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 treated patients were responders (p<0.0001). Other end points include: cost-effectiveness of intervention; effect on non-GI symptoms; differences in treatment satisfaction; differences in patients' knowledge and follow-up; differences in patient-reported outcomes; and differences in patient-reported outcomes. 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 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) interventional using our algorithm provides benefit and sustained IBS degree-of-relief response at 12 and 26 wks were seen for both linaclotide-treated and 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.


Oesophageal free papers

OC-084 THE CLONAL PROGRESSION OF BARRETTS 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) which develops through a metaplasia: dysplasia: carcinoma sequence. Initial studies suggested that BO lesions were genetically clonal. However, our group has shown, by gland micro-dissection, that multiple clones are present within BO and it is therefore a genetically heterotypic disease. Furthermore, Malley et al 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 p16INK4A, 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 p16INK4A.