

Patients with radiologically, endoscopically or surgically proven SBNETs were included in this study, patients with unknown primary were excluded. A total of 623 patient year's follow-up, with a mean duration of follow-up of 5 years. The median age 61 years (range 24–84). Statistical analysis was performed using GraphPad Prism 5.1.

Results TNM staging and follow-up data were available in 118 cases. Due to low numbers of Stage 2 and 3 tumours these were group together for comparison. There were four cases with stage 2, 23 cases with Stage 3 and 91 cases with stage 4 small bowel NETs. Kaplan–Meier plots were constructed these demonstrated a significant difference in survival between patients with different stage of disease ($p=0.03$). There was no significant difference in survival between stage 2 and stage 3 diseases. There was a significant survival difference between G1 (Ki67 ≤ 2) vs G2 (Ki67 3–20) $p=0.049$. The overall 5-year and 10-year survival was 79.5% and 48.5% respectively for all patients independent of stage of disease. Of the patients that died the median time to death from diagnosis was 3 years (range 0–14). The cause of death was related to tumour burden in 50% (22 patients), carcinoid heart disease in 11.3% (five patients), post intervention (one case surgery, one case post-embolisation) 4.5%, small bowel obstruction or perforation 13.6% (six patients) and non-tumour related deaths in 24.5% (9) patients.

Conclusion This study demonstrates the overall 5-year and 10-year survival is higher than that published in the SEER data.² The cause of death demonstrates the non-tumour or disease related deaths account for 24.5% of cases. There is significant survival difference between Stage IV disease and Stage II and III. There was no significant difference in survival between stage II or III. Low grade tumours Ki67 $\leq 2\%$ was associated with better survival than Ki67 3–20. No patients had a Ki67 >20 ; therefore no analysis could be performed.

Competing interests None declared.

REFERENCES

1. Rindi G, Klöppel G, Couvelard A, *et al*. TNM staging of midgut and hindgut (neuro) endocrine tumors: a consensus proposal including a grading system. *Virchows Arch* 2007;**451**:757–62.
2. Yao JC, Hassan M, Phan A, *et al*. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *J Clin Oncol* 2008;**26**:3063–72.

PWE-126 SURVIVAL AND RECURRENT DISEASE IN PATIENTS WITH RESECTED PRIMARY SMALL BOWEL NEUROENDOCRINE TUMOURS

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Introduction Small bowel neuroendocrine tumours (SBNETS) are the most common of all GI NETs. The majority of patients present with metastatic disease. It is unclear whether resection of the primary tumour improves prognosis. Furthermore, the recurrence rate of disease in patients following "curative" resection is not previously been investigated.

Aims To demonstrate if primary SBNET resection leads to improved survival and time to development of recurrent disease in patients following resection of primary tumour +/- mesenteric disease in an attempted curative resection.

Methods 138 patients with SBNETs seen in our institution; median duration of follow-up was 5 years. Median age 61 (range 24–84 years). Only patients in whom current disease state was known were included in the study. Primary site: Duodenal 2.1% (3),

Jejunal 2.9% (4), ileal 95% (131). Kaplan–Meier plots were constructed to determine survival. Staging was performed retrospectively using the TNM staging system proposed by ENETs.¹

Results 100 patients had the primary resected, four patients had irresectable disease at laparotomy. The mean time to resection of primary from diagnosis was 5.8 months (range 0–78 months). There were no deaths within 30 days post surgery. Kaplan–Meier survival curves were constructed. There was a significant survival benefit in patients whom underwent resection of primary tumour compared to those who did not have the primary resected (120 vs 56 months, $p<0.005$). There were four patients with Stage 2, 23 patients with stage 3 disease and 91 with stage 4 disease. There were 10 patients in whom it was not possible to accurately stage of disease since the complete histology was not available, however, all of these patients had no evidence of recurrent disease in the initial post-operative period. No survival data were available for the remaining 10 patients. Of the patients who underwent attempted curative resection without distal metastatic disease at presentation, there were 36 patients suitable for analysis. Of these 15 of 36 (41.7%) patients have developed recurrent disease. Median period for development of recurrence was 55 months (range 11–606 months). There was no recurrence in the four patients with known stage 2 disease (4–168 months). Recurrence occurred in 8 of 23 patients (34.8%) with stage 3 disease.

Conclusion This study demonstrated a marked improvement in survival in patients who underwent resection of the primary tumour. Disease recurrence is common in patients following curative resection of locally advanced small bowel NETs. Surveillance for a period of only 5 years will not identify a number of patients who will proceed to develop recurrence.

Competing interests None declared.

REFERENCE

1. Rindi G, Klöppel G, Couvelard A, *et al*. TNM staging of midgut and hindgut (neuro) endocrine tumors: a consensus proposal including a grading system. *Virchows Arch* 2007;**451**:757–62.

PWE-127 TWO RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 TRIALS OF LINALOTIDE IN ADULTS WITH IRRITABLE BOWEL SYNDROME: EFFECTS ON QUALITY OF LIFE

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Introduction Linaclotide, a minimally absorbed guanylate cyclase-C receptor agonist, is an investigational drug for the treatment of irritable bowel syndrome with constipation (IBS-C) that has shown statistically significant improvements in abdominal and bowel symptoms in two Phase 3 clinical trials. IBS-C is a common functional gastrointestinal disorder that affects a significant portion of the population and leads to reduced quality of life (QOL).

Methods Data evaluating the efficacy and safety of oral once-daily linaclotide 290 μg (N=748) vs placebo (N=742) in patients with IBS-C were pooled from two Phase 3 clinical trials. Patients meeting modified Rome II criteria for IBS-C were randomised to receive either linaclotide or placebo treatment for 12 weeks. The Irritable Bowel Syndrome Quality of Life (IBS-QOL) questionnaire, comprising 34 items, each with a 5-point response scale (1= "not at all" through to 5= "extremely" or "a great deal"), was completed at baseline and also at the end of the treatment period. The IBS-QOL is scored "overall" and by eight subscales (Dysphoria, Interference with Activity, Body Image, Health Worry, Food Avoidance, Social Reaction, Sexual and Relationships). The change from baseline to week

12 scores were analysed using an analysis of covariance model. The IBS-QOL response rates (ie, patients with ≥ 10 -point and ≥ 14 -point increase) for the treatment groups were compared using Cochran-Mantel-Haenszel stratified by geographical region.

Results The changes from baseline in the IBS-QOL "overall" score and seven of the eight subscale scores (Dysphoria, Body Image, Health Worry, Food Avoidance, Social Reaction, Sexual and Relationships) were statistically significant for linaclotide-treated patients vs placebo-treated patients ($p < 0.0001$ for each comparison). The percentage of responders for the IBS-QOL "overall" score was statistically significantly greater for linaclotide-treated patients vs placebo-treated patients at week 12 (64.3% linaclotide-treated patients vs 52.6% placebo-treated patients for ≥ 10 -point change; 53.8% linaclotide-treated patients vs 39.1% placebo-treated patients for ≥ 14 -point change). The most common adverse event among linaclotide-treated patients was diarrhoea.

Conclusion Compared with placebo, once-daily linaclotide treatment for 12 weeks significantly improved "overall" QOL scores and seven out of eight important QOL domains, as measured by the IBS-QOL, in adults with IBS-C.

Competing interests R T Carson Employee of: Forest Research Institute, S Tourkodomitis Employee of: Forest Research Institute, B E Lewis Employee of: Ironwood Pharmaceuticals, J M Johnston Employee of: Ironwood Pharmaceuticals.

PWE-128 REVIEW OF SEHCAT USE AT ST. GEORGE'S 2005–2010: AN UNDERUTILISED INVESTIGATION?

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Introduction Bile acid malabsorption (BAM) is a frequently overlooked but easily treatable cause of chronic diarrhoea. The SeHCAT study is a simple non-invasive technique for diagnosing this condition. Three types of BAM are described. Type 1 is seen in patients with terminal ileal disease/resection or bypass. Type 2, known as primary or idiopathic BAM, is characterised by lack of discernable change in ileal histology or obvious clinical history or pathology to account for the malabsorption. Type 3 comprises all other causes of BAM including gastric surgery, pancreatitis, cholecystectomy or associated with microscopic colitis, coeliac disease, diabetes and small bowel bacterial overgrowth.

Methods Retrospective review of all SeHCAT studies performed between 2005 and 2010 at St George's Hospital.

Results Between 1 January 2005 and 31 December 2010 55 SeHCAT studies were performed. Basic details were available on all 55, however only 44 sets of notes were available. 36 (65%) patients were female and 19 were male. Age ranged from 19 to 77 years old. 62% of studies were abnormal showing $< 15\%$ retention at 7 days. Of these 11 (32%) demonstrated mild BAM, 8 (24%) moderate BAM and 15 (44%) severe BAM. Of the 34 patients with BAM 28 sets of notes were available. 10 (36%) had Type 1, 8 (29%) had Type 2 and 10 (36%) had Type 3 BAM. In those with proven BAM 46% underwent a trial of bile acid sequestrant (BAS). 88% of patients with follow-up details had good resolution of their symptoms. Response rates to treatment ranged between 60 and 100%. Six of the 10 type 1 BAM subjects had a trial of BAS; follow-up details are only available on 3, 2 of whom had noticed an improvement in symptoms (66%). Six of the 8 type 2 BAM subjects had a BAS, follow-up details are available on 5, 3 of whom had improvement of their symptoms (60%). Four of the 10 type 3 BAM subjects had a BAS, at follow-up details are only available on three all of whom had a good response (100%).

Conclusion As chronic diarrhoea is a common reason for GI referral, the small number of studies performed over a 5-year period suggests that SeHCAT is probably underused and bile acid malabsorption

under diagnosed. As bile acid sequestrants provide good symptomatic relief, bile acid malabsorption is a useful diagnosis to make.

Competing interests None declared.

PWE-129 SHOULD SEHCAT BE EARLIER IN THE ALGORITHM FOR INVESTIGATING CHRONIC DIARRHOEA?

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Introduction Bile acid malabsorption (BAM) is a potentially under-recognised cause of chronic diarrhoea. An accurate diagnostic technology exists in the form of the SeHCAT (⁷⁵Se—homotaurocholate) test. The British Society of Gastroenterology investigation algorithm places SeHCAT as a very late stage investigation, but if BAM is common or SeHCAT unavailable it may easily be overlooked. This is a treatable condition: the response to bile sequestrants as an empirical "investigation" is not an adequate approach. This study aimed to characterise the results of SeHCAT in a large cohort of patients, and also to determine how well adhered to were the British Society of Gastroenterology guidelines for the investigation of chronic diarrhoea.

Methods The electronic records of 276 patients who underwent SeHCAT scanning between 2005 and 2011 were retrospectively analysed as a medical student project.

Results Bile acid malabsorption (BAM) was very common in patients who underwent SeHCAT testing, found in 110 (40%) of the 276 patients. In the overall cohort, 136 patients had no prior underlying disease or surgery recorded that might cause diarrhoea, and 86 of these displayed no abnormalities on full screening including endoscopies and coeliac tests. Of the 110 with BAM, 28 had undergone neither endoscopy nor coeliac screening. Predictably, 22 of the 26 (85%) Crohn's patients with a history of ileal resection had positive results, as did 15 of the 21 (71%) ileally resected patients who did not have Crohn's disease. Sixteen patients (55%) with post-cholecystectomy diarrhoea showed evidence of BAM.

Conclusion BAM is common in subjects undergoing SeHCAT. The current guidelines should be revised to take into account BAM as an important and common cause of diarrhoea, with SeHCAT earlier in the process. It is apparent that clinicians are not widely using the BSG algorithm, presumably using clinical judgement in patients in whom BAM seems likely, and, for example, opting not to undertake colonoscopy in many cases. In the absence of a terminal ileum, the BAM diagnosis is almost universal and the test is probably superfluous. A broader and contemporary health technology assessment including all patients currently investigated for chronic diarrhoea is now required in order to define a new algorithm.

Competing interests None declared.

PWE-130 THE HUMAN GUT MUCOSAL COGNATE CELLULAR RESPONSE TO LIVE ORAL TYPHOID VACCINATION

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Introduction The human gut mucosal cellular response to oral vaccination has never been directly assessed. We studied the cognate cellular immune response to the live oral typhoid Ty21a vaccine in the gut mucosa of human volunteers, and compared it with that seen in peripheral blood.