0–10 scale) and 76% had no CSBMs (mean rate 0.2/wk). Significant improvements in linaclotide-treated patients were seen for both co-primary and all 12 secondary parameters. For the first co-primary parameter (≥30% reduction from baseline in mean abdominal pain or discomfort score with neither score worsening for ≥6 of the first 12 wks), 54.1% of linaclotide-treated patients and 38.5% of placebo-treated patients were responders (p<0.0001). For the second co-primary parameter ("considerably relieved" or "completely relieved" on the weekly degree-of-relief of IBS symptoms question for ≥6 of the first 12 wks), 39.4% of linaclotide-treated patients and 16.6% of placebo-treated patients were responders (p<0.0001). Similar improvements in both co-primary endpoints were seen at 26 wks (53.6% vs 36.0%, 37.2% vs 16.9%; both p<0.0001). Also, rates for sustained abdominal pain/discomfort response and sustained IBS degree-of-relief response at 12 and 26 wks were significantly greater in linaclotide-treated vs placebo-treated patients (all p<0.0001). Linaclotide significantly improved CSBMs, stool consistency, straining, bloating, SBMs, abdominal pain and abdominal discomfort vs placebo over 12 and 26 wks (p<0.0001). The most common adverse event (AE) was diarrhoea, causing discontinuation in 4.0% of linaclotide-treated and 0.2% of placebo-treated patients.

Conclusion Treatment of IBS-C with linaclotide produced statistically significant improvements in abdominal and bowel symptoms at 12 wks and were sustained over 26 wks. Diarrhoea was the most common AE.

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OC-083 OPTIMISING RADIATION BOWEL INJURY THERAPY, THE ORBIT STUDY, A RANDOMISED CONTROLLED TRIAL

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Introduction Chronic gastrointestinal (GI) symptoms after radical pelvic radiotherapy are common. There is no evidence whether medical intervention helps. Most affected patients are never referred to specialists. We developed a comprehensive, peer-reviewed management algorithm for patients with new onset GI symptoms after pelvic radiotherapy. A prospective three arm randomised controlled trial was performed to test two hypotheses: (1) intervention using our algorithm provides benefit at 6 months after randomisation compared to no intervention; (2) outcomes do not differ when patients are managed by nurse or doctor. Other end points include: cost-effectiveness of intervention; effect on non-GI symptoms; outcomes after 12 months.

Methods Consenting people who had completed pelvic radiotherapy >6 months previously with persisting GI symptoms were randomised to see a GI nurse or gastroenterologist, both following our algorithm, or to receive the MacMillan booklet "Pelvic radiotherapy: possible late effects". After 6 months patients in the booklet arm with persisting symptoms could see the gastroenterologist. Patients in the nurse arm, were transferred to the gastroenterologist if they had problems beyond the algorithm's scope. The primary end point was change in the modified Inflammatory Bowel Disease Questionnaire-bowel sub score (IBDQ-B). The trial was designed with 80% power to answer the 1st hypothesis after randomising 196 patients and the 2nd after closing the booklet arm, and randomising 22 more patients to gastroenterologist or nurse.

Results This 1st analysis includes 152 men, 44 women randomised to the three arms and followed for 6 months: booklet (n=68) vs combined treatment arms (66 nurse, 62 gastroenterologist). Median age was similar in both groups (69 years range 29–87); 25 patients had radiotherapy for GI, 30 gynaecological, 141 urological cancer. 18 (9%) withdrew/were withdrawn from the trial; 26 (38%) from the booklet group and 5 (8%) from the nurse arm crossed to the gastroenterologist. Intention to treat analysis showed a non-significant (p=0.056) improvement in IBDQ-B score of 2.8 points (95% CI 6.5 to −0.1). Planned per protocol analysis in 158 patients with complete data sets showed significant (p=0.041) improvement in IBDQ-B between treated and non-treated arms of 3.4 points (95% CIs 6.7 to 0.1).

Conclusion Medical intervention can ameliorate radiotherapy-induced GI symptoms. A 2nd analysis in December 2012 will address the other end points and the 2nd hypothesis. This study was funded by RFPB, NIHR.

Competing interests None declared.

Oesophageal free papers

OC-084 THE CLONAL PROGRESSION OF BARRETT'S OESOPHAGUS TO OESOPHAGEAL ADENOCARCINOMA

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Introduction Barrett's oesophagus (BO) is a common premalignant condition, wherein the normal squamous oesophageal epithelium is replaced by a columnar, intestinal phenotype. It is the predominant risk factor for the development of oesophageal adenocarcinoma (OA)[1] which develops through a metaplasia: dysplasia: carcinoma sequence. Initial studies suggested that BO lesions were genetically clonal.[2] However; our group has shown, by gland micro-dissection, that multiple clones are present within BO and it is therefore a genetically heterotypic disease.[3] Furthermore, Maley *et al*[4] have shown that genetic diversity increases the risk of BO progressing to cancer. Here, we demonstrate that although Barrett's dysplasia is polyclonal, oesophageal adenocarcinomas arising from Barrett's are typically clonal.

Methods DNA was macro-dissected from dysplastic and cancerous regions of endoscopic mucosal resection (EMR) and oesophagectomy specimens and screened for mutations in p16*INK4A*, *TP53* and *K-RAS*. Mutated specimens were serially sectioned; crypts and carcinomas were histologically graded and then micro-dissected using a P.A.L.M. laser capture microscope. DNA was extracted from dissected material and was sequenced for the point mutations identified in the initial screen.

Results Individual glands from 10 specimens (EMRs and oesophagectomies) were laser captured and sequenced for mutations identified as per above. Seven specimens contained *TP53* mutations and the three remaining specimens were mutated for p16*INK4A*.