 2 cm threshold (≤ 2 cm 87.0%, > 2 cm 80.3%; Z=0.151). Significant prognostic factors for the whole cohort included age (hazard ratio 1.07, P=0.004), diameter (HR 1.01, P=0.018), positive nodes (HR 2.041, P=0.026), TNM stage (P<0.05), extrabehatic disease (HR 2.42, P=0.019) and grade (G1 HR 0.11, Z=0.04), diameter (HR 1.01, P=0.018), positive nodes (HR 2.041, P=0.026), TNM stage (P<0.05), extrabehatic disease (HR 2.42, P=0.019) and grade (G1 HR 0.11, Z=0.04)

Extended analysis showed that tumours > 2 cm had significantly worse outcome (Z=0.018). Table shows significant factors in univariate and multivariate analyses. Z=0.018, P=0.003. Interestingly, surgical margin involvement and extent of nodal positivity (e.g. 2/27) were not prognostically significant. Subgroup analysis of tumours ≤ 2 cm showed that diameter was not prognostically significant (P=0.15).

Conclusions
1) 34% of PNETs ≤ 2 cm displayed malignant features.
2) Metastatic disease was reported in primaries as small as 6 mm, therefore making diameter based surveillance problematic.
3) 3-year survival was not significantly better for tumours ≤ 2 cm than for tumours > 2 cm, reflecting the malignant potential shared by all PNETs.

Figure 1 Prevalence of malignant features and overall malignancy (presence of any one feature) stratified by diameter in a cohort of 216 resected PNET patients

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OC3

Efficacy and safety of telotristat etiprate in patients with carcinoid syndrome not adequately controlled by somatostatin analog therapy: Analysis of the ongoing TELESTAR extension period
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Introduction
TELESTAR was a pivotal, randomized phase 3 study evaluating telotristat etiprate (TE), a tryptophan hydroxylase inhibitor, among patients (pts) with carcinoid syndrome (CS). When added to somatostatin analogues (SSA), 250 mg tid and 500 mg tid TE each produced significantly greater bowel movement (BM) frequency reduction averaged over 12 weeks (wks) than placebo (PBO) plus SSA (P<0.001). Ps crossed over to open-label (OL) treatment with TE 500 mg tid after Wk 12. The extension phase (Wk 13 to Wk 48) is still ongoing. Aim(s): Examine initial efficacy and safety in the crossover (CO) to OL, TE. Materials and methods: Changes from baseline (CFB) in BMs/day were examined at Wks 12, 24, and 36, and safety was reviewed.

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Results
Among 135 randomized pts, baseline BMs/day (prior to Wk 1) were 5.2, 6.3, and 6.0 respectively on PBO, 250 mg and 500 mg tid. At Wk 12, CFB were $-0.9$ (PBO), $-1.7$ (TE 250 mg), and $-2.1$ (TE 500 mg) ($n=108$ pts with BM data). 115 pts entered the extension, and at Wk 24, CFB were $-1.8$, $-2.1$, and $-2.1$ ($n=98$), and at Wk 36 CFB were $-1.8$, $-2.2$, and $-1.9$ ($n=73$), respectively, in pts originally assigned to PBO, 250 mg tid, and 500 mg tid TE. The Wk 12 CO to 500 mg tid TE was well tolerated. No safety signals were observed with the CO.

Conclusion
Decreases in BM frequency were observed in pts who received TE 500 mg tid after crossing over from either PBO or 250 mg and were sustained in those on 500 mg. BM reduction and favorable safety were observed in pts treated beyond Wk 12.

Keywords: telotristat, carcinoid syndrome, tryptophan

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Poster Presentations
P1
MicroRNAs associated with small bowel neuroendocrine tumours and their metastases
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Introduction
Novel molecular analytes are needed in small bowel neuroendocrine tumours (SBNETs) to better determine disease aggressiveness and predict treatment response.

Aim of the study
To profile the global miRNome of SBNETs, and identify microRNAs (miRNAs) involved in tumour progression for use as potential biomarkers.

Material and methods
Two independent miRNA profiling experiments were performed (n = 90), including primary SBNETs (n = 28), adjacent normal small bowel (NSB; n = 14), matched lymph node (LN) metastases (n = 24), normal LNs (n = 7), normal liver (n = 2) and liver metastases (n = 15). We then evaluated potentially targeted genes by performing integrated computational analyses.

Results
We discovered 39 miRNAs significantly deregulated in SBNETs compared with adjacent NSB. The most upregulated (miR-204-5p, miR-7-5p and miR-375) were confirmed by qRT-PCR. Two miRNAs (miR-1 and miR-143-3p) were significantly downregulated in LN and liver metastases compared with primary tumours. Furthermore, we identified upregulated gene targets for miR-1 and miR-143-3p in an existing SBNET dataset, which could contribute to disease progression, and show that these miRNAs directly regulate FOSB and NUA2K oncogenes.

Conclusion
Our study represents the largest global miRNA profiling of SBNETs using matched primary tumour and metastatic samples. We revealed novel miRNAs deregulated during SBNET disease progression, and important miRNA-mRNA interactions. These miRNAs have the potential to act as biomarkers for patient stratification and may also be able to guide treatment decisions. Further experiments to define molecular mechanisms and validate these miRNAs in larger tissue cohorts and in biofluids are now warranted. (Work published).

Keywords: microRNAs, biomarkers, small bowel neuroendocrine tumour

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P3
Health-related quality of life (HRQoL), anxiety, depression and impulsivity in patients with advanced Gastroenteropancreatic Neuroendocrine Tumours (GEPNETs)
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Background
In patients with advanced GEPNETs, psychological symptoms may result due to potential disturbances in biogenic amines, particularly serotonin. This study compared HRQoL, anxiety, depression, and impulsivity in patients with and without carcinoid syndrome (CS) and correlated with serum 5-HIAA.

Methods
Consecutive patients with advanced GEPNETs (with liver metastases) receiving treatment, with and without CS completed (single time-point) HRQoL, QLQ-C30 and QLQ-G.NET21, Hospital Anxiety and Depression Scale (HADS) [score of ≥8/21 cut-off for anxiety/depression] and Barrett Impulsivity Scale (BIS). First-order factors analysed included: attention, cognitive instability, motor, perseverance, self-control, cognitive complexity; second-order factors: attentional, motor and non-planning. Two-sample Wilcoxon (Mann Whitney test) was applied to assess differences in serum 5-HIAA; two-sample Mann-Whitney U test for HRQoL and BIS, and proportion test for HADS, between those with and without CS.

Results
Fifty patients were included (April-August 2016); 25 each with and without CS. Median age was 66 years, 29 (58%) male. Median Ki67 was 4% (range 0–100); primary site: small bowel: 29 (58%), pancreas: 11 (22%), gastric and large bowel: 10 (20%), recurrent disease in 8 (16%). Five patients (10%) were taking prescribed psychoactive medications. Median time since diagnosis was 39.5
months (95%-confidence interval 21.5–48.5). Current median serum 5-HIAA in patients with and without CS was 367 nmol/l and 86 nmol/l respectively ($P=0.003$). No statistically-significant differences were reported between patients with and without CS in responses on QLQ-C30 or QLQ-GI.NET21; responses relating to physical functioning and endocrine symptoms approached significance ($P=0.09$ for both). Fifteen patients (26%) scored ≥8/21 on anxiety scale; 8 had CS, and 6 (12%) scored ≥8/21 on depression scale; 3 with CS. There was no difference in median 5-HIAA between those scoring < or ≥8/21 on anxiety scale ($P=0.53$). Proportion test was not statistically significant between groups for anxiety ($P=0.76$) or depression ($P=1.0$). There were no statistically significant differences between groups in first or second-order factors (BIS) or total sum ($P=0.23$).

Conclusion
There were no significant differences in HRQoL, anxiety, depression or impulsivity between patients with advanced GEPNET with or without CS. Over one quarter of patients had high anxiety scores (unrelated to peripheral serotonin metabolism), indicating importance of psycho-oncological intervention.

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**P4**

**Measurement of urinary 5-hydroxyindole acetic acid: correlation between spot versus 24-hour urine collection**

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**Introduction**

In neuroendocrine tumours (NETs), the urinary concentration of the serotonin metabolite 5-hydroxyindole acetic acid (5-HIAA) is used to monitor disease progression or treatment response. The sensitivity and specificity in the presence of the carcinoid syndrome are approximately 70 and 90%, respectively. Collecting a 24 hour urine specimen is difficult and inconvenient for patients and increases analytical variability. In addition, serotonin-containing foods may increase urinary 5-HIAA levels and require food avoidance. Aim of the study: To assess the correlation between 5-HIAA concentration in a ‘spot-urine’ sample with the 24 h-urine collection.

**Methods**

Patients with NETs or symptoms suggestive of NETs seen in our Endocrine Oncology Clinic provided a 24 h-urine collection and a spot-urine for 5-HIAA assessment. Patients were advised to avoid serotonin-rich food for three days prior and during the collection period. Urine 5-HIAA was analysed by high-performance liquid chromatography (HPLC). Different laboratories give upper reference values for 5-HIAA excretion of 40 to 50 μmol/24 h depending on the laboratory. As suggested by the King’s Hospital London group, a cut-off value of 5 μmol/mmol for spot urine 5-HIAA was used as the upper reference limit.

Results
We included 130 paired samples from 108 patients: 61/108 were male, the mean age was 64.5y (SD 14.2) years, and 97/108 had a NET diagnosis: 74/130 (56.9%) measurements were ≥40 μmol/24 h (median concentration 50.5 μmol/24 h, IQR 26.75 to 145.5) and 63/130 (48.5%) from spot specimens were ≥5 μmol/mmol (median concentration 4.69, IQR 2.26 to 16.4). A spot-urine was concordant with the 24 h-urine results in 85% (median concentration 4.69, IQR 2.26 to 16.4). A spot-urine was concordant with the 24 h-urine collection.

Conclusions
These results suggest that the spot-urine is a simple and promising sample type for 5-HIAA analysis, in particular for follow-up in patients with known elevated 5-HIAA levels.

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**P5**

**Incidence and characteristics of ileo-colonic neuroendocrine tumours identified in the UK bowel cancer screening programme**

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**Background**

Colorectal cancer is the third most common cancer in the UK this had led to development of the bowel cancer screening programmes (BCSPs). It is known that ileo-colonic NETs are increasing in incidence in part thought to be related to increased endoscopy. There are few epidemiological data on rectal or ileal NETs diagnosed in BCSPs. This study aims to identify the number of NETs diagnosed through the UK BCSP.

**Methods**

UK bowel cancer colonoscopy data is stored on the Exeter database managed by Public Health England (PHE). Queries were developed by PHE to capture potential NET related search terms across relevant data tables in the Exeter database. Queries were run to identify BCSP participants attending for colonoscopy with NET-related coding from 2006 to December 2014. A written proforma was sent to the responsible BCSP clinician for all participants identified with NET related search terms. The proforma contained questions on tumour characteristics and further patient management.

**Results**

216/707 participants had colonoscopies. There were 146 unique BCSP participants with NET related codes across the 3 database tables in this time period. 60% of the 146 participants were male (n=87). Primary sites: colorectal region (n=102, 70%), ileum (n=24, 16%), unknown (n=18, 12%) and appendix (n=2, 1%). The incidence of ileo-colonic NETs was 67 per 100,000 colonoscopies per year. 83% of participants with this data available were reported as grade 1 (83/98) with 8% as grade 2 (8/89) and 7% as grade 3 (7/89). Data on the presence of metastatic disease was available in 95/110 (86%). Metastases were present in 24% of cases (23/95); colonic (10/ 17) or ileal NETs (9/27). 94% (102/108) with a validated NET were discussed in a multidisciplinary meeting (MDM), mostly in colorectal MDMs (82%, 89/108) rather than a specific NET MDM (12%, 13/108). Additional recommendations were made in 82% of instances (63/77).

**Discussion**

This is the first data reporting on incidence of ileo-colonic NETs within a national bowel cancer screening programme. It provides evidence of early stage of disease at presentation of ileo-colonic NETs.

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**P6**

**Whole-exome next generation sequencing of sporadic adrenocortical carcinomas - evidence for a proposed adrenoma-carcinoma carcinogenesis sequence**

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Limited survival of patients with adrenocortical carcinoma (ACC) makes it imperative to understand the genetic basis of disease and support development of new therapies. Between 2010–2015, tissues from nine adrenalecomy patients (5M:4F, age 30–68 years) were snap frozen in liquid nitrogen and DNA extracted. Adjacent normal adrenal tissue (n=3) excised at adrenalecomy was collected as matched ‘normal’ controls. Whole-exome sequencing of these 12 adrenal samples using Illumina Nextera library kits on HiSeq1000 next generation sequencing compared four groups: 3 ‘normal’ adrenal; 2 benign adrenocortical adenomas (bACAs); 5 ACCs; and 2 metastatic ACCs (mACCs). The ‘normal’ adrenal were pairs to ‘normal’ controls. The average depth of sample coverage was 35x–50x, and >2000 potentially deleterious genetic mutations were identified, after excluding those also found in paired ‘normal’ samples. The median number of mutations found in: paired bACAs was 453.5; and in mACC was 532.5. A known Multiple Endocrine Neoplasia type 1 (MEN1) mutation was confirmed in an MEN1 patient’s bACA. One ACC contained both MEN1 and
beta-catenin (CTNNB1) mutations. No Beckwith-Wiedemann syndrome gene variants were found in this study, however, one ACC and one mACC harboured Li-Fraumeni syndrome mutations (TP53). Numbers of mutually exclusive mutations found in each separate tumour group were: 24 in bACC, 1244 in ACCs and 712 in mACCs. Few mutations (0.1%) were common to both adenomas and carcinomas. However, 7.1% of mutations were found in both ACC and mACC groups. Finally, two oncogenes, MAGEC1 and PLIN4, were mutated in all three adrenal tumour groups and the most frequently mutated cancer-related genes were TYRO3 and KRT18, whose protein products are normally expressed in adrenal glands. Thus, MAGEC1, PLIN4, TYRO3, and KRT18 are novel candidate adrenal oncogenes, and our findings supports a proposed adenoma-carcinoma sequence for adrenocortical carcinogenesis.

Acknowledgment
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P7
Evaluation of quality of life after each cycle in patients treated with Peptide Receptor Radionuclide Therapy (PRRT)
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Background
NET-related symptoms such as flushing and diarrhoeas as well as disease related worries reduce quality of life in patients with neuroendocrine tumours (NETs). Peptide receptor radionuclide therapy (PRRT) is an established treatment in NETs and has been shown to prolong survival. However quality of life data post PRRT is lacking.

Aim
To evaluate the symptoms prevalence, intensity and their relation to quality of life in patients receiving PRRT.

Method
patients (mean age 63, range 36–79; 17 Female and 22 Male) completed 4 cycles of PRRT treatments (7.4 GBq of Lu177-DOTATATE) and filled in QLQ-GINET21 questionnaires before the first session of administration and prior to 3 succeeding treatments were available for analysis. The first questionnaire was used as a baseline.

QLQ-GINET21 is a disease-specific module, intended for use among patients with gut related carcinoid in varying disease stage. The response format of the questionnaire is a 4-point Likert scale with higher scores reflecting more severe symptoms. Responses to the questionnaire were linearly transformed to a 0–100 scale using European Organisation for Research and Treatment of Cancer (EORTC) guidelines.

The individual categories were analysed, looking at the mean change in score. In addition the global score (S) was evaluated according to EORTC guidelines.

Result
Results analysed according to change in overall score and change in category score.
See Table 1.

The mean scores within all categories (except treatment related effects) were reduced after 1 treatment and remained reduced prior to the 4th cycle of treatment (see Table). The biggest changes were seen in disease related worries followed by SF21 and ED.

Conclusion
This study demonstrates improved quality of life, reduction of symptoms, improved emotional and social function scale in patients who have received PRRT with improvement seen as quickly as after 1 cycle of treatment.

See Table 1.

Table 1. Results analysed according to change in overall score and change in category score.

<table>
<thead>
<tr>
<th>SCORE</th>
<th>ED</th>
<th>GI</th>
<th>TR</th>
<th>DRW</th>
<th>SF21</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>29.34</td>
<td>25.04</td>
<td>0.00</td>
<td>48.72</td>
<td>43.30</td>
<td>31.85</td>
</tr>
<tr>
<td>After 1st therapy</td>
<td>25.44</td>
<td>21.93</td>
<td>16.67</td>
<td>41.81</td>
<td>38.45</td>
<td>28.33</td>
</tr>
<tr>
<td>After 2nd therapy</td>
<td>24.22</td>
<td>18.12</td>
<td>17.95</td>
<td>38.60</td>
<td>36.47</td>
<td>26.45</td>
</tr>
<tr>
<td>After 3rd therapy</td>
<td>23.08</td>
<td>21.20</td>
<td>14.10</td>
<td>42.31</td>
<td>36.75</td>
<td>27.30</td>
</tr>
</tbody>
</table>

DOI: 10.1530/endoabs.46.P7

P8
Blood measurement of neuroendocrine gene transcripts defines the effectiveness of operative resection and ablation strategies
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Background
Surgery is the only curative treatment for gastroenteropancreatic neuroendocrine tumours (GEP-NETs), but the prediction of residual disease/recurrence is limited in the absence of optimal biomarkers. We examined whether a blood-based multianalyte neuroendocrine gene transcript assay (NETest) would define tumor cytodestruction and therapeutic efficacy.

Methods
The NETest is a polymerase chain reaction–based analysis of 51 genes. Disease activity is scaled 0–100%; minimal <14%, low 14–47%, and high >47%. A total of 35 GEP-NETs in 2 groups were evaluated. I: after surgery (R0, n = 15; residual, n = 12); II: nonsurgery (n = 8: embolization with gel-foam alone [bland: n = 3], transarterial chemoembolization (n = 2), and radiofrequency embolization (n = 3). Measurement (quantitative real-time polymerase chain reaction) and chromogranin A (CgA; enzyme-linked immunosorbent assay) were undertaken preoperatively and 1 month after treatment.

Results
NETest score was increased in 35 (100%) preoperatively; 14 (40%) had increased CgA (y2 = 30, P < 2 × 10–5). Resection reduced NETest from 80 ± 5% to 29 ± 5. (P < 0.001). CgA decrease was insignificant (14.3 ± 6.0 U/L to 12.7 ± 1.7 U/L). NETest decreases correlated with diminished tumor volume (R2 = 0.29, P = 0.03). Cytodestruction significantly reduced NETest from 82 ± 3% to 41% ± 6, P < 0.001. CgA was not decreased (21.4 ± 5.5 U/L to 18.4 ± 10.1 U/L). Four (36%) of 11 R0s with increased NETest at 1 month developed positive imaging (sensitivity 100%, specificity 20%). One hundred percent (ablated group) were transcript- and image-positive.

Conclusion

Keywords: Blood NET transcripts, NETest, gastroenteropancreatic neuroendocrine tumours

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P9
Whole-exome sequencing (WES) of samples from patients with advanced pancreatic neuroendocrine tumours (pNETs) with exceptional responses vs. poor responders to targeted therapies; a TransNET study
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Background
Despite encouraging advances in the systemic therapy options for patients with pNETs (sunitinib and everolimus), no predictive biomarkers have been established for these drugs. We aimed to identify distinctive genomic alterations associated with benefit from treatment in patients with pNETs, by comparing exceptional-responder (ER) to poor-responders (PO).

Methods
Patients who achieved an objective radiological response (complete or partial) by RECIST 1.1, due to its exceptionality (5% for everolimus and 9.3% for sunitinib) in landmark trials, were included in the ER group together with those with a progression-free survival (PFS) beyond the median reported in the registration
trials. Patients with a similar PFS to the placebo groups in the pivotal trials were classified as PO. Deoxyribonucleic acid (DNA) was extracted from archival formalin-fixed paraffin-embedded (FFPE) tumour samples (T) and normal tissue (NT) or blood (B). Paired-end libraries were prepared using Illumina’s Nextera Rapid Capture Expanded Exome enrichment kit. Illumina HiSeq2500 was used for the sequencing with a > 100x coverage of the exomes. VarDict software was used for variant calling. Manchester Cancer Research Centre biobank approval for the study was obtained; all patients provided written informed consent.

Results
Thirty-one patients were screened; following review of availability and quality of the FFPE samples, 12 were found eligible to proceed with DNA extraction and sequencing. For these 12 cases, paired DNA extracted from T and NT or B was obtained. Five of the 12 patients received treatment with both drugs (everolimus and sunitinib, respectively in each case). Overall, 11 received everolimus and 6 received sunitinib; 9 and 5 patients were classified as ER to everolimus and sunitinib, respectively. Only 3 PO were identified (everolimus (2 patients), sunitinib (1 patient)). All samples were sequenced and passed the standard quality check to proceed with the bioinformatic analysis. Interpretation of results is ongoing.

Conclusion
It is feasible to find patients with a pNET diagnosis phenotypically distinct in relation to their responses and to perform WES from FFPE samples. Final WES results of this TransNET study will be presented at the meeting.

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P10
Biomarkers for carcinoid heart disease
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Introduction
Carcinoid heart disease (CHD) develops in patients with small bowel NETs with carcinoid syndrome. Currently, NT-proBNP (NTP) is suggested as the best current biomarker to screen for CHD and monitor heart failure. A number of other markers have been investigated for heart failure, however, none of these have been explored in NET patients with CHD or carcinoid syndrome. Galectin-3 (GAL3) promotes fibroblast proliferation and correlates with worse outcomes in heart failure. Adrenomedulin is elevated in heart failure and Calcitrocin is an inflammatory protein increased in heart failure. ST-2 is an interleukin-1 receptor that signals for severity of cardiac remodelling and tissue fibrosis. In this study we have assessed these markers in three cohorts of NET patients to determine how they compared with NTP.

Methods
About 3 groups of NET patients (n=37) were identified with blood released from the King’s College Hospital Institute of Liver Studies biobank; CHD (Group A, n=10), non-functional (Groups B, n=12, normal CgA, SHHIA, BNP), functional (Group C, n=15, elevated chromogranin A (CgA) & urine SHHIA, normal BNP). Analysis was performed using NTP, GAL3, ST2, calprotectin and adrenomedullin assays. Statistical analysis was performed with SPSS.

Results
The median values for NTP in the CHD cohort was above the 260 µg/ml cut off. Median values for calprotectin were elevated across all three groups. ST2, GAL3 and adrenomedullin were not elevated. The Kruskal–Wallis test across the 3 patient groups was significant for NTP (P < 0.001) but not for ST2, GAL3. Adrenomedullin was significantly lower in the CHD group compared with the non-functional and functional groups. There was significant correlation between GAL3 and calprotectin.

Discussion
The results corroborate the role of NTP in CHD for NET patients. ST2 may play a role in combination with NTP for risk stratification in CHD and heart failure. GAL3 requires further evaluation given its possible role in the development of cardiac fibrosis. Its value may be for screening at an earlier stage of CHD.

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P11
Assessing treatment benefit of telotristat etiprate in patients with carcinoid syndrome: Patient exit interviews
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1University of Kentucky, Lexington, KY, USA; 2Zentraalkliniek Bad Berka, Bad Berka, Germany; 3RTI Health Solutions, Research Triangle Park, NC, USA; 4Dana-Farber Cancer Institute, Boston, MA, USA; 5Charité-Universitätsmedizin 13353, Berlin, Germany; 6UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; 7Royal Free Hospital, London, UK; 8Upstate University, Upstate, Sweden; 9Ichan School of Medicine at Mount Sinai, New York, USA; 10Stanford University, Palo Alto, CA, USA; 11University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, USA; 12Tom Baker Cancer Centre Calgary, AB, Canada; 13Royal North Shore Hospital, St Leonards NSW, Australia; 14Lexicon Pharmaceuticals, Inc., The Woodlands, TX, USA.

Background
Telotristat etiprate (TE), an oral tryptophan hydroxylase inhibitor, is intended to treat carcinoid syndrome (CS) by reducing serotonin production. TE was evaluated in TELESTAR, a phase 3 study; the primary endpoint showed significant reductions in bowel movement (BM) frequency for 2 TE dosages + standard of care (SOC) vs. SOC. TELESTAR patients had CS inadequately controlled on somatostatin analog therapy with ≥4 BMs per day. They were interviewed about baseline symptoms and clinical trial experiences.

Materials and Methods
Participating sites were asked to invite all TELESTAR patients (consent obtained prior to randomization) to phone interviews scheduled between Weeks 12 and 14. Patients and interviewers remained blinded to treatment assignment. Interview data were summarized with standard qualitative analysis methods.

Result
All interview participants (n=35) reported diarrhea and/or excessive BMs at baseline. Diarrhea (n=17), followed by BM frequency (n=9), and urgency (n=5) were identified as the most bothersome and important symptoms to treat. BM frequency negatively affected emotional, social, physical, and occupational well-being. When probed, most participants reported that a reduction of ≥30% would be considered meaningful. Improvements in CS symptoms were reported by 69% of participants. Among these, 88% reported reductions in BM frequency and 79% reported improvements in stool consistency. About 95% who reported reductions in BM frequency noted that it was meaningful, describing a better ability to enjoy life, leave the house, and participate in social and other activities. Among the 35 participants answering a question about treatment satisfaction, 55% reported it was somewhat or very satisfactory to achieve TE in relieving CS symptoms. Reports of “very satisfied” were 0% (0/9) on placebo (SOC) and 50% (17/34) on TE, with similar results in the 2 TE dosage groups.

Conclusions
Diarrhea and BM frequency were identified as the most impactful CS symptoms. The primary endpoint of TELESTAR is very meaningful to patients.

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P12
Evaluation of a novel microfluidic device for epitope-independent enrichment of circulating tumour cells (CTCs) in patients with neuroendocrine tumours (NET)
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UCL Cancer Institute, London, UK.

Background
The identification and characterization of CTCs as part of a minimally invasive “liquid biopsy” has potential as a real-time biomarker in cancer patients. Using blood samples from NET patients, we evaluate the epitope-independent Parsortix, which enriches CTCs based on size and rigidity, and compare to the EptCAM-dependent CellSearch platform.

Methods
About 10 patients with histologically confirmed metastatic NET had synchronous 7.5 ml blood samples collected for processing in the CellSearch and Parsortix. CellSave samples were processed in the CellSearch for identification and enumeration of CTCs as previously described. EDTA samples were run in the Parsortix and an automated protocol for fixing and staining within the separation cassette was applied. Cells were stained for cytokeratin, CD45, EptCAM and
P13
Role of palliative resection of the primary tumour in advanced pancreatic and small intestinal neuroendocrine tumours: A systematic review and meta-analysis
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University Hospital Birmingham, Birmingham, UK.

Introduction
The role of surgery to resect the primary lesion in incurable metastatic small intestinal (SI-NET) and pancreatic neuroendocrine tumours (P-NET) remains controversial. Recent evidence suggests that palliative surgery may increase survival even in asymptomatic patients with non-functioning tumours. The present study investigated the value of palliative resection of the primary tumour in SI-NET and P-NET by systematic literature review and meta-analysis.

Methods
MEDLINE and Embase databases were searched to identify articles comparing patients undergoing palliative primary tumour resection without metastasectomy vs. no resection. Relevant articles were identified in accordance with PRISMA guidelines. The primary outcome was overall survival. Included studies were evaluated for heterogeneity and publication bias.

Results
About 13 studies met the inclusion criteria, of which 6 presented data suitable for meta-analysis. No randomised controlled trials were identified. Analysis of pooled multivariate hazard ratios demonstrated significantly longer overall survival in patients undergoing resection of both P-NETs (HR 0.43; 95% CI: 0.34–0.57, P < 0.001) and SI-NETs (HR 0.47; 95% CI: 0.35–0.55, P = 0.007). No significant heterogeneity was detected across the studies (I² = 0%, P = 0.625). Additional survival in patients treated surgically relative to non-surgically ranged from 14 to 46 months in P-NET, and 22 to 112 months in SI-NET. The number needed to treat in order that one additional patient was alive at five years, ranged from 14 to 46 months in P-NET, and 22 to 112 months in SI-NET. The number of additional survival in patients treated surgically relative to non-surgically ranged from 14 to 46 months in P-NET, and 22 to 112 months in SI-NET. The number of CTCs were then reviewed independently by the second observer in order to establish a final CTC count.

Conclusion
The epitope-independent Parsortix can be used to increase the yield of CTCs captured from NET patients when directly compared to CellSearch. In view of the inter-observer variability seen, Parsortix does not appear to be the ideal platform for enumeration but may be of value in increasing the yield of CTCs available for downstream molecular and functional analysis.

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P14
Perioperative carcinoid crisis during surgery-who benefits from octreotide?
Khalil ElGendy1,2, Sarah Johnson1,3, Jeremy French1,3, Steven White1,3, Richard Charnley1,2, Derek Manas1,2 & Colin Wilson1,2
1NET Service, Newcastle-upon-Tyne Hospitals Trust, Newcastle-upon-Tyne, UK; 2Hepato-pancreatico-biliary Surgery, The Freeman Hospital, Newcastle-upon-Tyne, UK; 3Histopathology service, RVI, Newcastle-upon-Tyne, UK.

Introduction
Carcinoid crisis, as an entity is poorly defined, but can be seen in patients with small bowel NET tumours after open bowel surgery or tumour unrelated procedures as cardiovascular instability (CI). Recent evidence suggests that cardiovascular instability (CI) during NET surgery is more common than previously considered.

Aims and methods
We audited the incidence of CI during procedures and determined the relationship to perioperative octreotide; considering the patient’s underlying disease burden. Patients were identified from the hospital pathology database having had their primary tumour resected in our institution between January 2011 and December 2015. Our prophylactic octreotide protocol is an intravenous infusion of 50 micrograms an hour for 24 hours prior to surgery.

Results
About 54 patients underwent 65 procedures. About 24% (n = 13) had carcinoid symptoms or syndrome prior to surgery. There was no postoperative mortality or direct morbidity related to CI in the 65 procedures. About 77% of patients had preoperative octreotide for at least 4 hours. Most procedures (67%) were complicated by CI not related to blood loss (Table 1). About 31 detailed anaesthetic charts were available for review.

Conclusions
Octreotide infusion does reduce the incidence and severity of cardiovascular instability during surgery- but is not universal. Almost all patients undergoing bowel or liver resection in the presence of liver metastases will have some form of cardiovascular instability during the procedure. The postoperative effects are not directly discernible.

Table 1 Presence of CI in relation to Octreotide therapy.

<table>
<thead>
<tr>
<th>Cardiovascular Instability</th>
<th>(Oct vs. No Oct)</th>
<th>Chi χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel resection, no liver mets (n=13)</td>
<td>45.5% vs 50%</td>
<td>P = 0.9</td>
</tr>
<tr>
<td>Bowel resection, liver mets (n=9)</td>
<td>50% vs 100%</td>
<td>P = 0.35</td>
</tr>
<tr>
<td>Simultaneous liver/bowel resection (n=9)</td>
<td>87.5% vs 100%</td>
<td>P = 0.6</td>
</tr>
</tbody>
</table>

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P15
Low rate of psychological ill health in patients with GEP NETs attending an ENETS Centre of Excellence
Kamani Liyanarachchi1, Maheshi Amarawardena1, Eleanor Smith3, John Newell-Price1,2 & Alia Munir1
1University of Sheffield, Sheffield, UK; 2Royal Hallamshire Hospital, Sheffield Teaching Hospitals, Sheffield, UK; 3Wesley Park Hospital, Sheffield Teaching Hospitals, Sheffield, UK.

Background
Assessment of psychological burden of disease forms one criterion for accreditation of a cancer specialist center. Patient Health Questionnaire-4 (PHQ-4), a validated self-report ultra-short questionnaire was used to assess anxiety and depression level in patients with GEP NETs, attending the clinics at an ENETS Centre of Excellence.

Methods
PHQ-4 was completed during routine outpatient visits over a three month period by 48 patients, who were randomly selected from the GEP NET database. Composite score of PHQ-4 was calculated. Depression and anxiety was suggested by a score of 6–8, and strongly suggested by a score above 9. Association between the cumulative score and demographic and disease related factors were also assessed.
Results
The majority (45.8%) of patients were above 70 years and mean age was 64.4 years. (SD-4.6). Most were males (52.2%) and majority were married (72.9%). Eighty five percent of the study population had gastrointestinal NETs, and 18.8% had pancreatic NETs. Small bowel NETs (58.3%) were the commonest. In more than half (56.3%) the disease duration was less than 2 years whereas in 27.1% disease duration was more than 5 years. Metastatic disease was present in 87.5% and 52% had symptoms of carcinoid syndrome.

The mean depression score was 2.14 (SD-3.1). About 83.3% had scores ≤ 6 and only 2.1% had scores ≥ 9. There were no significant associations between the scores and demographic factors [sex (P=0.769), age (P=0.716), and marital status (P=0.162)] and the presence of co-morbidities (P=0.424). Furthermore, depression and anxiety was also not associated with the factors related to the disease itself such as presence of metastasis (P=0.242), presence of carcinoid syndrome (P=0.155), duration of the disease (P=0.33), hormonal activity of the tumour (P=0.39). In addition scores did not differ between pancreatic and non-pancreatic lesions (P=0.62).

Conclusion
Anxiety and depression affects a minority of patients with NETS attending a dedicated NETS centre. There were no statistical significant associations between demographic and disease related factors. These scores concur with a larger recent publication but that anxiety score were higher in recurrent disease.

DOI: 10.1530/endoabs.46.P15

P16
Knockdown of Ga15 in BON cell line enhances pancreastatin inhibitory effect on neoplastic proliferation
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Although initially considered rare, the incidence of pancreatic neuroendocrine tumours (P-NETs) has progressively increased. A population-based study conducted in England and Wales (1986–1999) found that 5-year survival was 29% for non-functioning and 41% for functioning tumours when considering well-differentiated P-NETs. Traditional treatments show very limited effectiveness; novel targeted therapies are, therefore, required and identification of key molecules driving neoplastic proliferation will facilitate this process. Ga15 is a heterotrimeric G protein belonging to the Gαq/11 family. It promiscuously recognizes most G-protein coupled receptors (GPCRs) and is poorly affected by β-arrestin dependent desensitization. In gastro-entero-pancreatic (GEP)–NETs and in vitro model, Ga15 is significantly over-expressed with respect to normal tissue and its involvement in tumour progression has been suggested. Pancreastatin is one of the biologically active regulatory peptides derived from chromogranin A (CgA) processing and it has been shown to have the potential to be a diagnostic and predictive tumour marker in detecting GEP-NETs, including P-NETs. It is coupled to a GPCR and exerts a proliferative inhibitory effect on a variety of pancreatic and hepatic cell lines. We hypothesized that Ga15 protein is involved in the activation of CgA signalling pathway through stimulation with Pancreastatin in BON cell line. Silencing Ga15 gene with small interfering RNA (siRNA) resulted in a reduction in Ga15 mRNA expression of 82% (Fig. 1); however cellular proliferation was not affected by knocking down Ga15 (Fig. 2). Stimulation with CgA fragments (rhCgA (1-439), pancreastatin and CgA (Y) 410-439) in BON cells had little anti-proliferative effect while vasostatin I and II showed no effect (Fig. 3). On the contrary, when Ga15 silenced cells were stimulated with 1 mM Pancreastatin for 48 hours, a significant reduction in cell proliferation of 48% was observed compared to untreated cells, in the same experimental setting (Fig. 4). The findings from this project showed a role for Ga15 protein in regulating cell proliferation in P-NET cells through CgA signalling pathway. These findings support the need for further investigations regarding the role of Ga15 in metastatic tumours considering also that at the time of diagnosis, most patients have either metastatic (60.2%) or regionally advanced (20.7%) tumours.

DOI: 10.1530/endoabs.46.P16
P17
UK Phase IV, Observational study to assess Quality of Life in patients (pts) with pancreatic neuroendocrine tumours (pNETs) receiving treatment with Everolimus; The “Real-World” OBLIQUE Study
John Ramage1, Pankaj Punja1, Faluoyi Olusola1, Andrea Frilling1, Tim Meyer1, Gaurav Kapur2, Judith Cave3, Johnathan Walsley4, Sebastian Cummins2, David Farrugia1,11, Naureen Starling11, Lucy Wall12, Ruby Saharan*1 & Juan Valle6
1Kings College Hospital, London, UK; 2Queen Elizabeth Hospital, Birmingham, UK; 3Chatterbridge Cancer Centre, The Wirral, UK; 4Hammersmith Hospital, London, UK; 5Royal Free Hospital, London, UK; 6Norfolk & Norwich University Hospital, Norfolk, UK; 7Southampton University Hospital, Southampton, UK; 8West Park Hospital, Sheffield, UK; 9Royal Surrey County Hospital, Guildford, UK; 10Cheltenham General Hospital, Cheltenham, UK; 11Royal Marsden Hospitals, London, UK; 12Edinburgh Cancer Centre, Edinburgh, UK; 13Novartis Oncology UK, Surrey, UK; 14University of Manchester/The Christie Hospital NHS FoundationTrust, Manchester, UK.

Background
Everolimus, a mammalian target of rapamycin inhibitor, is licensed for use in adult pts with advanced well-differentiated pNETs in the UK. Limited Health-Related Quality-of-Life (HRQOL) data are available for everolimus therapy in these pts.

Methods
This prospective study assessed changes in HRQoL, (by monthly patient-reported EORTC QLQ-C30, -G1NET21 and EQ-5D questionnaires), in pts with pNETs during the first 6 months (mo) of treatment with oral everolimus 10 mg o.d. in routine clinical practice. Endpoints included change in EORTC QLQ-C30 score at 6mo of treatment (primary); and changes in QLQC30/G1NET21/EQ-5D scores, efficacy and safety data (secondary).

Results
Of 52 enrolled pts, 48 met eligibility criteria and 46 criteria for inclusion in the Full Analysis Set. No significant worsening of the Global QLQ-C30 score was seen from baseline (Mean Score (MS) = 56.9; 95%CI, 50.3–63.6) to 6 mo (MS = 55.0; 95%CI, 48.1–61.9; P = 0.660). An initial decline in -C30 physical functioning scale from baseline (MS = 74.2; 95%CI, 67.5–80.9) to 3 mo (MS = 65.2; 95%CI, 56.5–73.9; P = 0.007), returned to baseline by 6 mo (MS = 72.7; 95%CI, 64.8–80.5). Disease-related worries (G1NET21) increased from baseline (MS = 48.3; 95%CI, 39.5–57.1) to 1 mo (MS = 37.4; 95%CI, 31.0–43.8; P = 0.002), returning to baseline by 6 mo (MS = 43.7; 95%CI, 33.6–53.8). Treatment-related symptoms (G1NET21) increased from baseline (MS = 10.1; 95%CI, 2.6–17.7) to 3 mo (MS = 22.0; 95%CI, 16.8–27.3; P < 0.009), with recovery toward baseline by 6 mo (MS = 14.1; 95%CI, 9.3–18.9). The EQ-5D utility score decreased from baseline (MS = 0.72; 95%CI, 0.67–0.77) to 3 mo (MS = 0.67; 95%CI, 0.61–0.73); with recovery by 6 mo (MS = 0.73; 95%CI, 0.67–0.78). One patient stopped treatment due to adverse events in months 1–3, and 4 in months 3–6; with 32 pts still on treatment at week 24.

Conclusion
OBLIQUE has shown there is no significant decline in Global QLQ-C30 score from baseline to 6 mo following initiation of everolimus in pNET pts. An initial significant decline in some individual scales was observed during the first 3 mo, with recovery to baseline with continued treatment.

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P18
High-grade neuroendocrine tumours of the oesophagus: a single centre experience
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Background
High-grade neuroendocrine tumours (HGNETs) of the oesophagus are extremely rare and few cases have been reported worldwide. Here we aim to understand clinical profile, treatment strategy and outcomes for oesophageal HGNETs.

Methods
We report a single-centre retrospective review of 21 patients with oesophageal HGNETs treated between 2011–2016. Data on incidence, tumour location, stage at presentation, histopathology, treatment protocol and clinical outcomes was collected and analysed.

Results
Among >2000 cases discussed at upper GI multidisciplinary team meetings in the Christie between 2011–2016, 21 cases of oesophageal HGNET were identified. Median age at presentation was 70 years (range, 47–85). Female:male ratio 57.1% (n = 12) and 42.9% (n = 9) respectively. Histology confirmed small-cell NET in the majority (76.2%, n = 16), NOS 19% (n = 4) and large cell 4.8% (n = 1). At diagnosis (9/21, 42.9%) of patients had distant organ metastasis. The most common site of metastatic disease was the liver. All but one patient were deemed suitable for active anticancer treatment. Twelve patients (57.1%) were considered candidates for radical treatment. Among them, 9 (75.5%) commenced neo-adjuvant chemotherapy with intent to proceed to chemoradiotherapy (CRT); only 7 (58.3%) received CRT, while 2 (16.7%) progressed during neo-adjuvant chemotherapy. Three patients (25.0%) underwent radical surgery with or without chemotherapy. Of 8 patients not amenable for radical treatment, all received platinum/etoposide doublet chemotherapy. 70% (n = 7) received cisplatin and 30% (n = 3) carboplatin. Median number of cycles was 4 (range, 1 – 6). Best response was stable disease in 2 patients (25%) and partial response in 2 patients (25%). Median survival 16.4 months for patients treated with surgery, 14.6 months for patients who followed the radical CRT pathway and 14.1 months for those treated with palliative chemotherapy (P = 0.1).

Conclusion
HGNETs of the oesophagus are a rare aggressive malignancy generally resistant to approved treatments for typical oesophageal cancer. Response rate to platinum-based chemotherapy is much lower than with high-grade lung NETs, while long-term disease-free interval after radical surgical resection is a rare phenomenon. In view of their poor prognosis, patients with local or locoregional disease might be better treated conservatively with radical chemoradiotherapy, while newer therapeutic agents should be studied in patients with metastatic disease.

DOI: 10.1530/endoabs.46.P18

P19
Patient outcomes after cardiac surgery for carcinoid heart disease are dependent upon successful cytoreductive multimodal treatment and control of metastatic neuroendocrine disease
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Introduction
Carcinoid Heart Disease (CHD) can occur in up to 50% of patients with long standing carcinoid syndrome as a result of metastatic neuroendocrine tumour (NET). It is associated with poor prognosis due to the development of right side heart failure. High circulating levels of serotonin cause cardiac fibrosis leading to tricuspid and pulmonary valve regurgitation and poor ventricular function. Cardiac surgery with valve replacement in combination with cytoreductive surgery and control of hormonal symptoms may offer patients improved long term survival.

Methods
We describe our series of patients who presented to the regional NET multidisciplinary meeting over a 5 year period who underwent cardiac surgery for CHD.

Results
Between 2011 and 2016, eleven patients (9 female), median age 62 years with metastatic NET and CHD underwent valve replacement. The commonest tumour site was midgut (10) and 1 unknown. Histology identified. Median age at presentation was 70 years (range, 3–144) months. There were 4 early deaths at 3,4,4&12 months all as a result of cardiac failure from progressive (3) or untreated (1) disease. Of the remaining patients, at
median follow-up 23(range 4–56) months, 5 of 7 have undergone complete cytoreductive surgery and have stable disease, 1 awaiting surgery, 1 non surgical treatment.

Conclusion
Cardiac surgery is a therapeutic option for treatment of CHD. It is associated with high mortality in the presence of untreated or progressive metastatic disease. Good outcomes are achievable when patients have undergone successful cytoreductive surgery leading to good disease control.

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P20
Initial experience of a novel technique for endoscopic full thickness resection of rectal neuroendocrine tumours
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Introduction
Standard endoscopic resection of rectal neuroendocrine tumours (NETs) is often associated with histological incomplete excision due to the submucosal position of the tumour within the bowel. This can lead to multiple attempts to achieve a complete excision or uncertainty leading to ongoing endoscopic surveillance. Endoscopic full thickness resection may allow early definitive management. We report a simple definitive technique for the full thickness excision of rectal NETs using a novel endoscopic full thickness resection device (FTRD).

Methods
All patients who presented to the regional NET multidisciplinary team (MDT) meeting with a histologically confirmed rectal NET between January 2015 and August 2016 were included. Electronic records of endoscopy and histology reports, as well as MDT discussions were identified and prospectively analysed.

The procedure was undertaken using an over-the-scope FTRD.

Conclusion
Full thickness endoscopic resection with FTRD is a promising technique, offering a simple and safe method for obtaining or confirming complete excision of the tumour. The close deep resection margins achieved even with this technique highlight the difficulties in obtaining a deep resection in order to confirm adequate local treatment. Further data are needed to confirm its position in the management algorithm of rectal NETs.

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P21
Efficacy of the combination of Capecitabine and Temozolamide in patients with advanced Pulmonary Carcinoid Tumors: A single institution experience
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Background
Pulmonary carcinoids (PC) are rare neuroendocrine tumors (NETs). The course of PCs is considered to be indolent, but patients with advanced disease have low survival rates and their treatment options are limited. As PCs are under-represented in trials, therapeutic decisions are based on evidence extrapolated from other types of NETs. Capecitabine-Temozolamide (CAPTEM) has demonstrated significant efficacy in pancreatic NETs. However, its role in PCs is still unexplored. The aim of this retrospective study was to examine the efficacy of CAPTEM in patients with advanced PC.

Methods
Patients with advanced PCs, received treatment with Capecitabine 750 mg/m2 twice daily (day 1–14) and Temozolamide 200 mg/m2 once daily (day 10–14), in a 4 week cycle, up to 6 cycles. Patients were treated at the Christie NHS Hospital from March 2014 to August 2016.

Results
Twenty four patients were included in the analysis; 12 males, 12 females. Eight (33%) had typical and 15 (62.5%) had atypical histology. Median age was 63.5 years (range, 47–79). EGOC performance status ranged from 0 (10 patients, 47.5%), 1 (9 patients, 37.5%) to 2 (5 patients, 20.8%). Six patients (25%) had previous chemotherapy; 5 of them (20.8%) received CAPTEM as second line cytotoxic treatment and 1 (4.2%) as a third line. The rest 18 patients (75%) were chemo-naïve. Ten patients (41.7%) completed all 6 cycles. The median number of cycles was 4 (range, 1–6). From 23 assessable patients, disease control rate with CAPTEM was 73.9%. Four (17.4%) patients had partial response, 13 (56.5%) had stable disease and 6 (26.1%) progressed. No patient achieved complete response. After a median follow up of 11.1 months (range 2.7–21.2) 15 patients progressed (62.5%) and 8 patients deceased (33.3%). Median time to progression was 5.5 months (95% CI: 4.4–6.7). Overall survival has not been reached yet.

Conclusions
CAPTEM is an active treatment for PCs. The responses obtained in this analysis are similar with those described in the literature for PCs and other non-pancreatic NETs. Prospective trials are needed to confirm this efficacy and provide more information about predictive factors and the correct line of administration to optimise outcomes.

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**P22**

Multivisceral transplantation and vascularised sentinel forearm flap for a metastatic small bowel neuroendocrine tumour: Update on follow-up

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**Introduction**

We previously reported the first documented case of a novel approach in a patient with extensive mesenteric metastases from a small bowel (SB) NET: this combined multivisceral transplantation (MVT) and a vascularised sentinel forearm flap (VSFF) from the same donor.

**Aim(s)**

We re-present this case after 38-month follow-up post-MVT/VSFF.

**Materials and methods**

A 44-year-old male patient was diagnosed with a well-differentiated, grade 1 (Ki67 < 1%) neuroendocrine tumour. Initial gut hormones were raised: chromogranin A 395 pmol/l (normal < 60), chromogranin B 349 pmol/l (normal < 150) and 24-hour urinary 5-HIAA 643 pmol/l (normal < 40). Pre-operative 68-Ga DOTATATE PET/CT showed uptake in an aorto-caval lymph node and bulky mesenteric disease, which was confirmed at laparotomy as stage IV disease encasing the mesenteric root. Numerous lymph nodes and multifocal primary tumour (7 sub-centimetre lesions) were also found at surgery.

**Results**

4 cycles of neoadjuvant 177-Lu PRRT were followed by modified MVT (stomach, pancreas, spleen, small bowel, right hemi-colon), VSFF and resection of the aorto-caval lymph node. Disease stage was pT3 N1 MO LI VO R0.

**Conclusion**

38 months post-MVT/VSFF the patient is well and fully physically active with no evidence of disease recurrence following up-in imaging or biochemistry. There was never any rejection in the visceral graft, with one mild, easily treated reaction in the VSFF. (Work published).

**Keywords:** neuroendocrine, transplantation, multivisceral, forearm flap

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**P23**

Evaluation of faecal elastase 1 in symptomatic patients with neuroendocrine tumours

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Monitoring patients with NETs reveals a significant prevalence of gastrointestinal symptoms, often unrelated directly to the tumour. Exocrine pancreatic insufficiency exemplifies a common treatable cause of gastrointestinal symptoms in NET patients undergoing treatment with somatostatin analogues. There is a paucity of data regarding this important issue which affects quality of life in NETs. We explored the use of faecal elastase (FE) as a marker of exocrine pancreatic insufficiency in patients with NETs.

**Methods**

Thirty-nine patients with NETs (27 midgut, 5 pancreatic, 7 other) consecutively referred to a gastroenterology NET clinic, from oncology and endocrine clinics, completed standardised questionnaires regarding symptoms and quality of life (QoL), as part of clinical care: Gastrointestinal symptoms rating scale and NET QoL questionnaires (EORTC QLQ – G1.NET21). FE was prospectively evaluated to investigate gastrointestinal symptoms. Data from questionnaires and medical records was analysed for an association between low FE (< 200 µg/g) and steatorrhoea.

**Results**

Of 39 patients, 69% had well-differentiated low-grade (G1) tumours with the remainder intermediate (G2) or unknown grade. Median duration of disease was 69 months (range 9–265). 35/39 NETs (90%) had metastatic (stage IV) disease. 33/39 NETs had complete data, 78% (25/32) of which were established on long-acting somatostatin analogue therapy and 81% (26/32) complained of steatorrhoea. Only 6/32 patients had a low FE, four of whom complained of steatorrhoea (12.5%). 22/32 patients had steatorrhoea with a normal FE, 77% (17/22) of whom were taking regular somatostatin therapy. Sensitivity of FE in detecting steatorrhoea in NET patients was 15.4%. Less than one fifth of patients exhibiting signs of pancreatic insufficiency had an abnormal FE prior to commencing a trial of pancreatic enzyme replacement therapy.

**Conclusions**

There appears to be a lack of association between FE and steatorrhoea in patients with NETs. Many patients experienced steatorrhoea on somatostatin analogues despite normal FE; thus FE should not be used to evaluate pancreatic function in this group. Further studies are required to evaluate exocrine pancreatic insufficiency in patients with NETs undergoing treatment or surveillance.

**Williams M et al, Exploring gastrointestinal symptoms in patients with neuroendocrine tumours ENETS 2016.**

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**P24**

Improving outcomes for patients with resectable small bowel NET tumours: 5 year experience from a tertiary centre

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**Introduction**

There remains controversy about which patients benefit from removal of their primary small bowel tumour and whether this should be performed in a specialist tertiary referral hospital as an elective procedure. Part of the decision making and consenting process in patients with metastases will be a shared decision about surgery with the patient in light of symptoms, morbidity from surgery and survival. The aim of this study was to elucidate important institution specific data.

**Methods**

Retrospective cohort study. Patients were identified from the hospital pathology database having had their primary tumour resected between January 2011 and December 2015 and the specimen reviewed by our specialist NET pathology centre; of these 59% (n = 29) had metastases (Stage IV) at the time of surgery. Overall mean survival was 182 months with 5 yr survival 87%. There was no postoperative mortality and 26% morbidity; 10.1% Clavien-Dindo Grade 3 within our institution. Median overall survival for patients with Stage IV disease having surgery was 156 months. Multivariate analysis of overall survival suggested age at presentation being the only significant factor (P = 0.03) with liver metastasis (P = 0.07) and surgery within the tertiary centre (P = 0.09) not significant.

**Conclusions**

Small bowel NET surgery in our institution is safe and maybe preferable to surgery in a peripheral hospital. Current indications and acceptance criteria for small bowel surgery yield acceptable surgical morbidity.

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**P25**

Prognostic factors that mandate long term follow up following surgery for appendix neuroendocrine tumours (aNETs)

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**Background**

Appendiceal neuroendocrine tumours (aNETs) are usually diagnosed incidentally at appendicectomy, are indolent and rarely recur. Current ENETS guidelines inform aNETs management and highlight areas of uncertainty. We aimed to identify risk factors that predict lymph node metastasis, residual disease at Endocrine Abstracts (2016) Vol 46
collection surgery, or disease recurrence and also assessed survival according to ENETS stage. Methods We retrospectively analysed a prospectively database of patients diagnosed at our centre with aNETs from 1990 to 2016. We assessed risk factors for nodal metastases detected at primary or completion surgery, for residual disease at completion surgery, or for disease recurrence using logistic regression models. We assessed overall and aNET-specific survival using Kaplan-Meier analysis. Results 93 patients (39 males, 54 females, median age 47.9 (range 16.3–78.8) years) were included. Unsurprisingly, lymph node metastases significantly (P = 0.0015) correlated with tumour size >2.0 cm. Residual disease was significantly predicted by tumour grade ≥G2 (P = 0.0418) and goblet cell carcinoma (GCC) histology (P = 0.0390). Disease recurrence was significantly predicted by GCC histology (P = 0.0002). In the only recurrence where the primary aNET was non-GCC, the patient had undergone R1 resection of an ENETS stage 3a tumour 16 years earlier. Disease-specific 5 year survival for ENETS stages 1, 2a, 2b, 3a, 3b, and 4 were 100, 100, 93, 100, 71, and 67% respectively. Overall 5 year survival mirrored these figures except for ENET stage 1 disease, where two non-NET related deaths occurred, hence survival of 92%. Significantly worse overall and disease-specific 5 year survivals occurred in ENETS stages 3b and 4 compared to others (P ≤ 0.016).

Conclusion Tumour size >2.0 cm remains prognostic for lymph node metastasis. GCC histology was not only prognostic for recurrence after aNET resection, but, also prognostic for residual disease along with grade ≥G2. We suggest that extended follow-up (10 years or more) is appropriate for patients with ENETS stage disease (3b and 4), GCC histology, or following R1 resection because of their higher rates of disease recurrence and poorer overall survival.

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P27 Modality to detect pancreatic NETS in MEN1: EUS or MRI? Manta Joshi, Barbara McGowan, Jake Powrie, Louise Breen, Audrey Jacques, Louise Izatt & Paul Carroll Guy’s and St Thomas’s NHS Foundation Trust, London, UK

Background Pancreatic neuroendocrine tumours (pNETs) are commonly reported in patients with MEN1. The estimated incidence is reported as 40–80% of adults with MEN1 and pNETs are frequently multifocal. Guidelines recommend that CT, MRI and endoscopic ultrasound (EUS) can be used for detection and surveillance of pNETs in MEN1. MRI has been the most commonly used modality, but EUS may be more sensitive in detecting pNETs. Objective To compare the sensitivity of CT/MRI and EUS in detecting pNETs in adults with MEN1.

Methods Extensive review of electronic and paper records was undertaken from 2005–2015. We identified forty three MEN-1 patients, of whom 25 were shown to have pNETs. Of these patients, five did not have EUS for comparison and hence only 20 patients were included in the analysis.

Results Twenty patients were included (8 M, 12 F; mean age 41.3 years (range 21–56)). All had a confirmed pathogenic mutation in the MEN1 gene. Gut peptides were measured in all patients. Pancreatic imaging using CT and/or MRI was compared with EUS findings. Cross-sectional imaging using MRI/CT detected abnormality in 14 out of 20 (70%) compared to EUS which found at least one lesion in all 20 patients (100%). Those with negative MRI/CT, had EUS lesions ranging from 3.5–13 mm. Five of these six imaging negative patients were symptomatic, three patients of which included gastrin excess features, two patients with non-functional lesion were symptomatic. Seven patients had normal gut peptides; gastrin was elevated in 8 patients, 4 patients had elevation of other gut peptides, while 1 patient had insulinoma.

Conclusion EUS invariably detected at least one pNET in these adults with MEN1, compared with approximately 70% detection using MRI/CT. Current guidance exists regarding treatment decisions when pancreatic lesions are >2 cm or associated with hormone hypersecretion. In this series, EUS commonly detected small pNETs in MRI negative symptomatic individuals but the optimal management of these tumours is less established. We conclude that routine use of EUS in pancreatic surveillance for MEN1 patients identifies lesions less than 2 cm more reliably than MRI and should be an integral part of MEN1 surveillance.

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P26 The use of continuous glucose monitoring to investigate and manage a rare cause of spontaneous hypoglycaemia Emma Walkinshaw1, Hugh Jones2 & Alia Munir1 1Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; 2Barnsley Hospital NHS Foundation Trust, Barnsley, UK; 3University of Sheffield, Sheffield, UK

Insulin autoimmune syndrome (Hirata syndrome) is a rare cause of hypoglycaemia. It was described by Hirata in 1970 and characterised as spontaneous hypoglycaemia, with elevated insulin levels, and associated high titres of insulin autoantibodies. It is most commonly reported in Japan and is associated with autoimmune disease or exposure to sulphonyl-containing drugs. Continuous glucose monitoring (CGM) devices measure interstitial glucose and were initially developed as an adjunct to blood glucose monitoring for use in individuals with diabetes mellitus. First generation devices provided short term, retrospective data, but newer devices allow real time monitoring with trend analysis and alerts predicting hypoglycaemia. NICE now recommends CGM for patients with type 1 diabetes with frequent or severe hypoglycaemia. Here we use this technology in the investigation and management of non-diabetes mellitus hypoglycaemia.

We present a case of a 76 year old, Caucasian gentleman, presenting with spontaneous hypoglycaemia in 2013. He gave a 12 month history of episodes of severe sweating associated with feeling vacant. Blood glucose was 1.5 mmol/l, insulin 2571.0 pmol/l (178–173) and C-peptide 652 pmol/l (298–2350). Subsequent imaging including an MRI of the pancreas, NM Octreotide scan with SPECT and NM whole body PET FDG did not reveal any evidence of an insulinoma. This gentleman was reassessed in 2016 following suspension of his driving licence and ongoing symptoms despite treatment with diazoxide. He underwent two 72 hour fasts that did not precipitate any spontaneous hypoglycaemia. A mixed meal test revealed blood glucose of 1.6 mmol/l at 300 minutes with insulin levels >6945 pmol/l. CGM showed large periods of time with hypoglycaemia. Insulin antibody IgG > 200 mg/l (0–5).

His glycaemia continues to be difficult to control despite dietary advice and diazoxide. He finds the use of CGM invaluable as it predicts hypoglycaemia and allows prevention of episodes. As CGM is now real-time, more readily available, better tolerated and easy to use it may have an important role in the investigation and treatment of endocrine hypoglycaemia. To our knowledge this is the first use of this technology in the work up and management of non-diabetes mellitus hypoglycaemia.

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P28 Outcome of Surgical Resection after Neoadjuvant Peptide Receptor Radionuclide Therapy (PRRT) for Pancreatic Neuroendocrine Neoplasms: a case-matched analysis Stefano Partelli1, Emilio Bertani2, Mirco Bartolomei1, Francesca Muffati1, Chiara Maria Grana2, Claudio Doglioni1, Nicola Fazio3 & Massimo Falconi1 1San Raffaele Scientific Institute, Milan, Italy; 2European Institute of Oncology, Milan, Italy; 3“M. Bufalini” Hospital, Cesena, Italy

Background Peptide receptor radionuclide therapy (PRRT) can be an option for advanced pancreatic neuroendocrine neoplasms (PNNs) to allow patients undergo resection. Whether or not neoadjuvant PRRT increases postoperative morbidity remains unclear.

Methods Patients with initially metastatic and/or locally advanced PNN who underwent neoadjuvant PRRT (neoadjuvant group) were compared with a group of patients who underwent upfront surgery (control group). Patients were matched for tumor size, grading, and intent of resection.

Results Overall, 20 patients underwent sequential PRRT and pancreatic resection. The rate for neoadjuvant PRRT was the presence of liver metastases in 6 patients (30%), the presence of organ/vascular infiltration in the remaining 14 (70%). After PRRT the median tumor size decreases from 59 mm to 50 mm (P = 0.047). The majority of patients (n = 15) underwent distal pancreatectomy whereas the remaining 5 underwent pancreaticoduodenectomy. The rate of curative resection was 65%. Histology revealed a PNN-G1 in 10 cases, a PNN-G2 in 7 patients, and a PNN-G3 in 3 patients. Preoperative and postoperative tumor grading was concordant in 13 patients whereas 5 patients were upstaged and 2 patients were
Pancreatic resection for PNEN after neoadjuvant PRRT is safe and associated with a lower risk of developing pancreatic fistula.

Conclusions

Pancreatic resection for PNEN after neoadjuvant PRRT is safe and associated with a lower risk of developing pancreatic fistula.

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P29
Succinate dehydrogenase subunit-B mutation with associated pro lactinoma and typical carcinoids
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Case Report
A 42 year-old male, with a family history of phaeochromocytomas and paragangliomas, was diagnosed as a carrier of the succinate dehydrogenase subunit-B (SDHB) mutation. He was also diagnosed with macroprolactinoma and treated with cabergoline (currently 250 mcg weekly). A contrast CT chest scan, performed as part of the surveillance program for SDHB-associated tumours, revealed a small right lung lesion, which was found to be Octreoscan positive. The patient was asymptomatic and previously smoked ten cigarettes daily. Urinary and plasma metanephrines were normal. He underwent a right VATS (video-assisted thoracoscopic surgery) sublobar wedge resection. Two typical carcinoids (TCs) were found (according to the WHO 2015 classification) measuring 7 and 6 mm in diameter. TNM was pT1a (2) Nx L0 V0 PL0 R0. The cellular marker of proliferation, Ki-67, was 1 and 5% respectively. Immunohistochemical analysis showed that the neoplastic cells expressed neuroendocrine markers including chromogranin A and synaptophysin. At 1 year follow-up CT scan, a new 34 mm octreotide-avid mass was found at the site of the original resection. The multidisciplinary team referred the patient for a right lobectomy. The pathology report indicated another TC: pT1b (25 mm) N0 Mx PL0 R0, Ki-67 4%. Biochemical markers including plasma chromogranin A and metanephrines remained within the normal range. The follow-up plan was a FDG-PET CT scan after 6 months in order to early detect a possible lung carcinoid recurrence or the presence of phaeochromocytomas/paragangliomas.

Discussion and Conclusions
Germline mutation of SDHB predispose to head-and-neck-paraganglioma, sympathetic paraganglioma, phaeochromocytoma and renal cell carcinoma. Recently it has been suggested that germlne SDH mutations can rarely be associated with pituitary adenomas, most frequently macroprolactinomas. To our knowledge, this case represents the tenth patient with an SDHB-associated pituitary adenoma.

TCs occur in the fourth to sixth decades of life and tend to grow very slowly. The majority are sporadic, though somatic MEN1 (multiple endocrine neoplasia type 1) gene mutations have been reported. This is the first case of an SDHB-associated TC. Interestingly, the TCs showed aggressive behaviour. Given the rarity of both diseases, the possibility of a new phenotype-genotype correlation should be considered.

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P30
Evaluating the impact of the Specialist Nurse
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The Beatson West of Scotland Cancer Centre (BWoSCC) is a Regional Service for the West of Scotland and beyond. It is considered to be a Centre of Excellence in the delivery of 21st century cancer care. Whilst the role of site specific specialist nurses has been integral to many cancer teams for in excess of 20 years, this has not been the case for neuroendocrine tumours in Scotland until May 2016. An international study carried out by Bouvier (2015) revealed that NET ± their treatment had significant impact physically, socially, psychologically and functionally on many patients. Few patients if any experienced no deleterious effect. The role of any nurse is to provide person centred and holistic care to those who are well. The specialist nurse combines that with specialist experience, knowledge and skills to support patients with complex needs. Without a nurse in the NET team at the Beatson gaps in care and support were very apparent. The European Neuroendocrine Tumour Society (2014), Scottish Neuroendocrine Tumour Group (2015) and the Scottish Government (2016) all state vehemently that a Clinical Nurse Specialist is an essential part of the Neuroendocrine Cancer care team.

In May 2016 an Advanced Clinical Nurse Specialist in Neuroendocrine Tumours and Thyroid Cancer was appointed in the BWoSCC. To assess if the role was having an impact on needs of patients a feedback survey was carried out supported by the West of Scotland Cancer Network. A convenience sample was taken from the out patient clinic and 40 questionnaires were distributed. The response rate was 62%. There were 10 questions and 2 opportunities for comments. Questions asked were, for example perception of support, symptom management, liaison with other healthcare professionals. The responses were very favourable with 86-94% rating care as being done well or very well. The comments highlighted specifics such as helping with depression and financial problems. There were no negative comments. This work will be continued as an integral part of the team’s work to meet with 12.2.1 of the ENET specification for Center of Excellence.

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P31
A single centre analysis of the management of appendiceal neuroendocrine neoplasms (NENs) including goblet cell carcinoids (GCC)
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Introduction
Appendiceal NENs are usually diagnosed incidentally on histology following an appendicectomy. They include carcinoid tumours (appendiceal neuroendocrine tumours, NETs) and GCC. GCC neoplasms are able to transform to an adenocarcinoma phenotype. There are several important criteria to review when deciding on the treatment and follow up for appendiceal NENs, in particular when to offer further surgery to patients.

Aim
To assess whether the management of appendiceal NENs, including surgical management is appropriate, according to the histology of the appendicectomy specimen.

Method
A retrospective analysis of the prospectively kept NETs database was performed. Data including the type, staging, size and Ki-67 index of appendiceal NETs, and outcomes of right hemicolectomies (RHCs) was extracted.

Results
The database contained 74 patients: 51 well differentiated appendiceal NETs, 20 GCC, and unknown type in 3 patients. A completion RHC was performed in 23 patients with appendiceal NET: 10 patients had evidence of lymph node (LN) metastases, distant metastases or residual disease. 13 patients with GCC had a completion RHC performed.

Discussion
In the appendiceal NET group who had a completion RHC, cases where the size of the tumour had a T stage of pT1b (5 cases total), 2 patients had evidence of LN metastases but no residual disease seen in any of the patients. 2 of the 3 appendiceal NETs > 2 cm where a RHC was performed, more advanced disease was seen with evidence of LN and distant metastases. Our data shows that GCCs are more aggressive, presenting at a later stage. 2 of 13 patients who had a completion RHC (GCC) had evidence of LN involvement in the RHC specimen and 1 patient had evidence of residual disease at the appendix base. 2 patients (GCC) who did not have a completion RHC, presented later with small bowel obstruction.
Conclusion
Our results show that GCC are more aggressive than appendical NETs, and therefore a more aggressive surgical approach should be considered. The definite management in cases (appendiceal NET group) that fall in the pT1b group, remains most challenging; in cases where the size was ≥1.5 cm and a RHC was performed, deeper local invasion was seen.

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P32
Orbital neuroendocrine tumor metastases: diversity of presentation
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Introduction
Orbital metastases from Neuroendocrine tumours (NET) are reported to be very rare, and can be the primary presentation or become evident up to 20 years after diagnosis. We report a series presented in the NET MDT, where ocular metastases occurred.

Case series
A 69 year-old woman presented with blurred vision, pain and perception of a lump around the left eye. MRI showed a lacrimal gland mass within the orbit. Excision biopsy revealed a TTF1-positive, grade 2 NET (Ki-67 index – 10%). Carcinoïd syndrome was absent. FDG PET revealed a right lung nodule, with associated mediastinal lymphadenopathy. Octreotide scan was negative. She was treated with Cisplatin and Etoposide based chemotherapy but this was poorly tolerated and discontinued. One year later imaging revealed progression and vertebral metastasis and she received palliative radiotherapy (8Gy).

A 90 year old man presented with proptosis and restricted movements of left eye. Imaging showed a well-defined mass in the left globe with lateral rectus involvement. He underwent an R0 resection, with complete recovery. Histology showed a grade 2 NET (Ki-67-5%) highly suggestive of a GEP NET metastasis. A 60 year old man presented with symptoms of carcinoid syndrome and was found to have a sigmoid NET with hepatic metastasis. He underwent anterior resection and debulking. Histology confirmed a well differentiated NET with Ki67 index 5–10%. He was treated with somatostatin analogues and radionuclide therapy. Six years later, he presented with blurring of vision and was found to have a well-defined mass involving levator palpebre and superior rectus muscles. After ophthalmic consultation excision biopsy showed de-differentiated grade 3 NET with Ki67- 30%. Progression of liver metastasis with multiple metastases elsewhere was seen on imaging. He was referred for palliative chemotherapy.

Conclusion
Orbital metastases are rare, but may be the first or late presentation of NETs. Careful co-ordination between ophthalmology and NET MDTs is recommended. Although some recent publications advocate use of radionuclide therapy for these lesions this is not a current option in the NHS.

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P33
A case report of bicaval stents and inferior vena cava valve implantation to control carcinoid symptoms in order to safely allow surgical valve replacement
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Severe tricuspid regurgitation (TR) leads to a reduction in cardiac output and an increase in the central venous pressure, resulting in secondary organ dysfunction. Surgery for severe TR is a high-risk procedure, particularly in the presence of uncontrolled carcinoid syndrome (CS) symptoms. Replacement of leaking tricuspid valves can lead to reduction in tumour markers and improvement in carcinoid symptoms. Transcatheter valve implantation into the vena cava may be an alternative treatment for reducing the complications and symptoms associated with TR.

We report a case of a 69-year-old female with severe CS and severe carcinoid heart disease (CHD) affecting daily activities despite being on a somatostatin analogue (SSA). Uncontrolled CS symptoms deemed her too high risk for open-heart surgery. She had only 30% liver replacement by tumour and good liver function. She was deemed to have a good prognosis provided she could undergo heart valve replacement followed by transarterial embolisation (TAE) of the liver metastases. We planned a percutaneous approach to control the effects of tricuspid regurgitation on the liver to enable transarterial embolisation of liver metastases to be performed. Adequate control of CS would then allow heart surgery to be performed safely. An octreotide infusion was commenced pre-procedure and continued post-procedure. Two stents were implanted into the IVC and SVC. A 29 mm S3 valve was then deployed within the IVC stent. Prior to valve deployment, phasic pressure in the IVC was 32/20 mmHg with a mean of 22 mmHg. Following valve deployment, the IVC pressure fell to 15/8 mmHg with a mean of 15 mmHg, and venography confirmed only minor paravalvular regurgitation. The procedure was well tolerated throughout. Unfortunately, following the procedure, the patient became very unstable and despite very high doses of SSAs, she passed away as a result of severe carcinoid crisis.

IVC valve implantation specifically to improve CS has not been attempted before. Sadly, this novel approach to managing severe tricuspid regurgitation and carcinoid syndrome was unsuccessful in this case. Further work is needed to devise successful strategies for managing this difficult but potentially salvageable group of patients.

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P34
An exploration of psychological symptoms in vasoactive hormone-secreting neuroendocrine tumours (carcinoid syndrome)
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Introduction
Psychological symptoms such as aggression, confusion, irritation, anxiety and depression have been observed clinically in patients with carcinoid syndrome. It has been suggested that vasoactive-hormone secretion are involved in provoking psychological symptoms. The objective of this qualitative study is to explore the presence and experience of specific psychological symptoms in vasoactive hormone-secreting NET (carcinoid syndrome).

Methods
Nine patients with mid gut NET with carcinoid syndrome with psychological issues currently or in the past one year from two NET specialist centres were recruited. They participated in in-depth qualitative interviews focusing on the previous and current experience of physical and psychological symptoms.

Results
Patients experienced various psychological symptoms, including anxiety, agitation and irritability and occasional low mood, mood swings, and mild aggressive tendency. The unpredictable nature of physical distress from physical symptoms resulted in psychological symptoms. Although many patients had anxiety from cancer-related issues, there was a close link between anxiety and flushing in a minority. Positive mood and being socially active alleviated a low mood but had little influence on irritability, agitation and anxiety-induced flushing.

Conclusion
Cancer-related issues, the impact of physical symptoms, external issues and vasoactive-hormones are all implicated in producing psychological symptoms in carcinoid syndrome. Psychological symptoms affect all aspects of daily life. By clinicians becoming more aware of the issues and by identifying contributing factors, patients at risk can be more closely monitored and psychological support be provided.

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P35
Cardiac metastases from ileal NETs
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Background
Intracardiac metastasis of carcinoid tumours are rare (incidence 2–4%). Their presence without carcinoid valvulopathy or carcinoid syndrome is unusual.
A 70 year old male presented with abdominal pain. CT imaging revealed a small intestinal tumor with liver and mesenteric metastasis. Biopsy showed a neuroendocrine tumour (NET). Clinical and biochemical evidence of functioning was absent. He underwent definitive small bowel and liver metastases resection. Histology confirmed a well differentiated NET with Ki 67–5%. Two years later, he developed carcinoid syndrome and was commenced on somatostatin analogues. Subsequent imaging showed multiple liver metastases and a high intensity lesion in the intraventricular septum (IVS). Echocardiogram confirmed the cardiac finding without significant valvulopathy. Cardiac MRI displayed a well-defined mass measuring 2 cm × 1.5 cm in the mid IVS with high signal intensity in T2 suggesting metastasis. To date the patient has remained haemodynamically stable.

A 69 year old male presented with a 9 year history of carcinoid syndrome. Imaging revealed a terminal ileal NET with liver metastases. Multiple areas were octreotide avid including a pericardial apical region. Somatostatin analogues were commenced. Two years later he underwent CABG for underlying coronary artery disease. A surprising finding of large firm deposits over both ventricles extending and encasing the aorta was noted.

Discussion
Cardiac metastasis are a rare presenting feature of NETs. The absence of significant valvulopathy was likely to be related to the duration of syndrome. Here the cardiac metastases have been not caused any compromise.

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