Endocrine Abstracts

December 2022 Volume 87
ISSN 1479-6848 (online)

20th Annual Meeting of the UK and Ireland Neuroendocrine Tumour Society 2022

Monday 5 December 2022, London, UK

UKI NETS

UKI NETS 20th National Conference
Monday 05 December 2022
London, UK

published by bioscientifica

Online version available at
www.endocrine-abstracts.org

Endocrine Abstracts

Volume 87
December 2022

20th Annual Meeting of the UK and Ireland Neuroendocrine Tumour Society 2022

Monday 5 December 2022, London, UK

Programme Organising Committee

Mairéad McNamara (Programme Organising Committee Chair)
John Ayuk
Bahram Jafar-Mohammadi
Shaunak Navalkissoor
Anguraj Sadanandam
Jonathan Wadsley

Abstract Marking Panel

John Ayuk
Jorge Barriuso
Amy Eccles
Olusola Faluyi
Andrea Frilling
Shaunak Navalkissor
Raj Srirajaskanthan
Jonathan Wadsley

UKI NETS 2022 Sponsors

Advanced Accelerator Applications
Esteve
Ipsen

CONTENTS

Oral Communications

OC1

Urine 5-HIAA levels and quality-of-life in neuroendocrine neoplasia. Is there an association?

Rayhan Chaudhry[1], Benjamin White[1], Chandrakumaran Kandiah[1], Royce Vincent[2], Rajaventhan Srirajaskanthan[2], Dominique Clement[2] & John Ramage[1,2]
[1]Dept of Gastroenterology, Hampshire Hospitals NHS Foundation Trust, Basingstoke, United Kingdom; [2]ENETS Centre of Excellence, Kings College Hospital, London, United Kingdom

Introduction
Patients with neuroendocrine neoplasia (NEN) may experience psychological distress related to secretory effects of the tumour. 5-hydroxyindoleacetic acid (5-HIAA) is a metabolite of serotonin, the most important secretory product in carcinoid syndrome. This study aims to determine if urine 5-HIAA levels correlate with health-related quality of life (HRQoL) in patients with NEN.
Methods
A retrospective single-centre cohort study was conducted including 741 patients with a histological or radiological diagnosis of NEN. Patients at King's Health Partners ENETS Centre of Excellence completed standardised questionnaires at clinic appointments. Temporally related spot urine 5-HIAA levels were correlated with PHQ-9 (depression), GAD-7 (anxiety), QLQ-GINET21 and EORTC QLQ-C30 scores. Correlation was evaluated with the Spearman rho test.
Results
258 (34.8%) out of 741 patients had completed HRQoL data. Of these, 132 (51.2%) were male. 145 (56%) had a small intestine primary. The median age was 65 years (interquartile range, IQR: 54 - 72). Median urine 5-HIAA was 8.1 μmol/mmol (IQR: 4.0 - 13.6). Males had significantly higher (P =0.001) 5-HIAA (median:10.1, IQR: 6.2 - 16.2) compared to females (5.6, IQR: 3.3 - 11.6). Males also reported significantly higher Global Health Status (P= 0.018) and lower NET21 (P= 0.001), GAD-7 (P= 0.001) and PHQ-9 (P= 0.009) scores. Within the collective cohort, there was a significant association between high urine 5-HIAA levels and low GAD-7 (P= 0.037); similarly, between high urine 5-HIAA and low QLQ-GINET21 GI symptoms (P= 0.024). No significant association was found between urine 5-HIAA levels and EORTC QLQ-C30 Global Health Status (P= 0.527), EORTC QLQ-C30 diarrhoea score (P= 0.232), QLQ GINET21 endocrine symptoms scale (P= 0.151) and PHQ-9 (P= 0.515).
Conclusions
No significant correlation was detected between Urine 5-HIAA and patient reported depression (PHQ-9) or overall HRQoL (EORTC QLQ-C30 Global Health Status). The significant correlation between a low GAD-7 and high 5-HIAA may suggest high circulating levels of serotonin are associated with less anxiety. The sex differences in 5-HIAA values and HRQoL measures within this cohort warrants further studies to corroborate these findings.

DOI: 10.1530/endoabs.87.OC1

OC2

Glucagonomas: diagnostic features and outcomes of first line treatment in a series of 18 patients

Juliana Porto[1], Alexander Branton[1], Richard Heseth[2], Dalvinder Mandair[1], Martyn Caplin[1] & Christos Toumpanakis[1]
[1]NET Unit, ENETS Centre of Excellence, Royal Free Hospital, London, London, United Kingdom; [2]Department of Radiology- Royal Free Hospital, London, UK, London, United Kingdom

Introduction
Glucagonomas are rare functional pancreatic neuroendocrine tumours (p NETs), with an annual occurrence of 0.01 to 0.1 new cases per 100,000.
Objective
We focused on presenting symptoms, primary's size and location, presence of metastases, biomarkers at diagnosis, histology, response to first line treatment (clinical and biochemical), disease fee survival (DFS) and PFS (progression free survival).
Methods
Eighteen patients were identified and reviewed retrospectively. The diagnosis was based on relevant symptoms and/or raised plasma glucagon levels (>2 times upper normal limit). Assessment of primary and metastases was based on cross-sectional and molecular imaging at diagnosis. Follow-up was complete in 14/18 (78%) of patients.
Results
Presenting symptoms included migratory necrolytic erythema (MNE) in 8 (44%), diabetes in 6 (33%), weight loss in 5 (28%) and abdominal pain in 4 (22%) patients. In 2 patients, diagnosis was based only on glucagon levels. Pancreatic primary was located at the tail (33%), head (22%), body (6%) or unrecorded (39%), whilst in 85% patients, primary size was over 3cm. Thirteen (72%) patients had liver metastases at presentation. In the majority of those patients (75%), the metastatic volume occupied < 25% of the liver. Histologically, 22% of tumours were G1, 61% were G2, 6% were G3 and grade was not available in 11% patients. In 7 patients either with localized disease or small volume hepatic metastases, surgical resection was offered, as first line treatment, and mean DFS of 67 months (range 7 - 204 months). Of the remaining 11 patients, 9 had somatostatin analogues' (SSA) monotherapy as first line treatment, with clinical and biochemical response in > 50%, and mean PFS of 40 (range: 4 -143 months). Two patients had combination chemotherapy and SSA treatment, with PFS of 10 and 24 months, respectively.
Conclusion
Glucagonomas are large, usually grade 2 p NETs, diagnosed at a late/advanced stage of disease. MNE and diabetes are the most common presenting symptoms. SSAs represent an effective first line treatment option, for control of symptoms' and tumour growth. Large studies are needed to identify risk factors for PFS and overall survival, as well optimal treatments' sequence, in cases of further progression.

DOI: 10.1530/endoabs.87.OC2

OC3

Outcomes in patients with advanced well-differentiated gastroenteropancreatic neuroendocrine tumours receiving PRRT early versus later

Matthew D Robinson[1], Amarjot Chander[1,2], Tom Westwood[1,2], Prakash Manoharan[1,2], Was Mansoor[1,2], Angela Lamarca[1,2], Richard A Hubner[1,2], Juan W Valle[1,2] & Mairéad G McNamara[1,2]
[1]The University of Manchester, Manchester, United Kingdom; [2]The Christie NHS Foundation Trust, Manchester, United Kingdom

Background
Neuroendocrine tumours (NETs) are rare malignancies; over 60% of primary lesions arise in the gastrointestinal tract and pancreas. Despite several practice-changing clinical trials, uncertainty persists around the most efficacious treatment sequence in patients with advanced well-differentiated gastroenteropancreatic (GEP) NETs, particularly in relation to peptide receptor radionuclide therapy (PRRT). This study aimed to investigate the progression-free survival (PFS) of PRRT administered immediately after disease progression on a somatostatin analogue (SSA) (early) or following an alternative second-line therapy (later).
Methods
Data from patients who received PRRT for histologically-confirmed advanced GEP-NETs were analysed retrospectively. The Kaplan Meier method and Log-rank test were used to evaluate PFS and overall survival (OS) to assess any differences between the groups (PRRT early versus later).
Results
Of 147 patients who received PRRT for GEP-NETs between 24/05/2011-25/02/22, 134 potentially eligible participants were identified and 119 were included in the final analysis (15 excluded as they did not receive a first-line SSA) (median age 60 years; 51.3% male). Ninety-five patients [primary sites: small bowel: 61 (64%), unknown: 13 (14%), pancreas: 9 (10%), colon: 6 (6%), other: 4 (4%), rectum: 2 (2%); ECOG PS 0: 38 (40%), 1: 49 (52%), 2: 6 (6%); unavailable: 2 (2%), Grade: 1: 57 (60%), 2: 36 (38%), unavailable: 2 (2%)] received PRRT immediately after SSA (Group 1) and 24 patients [primary sites: pancreas: 11 (46%), small bowel: 9 (38%), rectum: 2 (8%), unknown: 2 (8%); ECOG PS 0: 11 (46%), 1: 13 (54%), Grade: 1: 12 (50%), 2: 12 (50%)] received PRRT later in their disease course (median number of intervening treatments: 1) (Group 2). Median PFS in Groups 1 and 2 was 40.7 (95% confidence interval (CI) 37.6-43.9) and 28.4 (95% CI 21.4-35.3) months, respectively (P= 0.297). Median OS for Groups 1 and 2 was 161.5 (95% CI 108.1-214.9) and 146.7 (95% CI 88.1-205.2) months, respectively (P= 0.308).
Conclusions
In this study, median PFS was not statistically significantly different in the group receiving PRRT early versus later. There was a trend towards improved PFS in the group receiving PRRT early, which may have been due to patient selection. Prospective studies are warranted.

DOI: 10.1530/endoabs.87.OC3

Poster Presentations

P1

Second primary malignancies in patients with a neuroendocrine neoplasm in England

Beth Russell[1], Benjamin E White[2], Brian Rous[3], Kwok Wong[3], Catherine Bouvier[4], Rajaventhan Srirajaskanthan[5], Mieke Van Hemelrijck[1] & John K Ramage[2,5]
[1]Translational Oncology and Urology Research, King's College London, London, United Kingdom; [2]Basingstoke and North Hampshire Hospital, Hampshire Hospitals NHS Foundation Trust, Basingstoke, United Kingdom; [3]NHS Digital, Leeds, United Kingdom; [4]Neuroendocrine Cancer UK, Holly House, Leamington Spa, United Kingdom; [5]King's Health Partners Neuroendocrine ENETS Centre of Excellence, King's College Hospital, London, United Kingdom

Background
Patients with neuroendocrine neoplasms (NENs) may often develop other malignancies. This study aimed to identify the frequency at which these second non-NEN malignancies occurred in England.
Methods
Data was extracted from the National Cancer Registration and Analysis Service (NCRAS) on all patients diagnosed with a NEN at one of eight NEN site groups between 2012-2018: appendix, caecum, colon, lung, pancreas, rectum, small intestine and stomach. WHO International Classification of Disease edition 10 (ICD-10) codes were used to identify patients who had been diagnosed with an additional non-NEN cancer. Descriptive tables were produced to characterise the study cohort. Standardised incidence ratios (SIRs) for tumours diagnosed after the index NEN were produced for each non-NEN cancer type by sex and site.
Results
A total of 20,579 patients were included in the study. Overall, 3,127 patients were diagnosed with a non-NEN cancer at any time point, of which 19% were diagnosed after NEN, 70% prior to NEN and 11% on the same date. All NEN sites were associated with an increased rate of at least one non-NEN cancer. The most commonly occurring non-NEN cancers after NEN diagnosis were prostate (20%), lung (20%) and breast (15%). Statistically significant SIRs were observed for non-NEN cancer of the lung (SIR = 1.85, 95%CI:1.55-2.22), colon (SIR = 1.78, 95%CI:1.40-2.27), prostate (SIR = 1.56, 95%CI:1.31-1.86), kidney (SIR = 3.53, 95%CI:2.72-4.59) and thyroid (SIR = 6.31, 95%CI:4.26-9.33). When stratified by sex, statistically significant SIRs remained for lung, renal, colon and thyroid tumours. Additionally, females had a statistically significant SIR for stomach cancer (2.65, 95%CI:1.26-5.57) and bladder cancer (SIR = 2.61, 95%CI:1.36-5.02).
Conclusion
This study found that patients with a NEN experienced a metachronous tumour of the lung, prostate, kidney, colon and thyroid at a higher rate than the general population of England. There was no clear pattern between the site of NEN and subsequent non-NEN tumour site. Based on our findings we would suggest screening for second cancers using one of the many imaging or biochemical methods available for these and taking care to counsel all NEN patients on risk of second tumours. Surveillance and engagement in screening programmes is required to enable earlier diagnosis of second non-NEN tumours.

DOI: 10.1530/endoabs.87.P1

P2

PREF-NET: a patient preference and experience study of lanreotide autogel administered in the home versus hospital setting among patients with gastroenteropancreatic neuroendocrine tumours in the UK

Mohid Khan[1], Louise Davies[2], Melissa Back[3], Tahir Shah[4], Mark Pritchard[5], Kathryn Cook[6], Diana Hull[4], Gail McKane[5], Melissa Day[5], Anne-Sophie Grandoulier[7] & Kate Higgs[8]
[1]Cardiff and Vale University Health Board, Cardiff, United Kingdom; [2]University Hospital Coventry and Warwickshire NHS Trust, Coventry, United Kingdom; [3]Royal Free London NHS Foundation Trust, London, United Kingdom; [4]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [5]Liverpool University Hospitals NHS Foundation Trust, Liverpool, United Kingdom; [6]Cardiff & Vale University Health Board, Cardiff, United Kingdom; [7]Ipsen, Boulogne Billancourt, France; [8]Ipsen, Slough, United Kingdom

Introduction
LAN, a somatostatin analogue, is a common first-line treatment for NETs. LAN comes as a pre-filled, ready-to-use syringe, administered every 4 weeks. In the UK, patients may receive LAN at home. The aim of PREF-NET was to generate real-world evidence describing patient's experience of LAN administered in homecare and hospital settings, and the associated impact of treatment setting on other areas of patients' lives.
Methods
PREF-NET was a multicentre, cross-sectional, patient-reported study of adults with GEP-NETs in the UK. The study had two parts: a quantitative online patient outcomes survey, and qualitative semi-structured interviews with a subgroup of respondents; here we report data from the online survey. Eligible patients (target, 80–90 patients across five clinical sites) were ≥18 years with GEP-NETs receiving a stable dose of LAN at home, but with recent experience in the hospital setting (switched to homecare 4–24 months earlier). The primary endpoint was overall patient preference for LAN administration at home versus the hospital setting. Secondary endpoints related to impact of treatment setting on healthcare utilisation, societal cost, work productivity, activities of daily living, and health-related quality of life.
Results
The study included 80 patients (mean age 63.9 years [SD 10.6]; 52.0% male. Participants had switched to homecare <6 months (29.5%), 6–12 months (29.5%) or >12 months (41.0%) prior to the study. In the primary endpoint analysis, 98.7% (95% CI 96.1-100.0) of participants preferred homecare (vs 1.3% [0.0–3.9] who preferred hospital care). Overall, 84.2% of participants reported that switching to homecare improved overall injection experience while 14.5% reported no change; additional secondary endpoints are reported in table.
Conclusions
In this survey, all but one patient with GEP-NETs receiving LAN preferred to receive their treatment at home versus in hospital, with most indicating that homecare had a positive impact on many other areas of their lives.

Homecare vs hospital	Somewhat/much better (%)
Time (travel, attending appointments)	93.6
Costs	90.9
Convenience	98.7
Independence	93.4
Confidence in self-management	76.3
Ability to plan/go on holiday	80.3
Ability to engage in social activities	73.7
Relationships with family members/friends	55.3
Ability to work	55.4

DOI: 10.1530/endoabs.87.P2

P3

Manipulating the composition of the culture medium promotes neuroendocrine cell differentiation in mouse and human gastric organoids

Klaire Exarchou[1,2], Carrie Duckworth[3], Nathan Stephens[2], Nathan Howes[2] & David Mark Pritchard[1]
[1]Department of Molecular and Clinical Cancer Medicine, Institute of Systems, Molecular and Integrative Biology, University of Liverpool and Liverpool ENETS Centre of Excellence, Liverpool University Hospitals NHS Foundation Trust, Liverpool, United Kingdom; [2]Department of Upper GI Surgery, Liverpool University Hospital NHS Foundation Trust, Liverpool, United Kingdom; [3]Department of Molecular Physiology & Cell Signalling, Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, United Kingdom

Aim
Organoid cultures are a powerful model system for the study of cell biology and human disease. Manipulation of the composition of the culture medium has been used to promote cellular differentiation in gastric organoids to allow more accurate modelling of the mature epithelial cells present in the stomach. However, methods to promote the differentiation of neuroendocrine cells and specifically enterochromaffin-like (ECL)-cells within a gastric organoid system have not yet been established.
Methods
Gastric organoids were produced from adult C57BL/6 mice and following ethical approval and informed consent from adult H. pylori negative patients who had a normal stomach at the time of diagnostic gastroscopy. We investigated whether altering the composition of the culture medium and the addition of a small molecule that is known to induce neural differentiation in other culture systems promoted neuroendocrine cell differentiation in mouse and human gastric organoids. The abundance of Chromogranin A and other markers of differentiated cells were assessed using reverse transcription quantitative polymerase chain reaction (RT-qPCR) and immunofluorescence.
Results
Mouse and human gastric corpus organoids that were cultured in conventional culture media showed high expression of the gastrointestinal epithelial stem cell marker Lgr5 and low abundances of the markers of differentiated stomach cell

types. Reduction of the amount of Wnt in the culture medium directed organoid differentiation towards the pit cell lineage, with a reduced abundance of Lgr5 and increased expression of the mucus neck cell marker MUC5AC. Incubation of mouse and human gastric organoids with a small molecule that is known to induce neural differentiation resulted in increased abundance of Chromogranin A as well as other markers associated with ECL-cell differentiation such as histidine decarboxylase and the gastrin/CCK-2 receptor.

Conclusions

Mature differentiated parietal and enterochromaffin-like cells were rare in tissue derived mouse and human gastric organoids that were cultured using standard conditions. Cellular differentiation could however be promoted by manipulating the media composition and we additionally established a novel method for promoting neuroendocrine cell differentiation in gastric organoid cultures. This methodology will hopefully provide a platform to investigate gastric ECL-cell physiology as well as the development of gastric neuroendocrine tumours.

DOI: 10.1530/endoabs.87.P3

P4

Exploring the potential benefit of epigenetic modification: The LANTana trial, an open label, single arm, phase Ib study to evaluate the effect of pre-treatment with ASTX727 (a demethylating agent) followed by Lutathera (^{177}Lu-DOTATATE) in patients with progressive, metastatic neuroendocrine tumours (NETs)

Ravindhi Murphy, Gurvin Chander & Rohini Sharma
Imperial College NHS Healthcare Trust, London, United Kingdom

Background

Neuroendocrine tumours (NET) are rare cancers arising from cells of the neuroendocrine system and frequently present with advanced disease. They are characterised by the presence of somatostatin receptors (SSTR) on the tumour surface. The presence of SSTR are associated with the inhibition of NET proliferation and have formed the basis of peptide receptor radionuclide therapy (PRRT), such as Lutathera. PRRT relies on SSTR tumour expression and patients without this biomarker do not benefit from Lutathera. ASTX727 is an oral fixed-dose combination of cedazuridine plus decitabine. Cedazuridine is a cytidine deaminase (CDA) inhibitor and decitabine is a nucleoside hypomethylating agent (HMA) known to induce demethylation through deoxyribonucleic acid (DNA) methyltransferase inhibition. ASTX727 may induce demethylation to increase expression of SSTRs on NETs. Therefore, pre-treatment with ASTX727 may allow patients previously unsuitable for Lutathera to gain benefit from treatment.

Methods

LANTana will recruit patients with a biopsy-proven NET without tumoural uptake or uptake less than liver on [^{68}Ga]DOTA-TATE imaging. Twenty-seven eligible participants will be recruited and are firstly administered 1st cycle ASTX727. Subsequently, they are assessed for SSTR expression (via [^{68}Ga] DOTA-TATE PET & tumour biopsy) and if proven, will progress to receive a further ASTX727 cycle and Lutathera. Lutathera will then continue every 2 months for 4 cycles until disease progression, patient withdrawal or completion of one year of treatment. The primary objective of the trials is to determine whether pre-treatment with ASTX727 results in re-expression of SSTR2 using [^{68}Ga] DOTA-TATE to image epigenetic modification of the SSTR2 locus, allowing subsequent treatment with Lutathera. Secondary objectives include tolerability of combination therapy and assessment of response to treatment. Exploratory outcomes include SSTR2 expression and methylation of its locus in tumours in conjunction with baseline PET uptake parameters. Response will be assessed by computed tomography imaging or magnetic resonance imaging (MRI).

Discussion

The trial is designed to provide prospective evidence on the efficacy and tolerability of epigenetic modification pre-treatment with ASTX727 in patients who were previously not eligible for PPRT. Outcomes will aim to improve prognosis in an otherwise poor-prognostic cohort and inform use of this imaging methodology to assess epigenetic modification.

DOI: 10.1530/endoabs.87.P4

P5

The role of laparoscopic surgery in the management of appendiceal and small bowel Neuroendocrine tumours

Abed Elbarah & Frances Goulder
Hampshire Hospitals NHS Foundation Trust, Winchester, United Kingdom

Introduction

There is controversy over the best technique for resecting small bowel NETs and performing right hemicolectomies in patients with appendiceal NETs at risk of nodal involvement. Most guidelines recommend open over laparoscopic surgery but a survey suggests that surgeons favour a laparoscopic approach. We have reviewed a series of 14 consecutive primary (not recurrent) small bowel NET resections and post-appendicectomy right hemicolectomies including operative technique and histology results.

Method

14 consecutive patients with surgically managed small bowel NETs or requiring a post-appendicectomy right hemicolectomy for an appendix NET (according to UKINETs guidelines) were identified and a database was created. This included operative technique and histology results including lymph nodes counts and adequacy of resection. Histology results were compared according to NET location and operative technique.

Results

- Appendix NETs: 4 patients underwent an elective right hemicolectomy for a histologically confirmed grade 1 well-differentiated appendiceal NET following an appendicectomy. All resections were attempted laparoscopically; 1 was converted to open due to adhesions. Histology revealed no lymph node involvement. Mean number of resected lymph nodes was 22.5 (range 12-51).
- Small Bowel NETs: 10 patients underwent an ileal or ileocolic resection for a (or multiple) well differentiated grade 1 & 2 ileal NETs. 3 cases were carried out via a laparoscopic or laparoscopic-assisted approach and 7 cases by laparotomy. Involved lymph nodes were present in all patients. An average of 14.6 nodes (range 12-18) were identified in the laparoscopic specimens and 6.1 nodes (range 1-9) in the open specimens. Histologically clear margins were achieved in all cases.

Conclusions

- Appendix NETs: A laparoscopic right hemicolectomy should be considered in all patients with appendiceal neuroendocrine tumours who require a nodal assessment.
- Small Bowel NETs: A laparoscopic approach can be safely utilised in selected patients with small bowel NETs, particularly when involved nodes are close to the bowel wall or along the ileocolic pedicle. The importance of palpating the small bowel and factors affecting the decision on surgical approach are discussed.

DOI: 10.1530/endoabs.87.P5

P6

The impact of the COVID-19 pandemic on Neuroendocrine tumour (NET) services and patients in the pandemic recovery period: A quantitative and qualitative analysis

Tanvi Dabke[1], John Finnen[2] & Alia Munir[2]
[1]University of Sheffield, Sheffield, United Kingdom; [2]Sheffield Teaching Hospitals, Sheffield, United Kingdom

Introduction

The COVID-19 pandemic has affected the delivery of NET services and patient care. We retrospectively analysed the recovery of NET service provision over the COVID-19 recovery period 2020-2021.

Method

The NET database was searched using 3 NET physician codes. Anonymised data was analysed, including PRRT, MIBG, endoscopy and bronchoscopy rates. In February 2022, patient satisfaction questionnaires were posted out to 87 randomly selected NET patients, treated between January and December 2021. The anonymised data was tabulated in an Excel spreadsheet and analysed.

Results

A total of 742 patients had recorded attendance at the NET centre, with 15% face-to-face, 83% telephone and 2% video. 693 patients were follow-up. Among new patient appointments, 59% were face-to-face and 41% telephone. The questionnaire received 51/87 responses. 18% had tested positive for COVID-19. 57% liked telemedicine follow-up. 96% felt cared for by their physicians and were satisfied with the information provided about their illness. 90% felt the wait period before examinations or treatments was acceptable, in comparison to 79% in 2020. None felt their chemo/radiotherapy was delayed. 33% reported an increase in anxiety and 82% felt psychologically supported. PRRT and MIBG were administered over 92 and 7 treatments in 2021 compared with 82 and 2 in 2020 respectively. The number of annual bronchoscopy procedures fell by 45% in 2020 compared to 2019 and increased by 20% between 2020 and 2021. The number of upper and lower GI endoscopies was 56% and 77% of 2019 levels in 2020 and 2021 respectively.

Conclusion

The COVID-19 pandemic saw a change in the delivery of NET consultations. The results demonstrate NET service provision has not fully recovered to pre-pandemic levels, which may have long term implications for NET patient care. It is important to assess the long-term impact of the pandemic on morbidity and mortality in NET patients and continue to monitor NET service recovery.

DOI: 10.1530/endoabs.87.P6

P7

Trans cather pulmonary valve replacement in carcinoid heart disease: a potential option in selected cases

Madushani Karunanayaka[1], Jamie Bentham[2], Helen Parry[2,3] & Alia Munir[1]
[1]Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom; [2]Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [3]Northern General Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Introduction
Established guidelines recommend carefully selected patients with Carcinoid Heart Disease (CHD) may undergo surgical valve replacement as definitive management. Right sided heart valve involvement is classical, occurring as result of plaque deposition on valve leaflets as a consequence of vasoactive peptides secreted by the NET because of carcinoid syndrome. Tricuspid and Pulmonary valve involvement leads to right heart failure (RHF) increasing mortality and morbidity independently. There is a paucity of studies reviewing percutaneous approaches in this group. Here we compare 2 patients with metastatic NET with carcinoid heart disease treated successfully by surgical valve replacement and percutaneous valve intervention and review short-term outcomes.
Case 1
56 years old female presented with carcinoid syndrome was diagnosed with metastatic small bowel neuroendocrine in 2015, developed rapid deterioration of pulmonary valve function (stenosis and regurgitation) with an element of TV thickening and mild TR with features of right heart failure in 2019. She had biochemical evidence of functioning NET with RHF evidenced by elevated N-terminal pro BNP of 436 ng/l, CgA (283ng/ml) and UHIAA 1321ng/24 hours. SSTR scintigraphy revealed widespread progressive multiple metastasis including bone, breast, liver, retro-orbital lesions. Her past treatment included Lutathera™ and Lanreotide autogel™. Her 2 – Echo, and CT-coronary angiogram confirmed thickened right heart valves with pulmonary affected more than tricuspid. She was not deemed suitable for surgical intervention. There were favourable pulmonary annular dimensions for percutaneous approach. This was undertaken with octreotide cover. Her RHF and quality of life dramatically improved immediately.
Case 2
65 years old male presented with carcinoid syndrome with metastatic small bowel NET developed features of right heart failure in 2020. Cardiac investigations revealed pulmonary and tricuspid regurgitation, and right coronary artery disease. He was treated with pulmonary valve replacement, tricuspid valve replacement and Coronary artery bypass graft. Recent Echo revealed TVR *in situ* and mild PVR. He is on Olatuton™. His disease remains stable, and his quality of life has improved.
Conclusion
Options for surgical valve replacement in patients with Carcinoid heart disease with stable NET disease exist, however percutaneous valve options should be further explored and studies in this area are needed.

DOI: 10.1530/endoabs.87.P7

P8

To determine potential prognostic factors influencing overall survival of patients with adrenocortical carcinoma

Niralini Thayaparan, Atirola Obileye & Alan Anthoney
University of Leeds, Leeds, United Kingdom

Adrenocortical carcinomas (ACCs) are a group of aggressive neuroendocrine cancers that affect 1-2 people/million/year (1) and are mostly diagnosed in advanced stages. ACCs have poor overall survival (OS) rates (2). This study aimed to determine potential factors influencing OS of ACC patients in Yorkshire by a retrospective investigation of potential factors and OS of all 30 adult patients with ACC seen at St James University Hospital (SJUH) from 01/01/2000 to 01/10/2021. Analytical statistics were performed on the data. Mann-Whitney U-tests showed that female patients had an insignificantly higher median OS (50 months) than male patients (24 months; $P=$ 0.142; U: 66.0). Mann-Whitney U-tests also showed that patients with co-morbidities had an insignificantly lower median OS (33 months) than patients without (39 months; $P=$ 0.374; U: 103). Mann-Whitney U-tests further showed that patients with left ACC had an insignificantly higher median OS (36 months) than patients with right ACC (32 months; $P=$ 0.689; U: 101). Furthermore, Mann Whitney U-tests showed that ACC patients with high cortisol had an insignificantly lower median OS (16.0 months) compared to that of ACC patients with low/normal cortisol (45.0 months; $P=$ 0.412; U: 60.5). Spearman rank analyses showed that there was an insignificant reduction in OS of patients diagnosed at an older age (rs: -0.312; p: 0.0935). However, spearman rank analysis showed that there was a significant reduction in OS of more deprived patients. Overall, deprivation has been shown in this study to be the only key contributor in influencing OS of ACC patients, which is important to consider upon making treatment decisions (3).
References
1. Allolio, B., & Fassnacht, M. Clinical review: Adrenocortical carcinoma: clinical update. The Journal of clinical endocrinology and metabolism. [Internet] 2006 [cited 2022 Oct 7]; 91(6):2027–2037. Available from: doi: 10.1210/jc.2005-2639
2. Bonnet-Serrano, F., & Bertherat, J. Genetics of tumors of the adrenal cortex. Endocrine-related cancer. [Internet] 2018 [cited 2022 Oct 7]; 25(3): 131–152. Available from: doi: 10.1530/ERC-17-0361.
3. Thayaparan N. An Investigation of Potential Factors Influencing Overall Survival of Patients with Adrenocortical Carcinoma in Yorkshire. ESREP Manuscript. The University of Leeds; 2022.

DOI: 10.1530/endoabs.87.P8

P9

Ocular neuroendocrine tumour metastases – presentation & outcome

Husnain Shah, Mohamad Roji, Ozgul Ekmekcioglu, John Ayuk, Stacey Smith, Zaira Khan, Suzanne Vickrage, Joanne Kemp-Blake, Sian Humphries, Simon Hughes, Salvador Diaz-Cano, Mona Elshafie, Salil Karkhanis, Shishir Shetty, Ian Geh & Tahir Shah[1]
Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom

Introduction
Here we present our experience of managing patients with orbital well-differentiated neuroendocrine tumour (NET) metastases.
Methods
Six patients were identified from the hospital NET database: four male; two female.
Results
Median age at diagnosis of primary NET: 69.5 years (range: 40-74 years). Three patients were alive at time of data capture. Of those who passed away: mean survival from diagnosis of primary NET = 326 weeks (range 135-447 weeks); mean survival from diagnosis of ocular metastases = 168 weeks (range: 39-408 weeks). Four patients had GI primary NET; one lung; one thymus. Median time between diagnosis of primary and ocular metastases: 68 weeks (range: 6-338 weeks). Ki67 at time of primary diagnosis: 4 patients were </=1%; 2 patients </=5%. Median 5-HIAA at time of primary diagnosis: 119.3 (range 20-334.3). Median 5-HIAA at time of ocular metastases: 108.1 (range 12-363). Additional to orbital metastases: 3/6 had liver metastases; 1/6 pancreas; 1/6 breast; 1/6 bone; 3/6 nodal disease. One patient had intracranial involvement. In five patients, the primary was identified first. Three patients were investigated on the basis of ocular symptoms, and diagnosed on the basis of histology. Those with eye symptoms: 2/6 patients suffered binocular diplopia; 2/6 patients ophthalmoplegia; 2/6 patients unilateral proptosis. The remaining patients were identified incidentally on the basis of Octreotide-Scan or DOTA-PET Scan. Two patients had prior ocular history separate from their metastatic disease: both had a diagnosis of glaucoma; one had bilateral early cataracts. Orbital involvement: 3/6 right orbital involvement; 1/6 left orbital; 2/6 both orbits. Superior rectus involved in 1/6; medial 2/6; inferior 2/6; lateral 3/6. 4/6 had rectus involvement; 3/6 had extra-global involvement. In terms of treatment: one patient received orbital radiotherapy. Two patients were provided spectacles with an occluded lens for symptomatic relief of diplopia. 4/6 patients had follow-up imaging of their ocular metastases. Median time from first orbital imaging to last follow-up imaging: 220 weeks (range: 68-331 weeks). Progression on follow-up imaging: one stable; two marginal increase; one progressed along anterior cranial fossa.
Conclusion
Orbital involvement by NETs is rare and thankfully does not require radical treatments.

DOI: 10.1530/endoabs.87.P9

P10

What is the prevalence of bile acid malabsorption in neuroendocrine tumour patients (NET) at the Queen Elizabeth Hospital Birmingham

Reena Mair[1], Tahir Shah[2] & Elizabeth Bradley[1]
[1]Nutrition and Dietetics, University Hospital Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [2]Department of Hepatology, University Hospital Birmingham NHS Foundation Trust, Birmingham, United Kingdom

Introduction
Bile acid malabsorption (BAM) may be a contributing factor causing diarrhoea in patients with NETs, particularly among those who have undergone previous

surgical resection of the terminal ileum and/or right colon or cholecystectomy (Naraev *et al* 2019).
Aim(s)
To identify the prevalence of bile acid malabsorption in neuroendocrine tumour patients (NET) at the Queen Elizabeth Hospital Birmingham (QEHB).
Materials and methods
Data was obtained via informatics looking back at the NET patients seen at QEHB from the past 10 years. A sample of 1665 patients was taken, of these 22 had a SeHCAT scan completed. Data was collected including; primary tumour location, surgery, whether the patient had been prescribed any bile acid sequestrants and the result of any completed SeHCAT scans.
Results
A SeHCAT scan result was available for 22 patients. 17 (77%) patients had a positive SeHCAT scan result, 5 (23%) patients had a normal result.
Of those with confirmed BAM;
- 82% had been prescribed bile acid sequestrants.
- 94% had previously undergone surgery with the majority having had some form of small bowel resection and/or right hemicolectomy.
- 88% had a small bowel primary tumour, 6% pancreatic and 6% lung.

Conclusion
NET patients that have undergone surgical resections of the right colon and small bowel are at a greater risk of bile acid malabsorption and this should be a factor considered when undertaking nutritional assessments and reviewing bowel habits. Due to the covid 19 pandemic SeHCAT scans were temporarily stopped, the data captured during this time frame does not include the patients that were empirically treated. More research needs to be conducted looking at the efficacy of bile acid sequestrants on symptom control and incidence of BAM as a whole.
Keywords: SeHCAT | Bile acid malabsorption | Bile acid sequestrants | Surgery | NET
DOI: 10.1530/endoabs.87.P10

P11

Metastatic VIPoma with Severe WDHA Syndrome: Natural History over 20 years documenting histological dedifferentiation - an illustrative case

Elspeth Saunders[1], Bruce Sizer[2], Jennifer Collins[1], Srinivasan Gopalkrishnan[2], Robert Skelly[1], Robert Petty[1] & Mary McStay[1]
[1]East Suffolk North Essex Foundation Trust, Colchester, United Kingdom; [2]East Suffolk North Essex Foundation Trust, Ipswich, United Kingdom

A 51 year old female patient presented in 2000 with a 7 month history of diarrhoea and weight loss. Bloods revealed hypokalaemia (1.9). Infection and malabsorption screen negative, but patient remained hypokalaemic despite maximum iv and oral replacement. No abnormality was found endoscopically. Fasting gut hormone profile showed raised Vasoactive Intestinal Polypeptide (VIP) >400 (NR <30). CT scan confirmed 5cm mass in body of pancreas, no metastatic disease. Response to Octreotide was confirmed initially and histology confirmed VIPoma with Ki67 <5%. Symptoms returned with hypokalaemic myopathy 5 months later and after repeat octreotide scan again showed no metastases, distal pancreatectomy was performed. On surveillance, repeat imaging and gut hormones remained normal. However, over 10 years later in 2011, patient developed further diarrhoea with CT scan revealing recurrence in pancreatic bed. She was started on sandostatin analogues, and in 2012 had further resectional surgery of pancreatic bed disease (Ki67 5%). By June 2014, patient developed diarrhoea and although CT scans remained stable, chromogranins were raised. A gallium PET scan revealed multifocal serosal metastases. Patient was treated with PRRT, 4 cycles from June 2015 to May 2016 stabilizing disease. She was then retreated in 2018 but then presented with small bowel obstruction and was operated on at Specialist Peritoneal Malignancy unit. This revealed metastatic NET (Ki67 now 33%) and was advised to have adjuvant chemotherapy which patient declined. There was further evidence of progressive disease by 2021, and patient commenced FCarbo-Strep. Unfortunately, mid-treatment serial CT scan confirmed progression. Octreotide infusion 600 mg/24h was started and regular Lanreotide increased to 120mg every 2 weeks, but there was no relief from symptoms, developing hypokalaemia, hypomagnesaemia and hypotension. A trial of dexamethasone 4mg OD was prescribed. We increased octreotide infusion to 1.2mg/24h. Diarrhoea improved to a manageable level and electrolytes normalised. She was readmitted 8 weeks later with hypoglycaemia and progressively worsening diarrhoea despite ongoing octreotide infusion. Octreotide was titrated up to 1.5mg/24h and diarrhoea again settled. With limited further treatment she was referred for further PRRT. Unfortunately, patient deteriorated and was not fit enough for further treatment. She died December 2021, 21 years after diagnosis.

DOI: 10.1530/endoabs.87.P11

P12

SIRT: adrenocortical carcinoma and liver metastases

Leo Baxendale-Smith[1], Karim El-Shakankery[1], Lucy Wall[1] & James Gordon-Smith[2]
[1]Department of Medical Oncology, Edinburgh Cancer Centre, Western General Hospital, Edinburgh, United Kingdom; [2]Department of Interventional Radiology, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

Introduction
Selective internal radiation therapy (SIRT) is a novel intervention used to treat both primary and metastatic malignant liver lesions. Adrenocortical carcinoma (ACC) is a rare cancer with limited treatment options; evidence for SIRT use in ACC liver metastases is limited to case reports only. In this case we report prolonged and successful disease control using recurrent SIRT in a gentleman with liver-limited ACC.
Case study
A 49-year-old gentleman, initially presenting with hypertension, underwent left-sided adrenalectomy for suspected phaeochromocytoma in August 2010. Histological examination of resected tissues was suggestive of ACC. As microscopic tumour cells were present at resection margins, adjuvant radiotherapy (45Gy to 25#) was given to the resection bed. Following re-presentation in January 2014 with liver-limited relapse, he underwent a left-sided hepatectomy. Two further hepatic lesions were subsequently identified on MRI in March 2015; radiofrequency ablation was used to achieve remission. Having reviewed the literature on mitotane toxicity, the patient declined its use in adjuvant and metastatic settings. In April 2018, follow-up imaging identified two further liver lesions too large for resection. Considering the non-surgical options available, SIRT was undertaken in July 2019, resulting in no toxicities and radiological response. This subsequently provided 18 months of progression-free survival with good quality of life. Following hepatic disease progression, repeat SIRT was performed in January 2021, inducing shrinkage of all new lesions without toxicity. Post-radiation fibrosis (described as 'residual arterial enhancement') at the site of recent SIRT was subsequently noted, managed with bland embolization in October 2021. In March 2022, a third round of SIRT was undertaken for hepatic relapse in previously untreated segments, alongside subsequent ablation of residual disease in May 2022. After presenting in July 2022 with spinal and base of skull metastases, the patient sadly passed away in September 2022.
Conclusion
Substantial unmet need exists for effective treatments in ACC, mindful that 75% patients present with incurable disease at diagnosis. Though ultimately developing widespread disease, SIRT offered 2 years of progression-free survival in our patient; the procedure was well tolerated on multiple occasions with minimal residual liver impairment. Its use in ACC liver-limited disease warrants further investigation.

DOI: 10.1530/endoabs.87.P12

P13

Parathyroid related peptide (PTHrP) secreting pancreatic neuroendocrine tumour (PNET): a case of PTHrP, hypercalcaemia and osteoarthrosis (OA) controlled by somatostatin analogue therapy (SSA)

Madushani Karunanayaka[1], Jon Wadsley[2] & Alia Munir[1]
[1]Royal Hallamshire Hospital, Sheffield Teaching Hospitals, NHS Foundation Trust, Sheffield, United Kingdom; [2]Weston Park Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Introduction
PNETs are rare with an annual incidence of 5 per million population. 75 % of pancreatic NET are functioning, PTHrP secretion regarded as a rarer entity and few case reports have been identified worldwide. Surgical resection is definitive management, however SSA treatment and Peptide Receptor Radionuclide Therapy (PRRT) have shown promising results in reducing PTHrP secretion.
Case report
Here we describe a 61 years old lady who presented with cough and clinical and features of hypercalcaemia in 2016. Biochemical evaluation revealed elevated calcium levels (2.85 mmol/l), Suppressed PTH level (0.8 pmol/l) with normal vitamin D level (59 nmol/l) and high Chromogranin A levels (49.7 nmol) with fully suppressed PTH, PTHrP was measured and found to be elevated (2.2 pmol/l, normal range 0-1.8). Radiological evaluation with CT and NM octreotide scan confirmed the presence of large pancreatic tail invasive mass measuring 8 cm with multiple Liver, splenic metastasis. USS guided biopsy confirmed ENETS grade 2 NET with Ki 67 index of 7%. She was treated with (PRRT-Lutathera™) and tumour size was reduced on follow up imaging. She discontinued her depot

analogue and switched to sc octreotide with normalization of calcium level. She was plagued by side effects including day time somnolence, insomnia and mood changes on the analogue and discontinued it. She developed marked hypercalcaemia and rapid bilateral hip osteoarthrosis. She has declined re-trial with analogue therapy. Currently she is managed IV Zoledronic acid treatment for hypercalcaemia and awaits bilateral hip replacements. Current imaging is stable. National assay shortage issues have meant repeat PTHrP levels have not been possible, calcium levels have been the marker for this.

Conclusion

We report a novel case of PTHrpoma with uncontrolled hypercalcaemia and accelerated osteoarthosis with intolerance to SSA therapy. Previous biomedical studies have reported an association between PTH deficiency and the risk of OA. The function and regulation of PTHrP in OA cartilage are still poorly understood and it is unclear if loss of PTHrP hormonal control accelerates OA.

DOI: 10.1530/endoabs.87.P13

P14

Somatostatin receptors in olfactory neuroblastoma: The rationale for peptide receptor radionuclide therapy

Juliana Porto[1], Aimee Hayes[1], Alexander Branton[1], Martyn Caplin[1], Martyn Alusi[2] & Ashley Grossman[1]

[1]Royal Free London NHS Foundation Trust, London, United Kingdom; [2]Barts and the London School of Medicine and Dentistry, London, United Kingdom

Olfactory neuroblastoma (ONB) is a rare neuroendocrine tumour with a slow onset of symptoms, and classically a propensity for recurrence and a poor prognosis. Due to its rarity, there is no agreed standard therapy, but treatment will usually include surgical resection, adjuvant radiotherapy and/or chemotherapy. However, such tumours very often show positive uptake on somatostatin receptor radionuclide scanning, and selective use of peptide receptor radionuclide therapy (PRRT) has been described in case reports, but currently only a handful of cases have been reported, with varying results. We describe a case of ONB where PRRT is planned in a patient with ONB. A 41-year-old lady presented with loss of sense of smell and right-sided facial swelling. She was diagnosed with nasal polyps and was planned for surgical resection, but this was delayed due to the COVID-19 pandemic. She subsequently developed an abscess on the right side of her face and was treated with drainage and antibiotics. It was then noted on CT scanning that she had a solid mass around her right maxilla that on biopsy was demonstrated to be an olfactory neuroblastoma. She underwent surgical resection followed by adjuvant external beam radiotherapy and cisplatin chemotherapy. Two years later she developed disease recurrence, biopsy confirming a recurrent ONB (Ki-67 40%-70%), with extensive infiltration of the right ethmoid sinus and septum, perineural and lymphovascular invasion, and involvement of 5 lymph nodes. A 68Gallium-DOTATATE PET/CT showed intense uptake in all the involved areas and following further debulking she is planned for PRRT with 177Lu-dotatate. The extensive expression of somatostatin receptors (SSTR) in patients with ONB supports the use of SSTR-dependent therapies, such as PRRT, which has shown excellent results in improving progression-free survival in other neuroendocrine tumours. Prospective studies evaluating PRRT efficacy, toxicity and quality of life in this rare cancer population are needed.

DOI: 10.1530/endoabs.87.P14

P15

Management and outcome of pituitary metastasis from a bronchial carcinoid tumour presenting with ocular symptoms

Husnain Shah & John Ayuk

Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom

Metastasis to the pituitary gland is a rare occurrence. Here we discuss our experience managing a patient with pituitary neuroendocrine metastasis who first presented with ocular symptoms. A 65-year-old lady presented in July 2015 with progressive diplopia. An MRI scan revealed a pituitary mass lesion with aggressive features and two abnormal enhancing nodules within the brain white matter, raising suspicion of metastatic disease. Radiotherapy was commenced on the basis that the lesion was equally infiltrative as compressive. External beam therapy of the pituitary lesion was initially successful at maintaining visual acuity (VA) (right VA 6/9, left VA 6/36) and stabilising Goldman visual field (VF) loss; however, the cranial nerve 3 palsy persisted. Six months after the initial presentation, the patient reported worsening vision, which was reflected in a decline in visual acuity (right VA 6/9, left VA 3/60) and further visual field loss. There was no evidence of pituitary lesion progression, and vision stabilised on follow-up six months later (right VA 6/7.5, left VA 2/60). Identifying and treating the primary lesion proved to be a challenge. CT-TAP revealed a likely right middle lobe primary, with local collapse and multiple hepatic foci. FDG-PET and octreotide scan were negative, and the tumour was not visible on bronchoscopy. However, liver biopsy revealed metastatic atypical bronchial carcinoid. The patient was started on interferon alpha 2a. The patient was able to tolerate this for only four months before stopping, by which time she had developed proximal muscle weakness. MRI revealed spinal drop metastases, and patient was placed on the palliative pathway. 19 months after diagnosis, the patient passed away. In summary, bronchial carcinoids can metastasise to the central nervous system and herald a poor prognosis.

DOI: 10.1530/endoabs.87.P15

Author Index