MONDAY, OCTOBER 17, 2016
08:00–10:00
OP001 LAPAROSCOPIC ILEOCecal RESECTION VERSUS INFliximAB TREATMENT OF TERMINAL ILEITIS IN CROHN’S DISEASE: THE LIERC TRIAL
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Introduction: The optimal therapeutic approach to ileocecal Crohn’s disease (CD) remains unclear.

Aims & Methods: The objective of this study was to compare infliximab with laparoscopic ileocolic resection in patients with thiopurine or steroid refractory recurrent CD of the terminal ileum, with respect to quality of life (QoL) and costs. A multicentre randomised controlled, open-label trial was performed in 33 centres in the Netherlands and the UK. Adult patients with CD of the terminal ileum who failed >3 months of thiopurine treatment or steroids without signs of a critical stricture were randomised to infliximab or laparoscopic ileocolic resection. Patients with a prior ileocolic resection, a disease length >40 cm, abdominal abscesses or fluid collections or an American Society of Anaesthesiologists (ASA) score of III or IV were excluded. The primary endpoint was QoL measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) at one year after follow-up. Furthermore, the mean direct costs per individual patient were prospectively documented and analysed according to intention-to-treat until one year after start of treatment. Dutch Trial Registry NTR1150.

Results: Between May 2008 and October 2015, 143 patients were randomised (32.9% male) with a median age of 27.0 years (interquartile range (IQR) 22.0–33.5) after start of infliximab treatment. CD related serious adverse events in the laparoscopic ileocolic resection group and in one patient allocated to infliximab eventually going for surgery. Three patients (4.1%) in the resection group were operated. On April 28th 2016, 96.5% of the patients have completed follow-up. Furthermore, the mean direct costs per individual patient were prospectively documented and analysed according to intention-to-treat until one year after start of treatment. Dutch Trial Registry NTR1150.

Results: Between May 2008 and October 2015, 143 patients were randomised (32.9% male) with a median age of 27.0 years (interquartile range (IQR) 22.0–40.0). Eventually, 65 patients started with infliximab treatment and 70 patients were operated. On April 28th 2016, 96.5% of the patients have completed follow-up. At baseline, the mean difference (MD) in IBDQ score was 4.9 points in favour of the resection group. After correction for the baseline difference, the MD at one year follow-up was 5.8 points in favour of resection (95% confidence interval (CI) –4.7 to 16.3, P = 0.28). The mean direct costs per patient at one year were €14,589 in the infliximab group and €10,318 in the resection group (MD €4,270, 95% CI 01,325 – 07,126, P = 0.005). Infliximab was stopped in 21 patients (30.0%) due to intolerance or insufficient response, 13 of whom underwent an ileocolic resection after a median time of 27.0 weeks (IQR 11.0–33.5) after start of infliximab treatment. CD related severe adverse events in terms of Clavien Dindo IIb complications occurred in three patients (4.1%) in the laparoscopic ileocolic resection group and in one patient allocated to infliximab eventually going for surgery. Three patients (4.1%) in the resection group were started on infliximab within one year. Readmissions (for flares or additional surgery or dilatation) during follow-up were comparable (21.4% of patients in the infliximab versus 17.8% in the resection group).

Conclusion: QoL at one year was not significantly different between the laparoscopic ileocolic resection and infliximab group. Given the lower bound of the 95% CI laparoscopic ileocolic resection can be considered a non-inferior alternative for infliximab treatment at significantly lower cost.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP002 CELL AUTONOMOUS AND NON-CELL AUTONOMOUS RESCUE OF NNOs DEFICIENT MOUSE COLON FOLLOWING IN VIVO ENTERIC NERVOUS SYSTEM STEM CELL TRANSPLANTATION
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Introduction: Enteric neural stem cells (ENSC) have been identified as a possible treatment for enteric neuropathies following successful colonization of recipient gut after transplantation. However, the ability of ENSC to rescue pathophysiologic conditions remains unclear. Loss of neuronal subtypes, including enteric nitric oxide synthase (nNOS), has been implicated in many enteric neuropathies. nNOS-/- mice display slow colonic transit providing a model to test ENSC rescue in a pathological setting.

Aims & Methods: Our aim was to assess the functional integration of transplanted ENSC within recipient nNOS-/- colon. Initially, donor ENSC were obtained from Wnt1-cre;YFP transgenic mice allowing specific fluorescent labeling. FACs selection and fate mapping of cells. YFP+ ENSC were transplanted to nNOS-/- distal colon at post natal day (P14). Subsequently, integration and functionality were assessed using immunolabelling and organ bath physiology after 4 weeks.

Results: After 1 month, YFP+/+nNOS-/- neurons were identified and transcriptional analysis showed specific expression of nNOS in recipient nNOS-/- colon. In NANC (non-adrenergic non-cholinergic) conditions, organ bath physiology revealed significant increases in electrical field stimulation (EFS)-induced relaxation (Area under curve/AUC) in transplanted nNOS-/- (–1.13 ± 0.16 g.s, n = 5) compared with non-transplanted nNOS-/- (–0.31 ± 0.08 g.s, n = 5; P = 0.0016). In transplanted colonic segments, addition of the nitric oxide synthase blocker L-NNAME resulted in significant reductions in the observed EFS-induced relaxation (–0.74 ± 0.17 g.s vs –0.12 ± 0.16 g.s, n = 4; P = 0.0389) demonstrating restoration of nitrergic responses after transplantation. Interestingly, significant increases in basal contractile amplitude were also observed in transplanted nNOS-/- colonic segments (0.30 ± 0.06 g.s, n = 5) compared with both C57BL/6J (0.10 ± 0.01 g.s, n = 5; P = 0.0093) and non-transplanted nNOS-/- mice (0.05 ± 0.008 g.s, n = 5; P = 0.0025). These high-amplitude contractions were unaffected by application of tetrodotoxin, suggesting that transplantation of ENSC can also lead to changes in underlying myogenic motility patterns. To assess the mechanisms involved in these non-cell autonomous phenomena we sought to investigate potential changes in gut morphology. No significant change was observed in the diameter of the distal colon between transplanted nNOS-/- mice (1.04 ± 0.13 mm; n = 3) compared to either non-transplanted nNOS-/- (1.12 ± 0.08 mm; n = 3; P = 0.6099) or sham-operated nNOS-/- (1.05 ± 0.02 mm; n = 3; P = 0.947). In addition, no change in muscle thickness was observed between transplanted nNOS-/- mice (55.33 ± 8.67 µm; n = 3) compared to either non-transplanted nNOS-/- (54.0 ± 8.9 µm; n = 3; P = 0.915) or sham-operated nNOS-/- (54.33 ± 2.96 µm; n = 3; P = 0.018). Ongoing work is targeting other potential processes such as modification of cell types involved in neuromuscular signaling, including intestinal cells of Cajal within the transplanted microenvironment.

Conclusion: Here we demonstrate, for the first time, that transplanted ENSC integrate and effectively restore function of, at the organ level, in a pathological GI disease model potentially via both ENSC-specific and non ENSC-specific processes.

Disclosure of Interest: All authors have declared no conflicts of interest.
Infected necrotizing pancreatitis is a potentially lethal disease that S. Van Brunschot

**RANDOMIZED CONTROLLED TRIAL**

**OP004 ENDOSCOPIC OR SURGICAL STEP-UP APPROACH FOR NECROTIZING PANCREATITIS: A MULTI-CENTER RANDOMIZED CONTROLLED TRIAL**

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**Introduction:** Infected necrotizing pancreatitis is a potentially lethal disease that almost always requires an invasive intervention. In recent years, the surgical step-up approach has become standard of care replacing primary open necrosectomy. A promising minimally invasive alternative is the endoscopic step-up approach. We conducted a multicenter randomized trial comparing an endoscopic and surgical step-up approach in patients with infected necrotizing pancreatitis.

**Aims & Methods:** We aimed to determine how two different diets affect gut microbiota and if bacterial profiles and modelling thereof can be used to predict patient intervention response in a secondary analysis of a previously published randomized control trial (Böhn et al.2015). After a 10 day screening period 61 IBs patients with at least moderately severe IBs symptoms according to IBs Symptom Severity Score (IBs-SSS) followed either a traditional IBs (n=30) or low-FODMAP (n=31) diet for 4 weeks. Faecal samples were collected and IBs-SSS were completed before and after the intervention. Food intake was recorded in 4-days food diaries before (baseline) and during the interventions. Responders were defined as having a reduction of IBs-SSS > 50 after the intervention. Faecal bacterial composition was evaluated by GA-map™ Dysbiosis Test which measures probe signal intensity (PSI) of 54 DNA probes targeting ≥300 bacteria on different taxonomic levels. Bacterial profiles were generated for each patient by multivariate discrimination analysis and graded from 1–5, relative to a healthy reference group. A dysbiosis index (DI) ≤ 2 signify normal microbiota composition, > 2 signify altered microbiota composition (dysbiosis). For all models, both strong and moderate outliers were sequentially excluded.

**Results:** At baseline, 45 patients (25 randomized to traditional diet and 20 to low-FODMAP) had a DI ≥ 3, i.e. dysbiosis; of these, 10 patients following the traditional diet and 9 following the low-FODMAP diet experienced an improvement in DI, while 6 following the traditional diet and 11 on the low-FODMAP diet had worsening of their dysbiosis; the rest experienced no change. In the low-FODMAP group, 9 of the non-diet group responders (n=19) had more severe dysbiosis than responders (n=12) ((3 (3-4) DI; 2 (2-3) DI; p=0.007) at baseline. Although patients on a traditional diet consumed significantly less protein, fat and alcohol, they experienced no change in overall bacterial composition after the intervention. Patients on a low-FODMAP diet ate significantly less carbohydrates, fibre, monosaccharides, fructose and total FODMAP, and had significant reduction in potentially beneficial Bifidobacterium after the intervention (33 (25-44) DI; 0.652; QQ 2 0.541), showing that bacterial profiles differed between responders and non-responders. A OPLS-DA model of the low-FODMAP intervention demonstrated satisfactory model fitting (R2Ycum=0.721; Q2 cum=0.652; QQ 0.005) which was even more prominent in non-responders. An OPLS-DA model of the low-FODMAP intervention demonstrated satisfactory model fitting (R2Ycum=0.721; Q2 cum=0.652; QQ 0.005), showing that bacterial profiles differed between responders and non-responders. An OPLS-DA model of the traditional diet group was inadequate, showing good model fit but poor predictive model (R2Ycum=0.742; QQ 0.004), demonstrating that bacterial profiles did not differ between responders and non-responders.

**Conclusion:** Faecal bacterial profiles predict patient responsiveness to a low-FODMAP dietary intervention. Thus, before considering dietary interventions, bacterial profiles could be determined in order to identify patients who are likely to respond favourably.

**Disclosure of Interest:** L. Öhman: Unrestricted research grants from AstraZeneca; L. Oehman: Unrestricted research grants from AstraZeneca; L. Oehman: Unrestricted research grants from AstraZeneca; L. Oehman: Unrestricted research grants from AstraZeneca; D. Jacobstein, J. L. Gao; J. Johanns; P. Szapary; J. Colombel, S. Targan; S. Ghozli; W. Sandborn; Icahn School of Medicine at Mount Sinai, New York/New York/United States of America/NY

**Conclusion:** The TENSION trial did not show superiority of the endoscopic step-up approach, as compared with a surgical step-up approach, in reducing major complications or death in patients with infected necrotizing pancreatitis. However, the rate of pancreatic fistula, length of hospital stay and costs were significantly reduced in the endoscopic group.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
OP006 VEDOLIZUMAB EXPOSURE CORRELATES WITH CLINICAL, BIOLOGICAL AND ENDOSCOPIC OUTCOME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab (VDZ) specifically targets the α4β7 integrin on gut-homing lymphocytes and has been approved for the treatment of patients with moderate to severe Crohn’s disease (CD) and ulcerative colitis (UC) (8). We studied the relation between serum VDZ trough concentrations (TC) and clinical, biological and endoscopic outcomes in real-life practice.

Aims & Methods: The first 75 patients (49 CD, 26 UC) who initiated VDZ therapy (300 mg IV administered) in our tertiary referral center were sampled at trough during induction (w2 and w6) and early maintenance (w10, w14 and w22) treatment. Clinical response (clinical symptoms and physician global assessment) was correlated to VDZ TC. All patients with UC received sibutrimidose at baseline and w10 and mucosal healing was defined as a Mayo endoscopic subscore of 0 or 1. Biological response (CRP decrease ≥50% from baseline) and remission (CRP <5 mg/L) were assessed at w6 and w22 in patients with CD. An ELISA for measuring serum VDZ TC was developed in house. TC are shown as median [IQR].

Conclusion: This is the first real-life experience with VDZ that shows substantial variability in exposure to VDZ between patients. A clear exposure-response correlation was observed as early as w2 and w6, with significant impact of higher VDZ TC on meaningful outcomes as biological response, remission and endoscopic healing. Our data support a potentially important role for early therapeutic drug monitoring also with VDZ.


S. Van Assche: Gert Van Assche is not financially supported for research from Abbvie and MSD, lecture fees from Janssen, Takeda, Ferrering, MSD, Abbvie and does consultancy for Abbvie, MSD, and Takeda.

All other authors have declared no conflicts of interest.

OP007 EARLY VEDOLIZUMAB DRUG LEVELS AND INDUCTION SUCCESS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab is an anti-α4β7 monoclonal antibody effective in ulcerative colitis (UC) and Crohn’s disease (CD). Data regarding pharmacokinetics/pharmacodynamics of vedolizumab are still scarce.

Aims & Methods: Aim: To assess whether early vedolizumab trough levels (weeks 2, 6) correlate with response to vedolizumab induction therapy. Methods: A 110 mLISA-based assay was developed for measuring Vedolizumab/Zeta, and employed in prospectively-followed IBD patients receiving vedolizumab induction therapy. Drug levels were assessed for association with clinical remission defined by HBI or SCD at week 6 and those who did not achieve clinical remission by week 6 were also not associated with drug level quartiles at week 6. Similarly, neither week 2 or 6 levels were predictive of clinical remission at week 14 (35.4 vs. 44.8 µg/ml respectively, p = 0.85). Clinical remission rates at week 6 were also not associated with drug level quartiles at week 6. Neither week 6 levels were predictive of clinical remission at week 14 (35.4 vs. 44.8 µg/ml respectively, p = 0.85). Clinical remission rates at week 6 were also not associated with steroid free remission (p = 0.1, p = 0.57) or with CRP normalization (p = 0.26, p = 0.73) at weeks 6 and 14, respectively. Among UC patients separately analyzed, week 2 levels were associated with clinical remission at week 14 (p = 0.04). However, statistical significance for this difference was not retained after Bonferroni correction for multiple testing. Finally, multivariable analysis for clinical remission at week 6 has been performed including baseline albumin level and patient weight. When adjusting for these co-variates, week 6 vedolizumab levels were not associated with clinical remission at week 6 (p = 0.56).

Conclusion: In this real-life cohort of consecutive IBD patients receiving vedolizumab, drug levels during induction were not associated with or predictive of clinical response to induction therapy and were not associated with CRP normalization or steroid-free clinical remission. Future studies are pertinent in order to elucidate the role of therapeutic drug monitoring of vedolizumab during induction and maintenance.

Disclosure of Interest: U. Kopylov: Dr. Kopylov received consultancy fees from Janssen, research support from Janssen and Takeda and lecture fees from Janssen, Takeda, Abbvie and CTS.

Y. Chowers: Prof. Chowers received consulting and lecture fees as well as grant support from Takeda, Abbvie, Janssen, Pfizer, Ferrering and Protalix.

R. Elaiikim: Prof. Elaiikim has received consulting and lecture fees from Takeda.

S. Ben-Horin: Prof. Ben-Horin has received consulting and/or advisory board fees from Janssen, Takeda, Celltrion, Abbvie, Schering-Plough and research support from Celltrion and Abbvie.

All other authors have declared no conflicts of interest.
**OP008 PREDICTORS OF NON-RESPONSE OR LOSS OF RESPONSE TO TUMOUR NECROSIS FACTOR ANTAGONIST THERAPIES IN INFLAMMATORY BOWEL DISEASE**

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Introduction: Tumour necrosis factor antagonist (anti-TNF) therapies are effective at inducing and maintaining disease remission in patients with moderate to severe ulcerative colitis (UC) or Crohn’s disease (CD). However, considerable proportions of patients do not respond to therapy or lose response over time.

Methods: This study uses real-world data to identify predictors of non- or loss of response to anti-TNF therapy. The study recruited UC and CD patients from 6 countries [Canada, France, Germany, Italy, Spain, and the United Kingdom (UK)] aged ≥18 years who initiated anti-TNFs (infliximab/adalimumab, certolizumab during June 2009 to June 2011) or adalimumab from January 2011 to June 2013 (CD). Data were collected on patient demographics, clinical characteristics and healthcare resource use. Patients were classified as having non- or loss of response if they: were hospitalized or required UC/CD surgery whilst on therapy, discontinued due to UC or CD flare, required dose-escalation or augmentation with steroids, or were on immunosuppressants 4 months after therapy initiation, or disease severity became worse after therapy initiation. Multilevel multivariate logistic regression was used to identify predictors of non- or loss of response.

Results: The study included 1195 patients (45% UC, 55% CD; 9.6% Canada, 13% France, 22% Germany, 23% Italy, 19% Spain and 14% UK). Mean age: 40.3 years (SD = 13.7); 51% male. Most patients had a Charlson comorbidity index (CCI) score of 0. The study had 52% females, and 32% of patients had a mean BMI of 24.8 (SD = 7.18) and mean disease duration of 8 years (SD = 8.07). Most patients had a physician global assessment of moderate (45%) at study entry. Mean follow up was 3.4 years (UC) and 4.4 years (CD). Overall, 22% of patients had a primary non-response and 71% were classified as having non- or loss of response to anti-TNF therapy in the maintenance period (4 months after initiating anti-TNF) over a mean follow up period of 32 months (SD = 20.4). Significant predictors of non-/loss of response are shown in the Table 1.

Table 1: Predictors of non-response or loss of response among patients with ulcerative colitis and Crohn’s disease

<table>
<thead>
<tr>
<th>Baseline Variables</th>
<th>Odds Ratio (95% Confidence Interval) P-value</th>
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<tbody>
<tr>
<td>Patients with Ulcerative Colitis</td>
<td></td>
</tr>
<tr>
<td>Rectal Bleeding (Reference: None)</td>
<td>1.12 (1.00–1.24) 0.04</td>
</tr>
<tr>
<td>· Passing blood alone</td>
<td>0.24 (0.06–0.97) 0.04</td>
</tr>
<tr>
<td>· Passing blood with stool ≥50% of time</td>
<td>0.35 (0.19–0.91) 0.05</td>
</tr>
<tr>
<td>· Passing blood with stool &lt;50% of time</td>
<td>0.17 (0.05–0.62) 0.02</td>
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<tr>
<td>Endoscopic Findings (Reference: Inactive; Mild)</td>
<td></td>
</tr>
<tr>
<td>· Moderate</td>
<td>3.19 (1.14–8.97) 0.02</td>
</tr>
<tr>
<td>· Severe</td>
<td>4.86 (1.61–14.7) 0.03</td>
</tr>
<tr>
<td>Patients with Crohn’s Disease</td>
<td></td>
</tr>
<tr>
<td>Number of Liquid or Soft Stools per Day</td>
<td></td>
</tr>
<tr>
<td>· 11.2</td>
<td>0.04</td>
</tr>
<tr>
<td>C-reactive Protein (CRP)</td>
<td></td>
</tr>
<tr>
<td>· 1.02 (1.00–1.03) 0.03</td>
<td></td>
</tr>
</tbody>
</table>

Note: Only the significant predictors are included in the table above. Other non-significant variables included age, gender, body mass index, disease duration, Charlson comorbidity index score, and use of corticosteroids or immunomodulators. Both were analyzed as continuous variables. The highest CRP values during the baseline period were used.

Conclusion: In this cohort the majority of patients did not respond or lost response to anti-TNF therapy over time. Predictors for patients with UC included the absence of rectal bleeding and moderate/severe endoscopic scores, and for patients with UC included CRP higher and number of liquid or soft stools per day. These predictors should be considered when evaluating treatment for patients.

**Disclosure of Interest:** L. Peyrin-Biroulet: Consulting fees from Merck, Abbvie, Janssen, Genentech, Mitsubishi, Ferring, Norgine, Tillots, Vifor, Therakos, BMS, UCB-pharma, Hospira, Celgene, Biogen Idec, Biogen Lyca, Biocompare. A. Armuzzi: Grant/support research from: MSD, Consultant for: Abbvie, Cellectirion, Hospira, Janssen, Lilly, MSD, Mundipharma, Pfizer, Sofar, Samsung, Takeda, Speaker bureau with: Abbvie, Astra-Zeneca, Chiesi, Ferring, Hospira, MSD, Mundipharma, Otsuka, Takoda, Zambon J.P. Gisbert: Grant/support research from and is on speaker bureau with MSD, Abbvie, Hospira, Kern Pharma, Takeda, Janssen, Pfizer, Ferring, Faes Pharma, Shire Pharmaceuticals, Dr. Falk Pharma, Chiesi, Casen Flet, Gebro Pharma, Osuka Pharmaceutical, Vifor Pharma. G.C. Nguyen: Consultant for: Janssen, Abbvie, and Takeda. B. Bokemeyer: Grant/support research from: Abbvie, Ferring, UCB, Consultant for: Abbvie, MSD, Shire, Ferring, UCB, Hospira, Takeda, Movets, Speaker bureau with: Abbvie, Ferring, MSD, Merckle, Falk, HLR, UCB. J. Lindsay: Grant/support research from and is on speaker bureau with: MSD, Abbvie, Hospira, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Vifor Pharma, Atlantic Health care, Actavis (Warner Chilcott), and Tillots. M. Smyth: Employee of Takeda Development Centre Europe Ltd, London, United Kingdom. S. Ramagopalan: Employee of Evidera and was commissioned by Takeda Development Centre Europe Ltd. to conduct the study J.M. Khalid: Employee of Takeda Development Centre Europe Ltd, London, United Kingdom.

**OP009 INFLAMMATORY BOWEL DISEASE COURSE AND THERAPEUTIC MANAGEMENT IN REAL LIFE PRACTICE IN THE CURRENT ERA OF ANTI-TNFs: ANALYSIS OF THE FRENCH ADMINISTRATIVE HEALTH DATABASES 2009–2014**

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Introduction: Management of inflammatory bowel disease (IBD) has evolved in the last decade. Clinical trials have shown that the combination of anti-TNFs and thiopurines is more effective than monotherapy with either of these. The impact of these results in real-life practice is unknown. Moreover, the frequency of treatment withdrawal has never been assessed in population-based cohort studies.

Aims & Methods: Our aim was to assess IBD course and therapeutic management including treatment withdrawal, surgery rates and hospital stays in the current era of anti-TNFs. Every patient affiliated to the French national health insurance with a diagnosis of IBD based on listed long-term diseases and/or hospital discharge diagnosis was included from 2009 to 2013, and followed up until 31 December 2014. Cumulative incidence rates were used to estimate the cumulative probabilities of medication use, surgery and hospitalization among prevalent and incident patients. Treatment sequences including treatment withdrawal after introduction of thiopurines, anti-TNFs and combination therapy were assessed for incident patients included between 2009 and 2012.

Results: 195,834 individuals were diagnosed with IBD (Crohn’s disease (CD), 106 436 (31,353 incident patients); ulcerative colitis (UC), 89,398 (27,578 incident patients)). Among incident patients treated with thiopurines or anti-TNFs (17 566 CD and 8035 UC patients), the first treatment was thiopurines, anti-TNFs monotherapy, and combination therapy in 69.1%, 24.8% and 6.1% of CD patients and 79.5%, 17.7% and 4.1% of UC patients, respectively. Subsequently, 36.8% and 20% of CD patients were exposed to anti-TNFs monotherapy and combination therapy, respectively, 5 years after diagnosis. More than 25% of CD and UC incident patients included between 2009 and 2012 withdrew thiopurines or anti-TNFs, during more than three months after a first treatment course. Drug withdrawal was related to hospitalization or surgical procedures in less than 30% of these patients. Nearly 50% of CD patients and 40% of UC patients went back to their initial treatment after withdrawal. Around 5% of CD and UC patients are 4% of UC patients stopped all IBD therapy during follow-up. Five years after diagnosis, the cumulative risks of first intestinal resection in CD, and colectomy in UC were 12.8% and 3.5%, respectively.

Conclusion: The step-up approach remains the dominant strategy in IBD, 5-year exposure to anti-TNFs is high and surgery rates are low. Treatment withdrawal in IBD is more common than expected. This study emphasizes the growing need of studying de-escalation strategy in IBD.

Disclosure of Interest: F. Carbonnel: Franck Carbonnel had consulting fees for Genentech, Otsuka, Vifor, and—in the past—for Hospira. All other authors have declared no conflicts of interest.
The identification of children at risk for failure to reach sustained remission despite exposure to anti-TNF remains challenging in Crohn’s disease between drug switching and dose or interval adjustments. When stratified by follow-up in the group failing sustained remission. There were no differences between age, was defined as inactive disease for score at diagnosis and yearly thereafter as inactive, mild and moderate-to-severe paediatric CD) were analysed after 5 yrs follow-up. Disease severity was of paediatric CD) in both groups and mild disease at diagnosis (45% vs. 16%; p = .03) more frequent in the group failing sustained remission. There were no differences between age, gender, WBC or CRP at diagnosis and treatment between both groups. Percentages of infliximab and adalimumab use were similar in both groups, including drug switching and dose or interval adjustments. When stratified by follow-up clinic, infliximab in paediatric follow-up was less frequently associated with failure to reach sustained remission compared to sustained remission.

Univariate analyses of the type of follow-up clinic and anti-TNF treatment between patients with or without sustained remission (more than one anti-TNF possible).

<table>
<thead>
<tr>
<th>Variable, number (%)</th>
<th>No sustained remission (n = 11)</th>
<th>Sustained remission (n = 55)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediatric follow-up and infliximab</td>
<td>3 (27)</td>
<td>37 (67)</td>
<td>.01</td>
</tr>
<tr>
<td>Paediatric follow-up and adalimumab</td>
<td>1 (9)</td>
<td>8 (15)</td>
<td>.63</td>
</tr>
<tr>
<td>Adult clinic follow-up and infliximab</td>
<td>6 (55)</td>
<td>14 (25)</td>
<td>.05</td>
</tr>
<tr>
<td>Adult clinic follow-up and adalimumab</td>
<td>2 (18)</td>
<td>4 (7)</td>
<td>.25</td>
</tr>
<tr>
<td>Paediatric follow-up and adjustments</td>
<td>1 (9)</td>
<td>8 (15)</td>
<td>.63</td>
</tr>
<tr>
<td>Adult follow-up and adjustments</td>
<td>1 (9)</td>
<td>3 (11)</td>
<td>.65</td>
</tr>
</tbody>
</table>

Higher average disease severity (2.1 (2.0–2.3) vs. 1.6 (1.3–1.8); p < .001), adult clinic follow-up (73% vs. 27%; p < .01), surgery for CD (1 vs. 0 (0–3); p < .01), receiving anti-TNF therapy for 5 yrs (91% vs. 24%; p < .05) were associated with failure to reach sustained remission. Both colonic disease and adult follow-up (AUC = .66; both p = .04) correlated with average disease severity (no correction for multiple testing). No other correlations were found.

Conclusion: Patient phenotype at diagnosis does not predict failure to reach sustained remission despite anti-TNF exposure. Mild disease may not trigger appropriate treatment and lead to active and complicated disease course. Sustained remission occurred most with infliximab in paediatric follow-up. Information on serum levels is lacking.


Disclosure of Interest: All authors have declared no conflicts of interest.
OP012 THE EFFECT OF CURRENT HELICOBACTER PYLORI INFECTION ON GASTRIC CANCER IN A LARGE POPULATION

Hanil Yu
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3National Cancer Center, Seoul/Korea, Republic of
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Introduction: Although the association between risk of gastric cancer and Helicobacter pylori (H. pylori) in case-control study have evaluated, the effect of current H. pylori infection on the risk of gastric cancer has not been studied in a large general population.

Aims & Methods: Their first Health check-up persons, who underwent comprehensive screening including endoscopy and H. pylori test from 2003 to 2013, were enrolled. Current infection of H. pylori was defined as positive rapid urease test. Negative current infection was defined as negative rapid urease test and absence of previous H. pylori eradication. Adjusted regression analysis was performed and estimated odds ratio (OR) and 95% confidence interval (CI).

Results: Among 35519 persons with 19396 men, 113 gastric cancers and 158 gastric adenomas were detected. In adjusted analysis, age (OR 1.06, 95% CI 1.01–1.08) and current infection of H. pylori (OR 2.39, 95% CI 1.53–3.74) first degree relatives with gastric cancer (OR 2.08, 95% CI 1.30–3.32) and high glucose (OR 1.66, 95% CI 1.04–2.65) increased the risk of gastric cancer, whereas high HDL (≥60 mg/dL) reduced the risk of gastric cancer (OR 0.49, 95% CI 0.22–0.94).

Conclusion: Current infection of H. pylori increased the risk of gastric cancer about 2.4-fold in a large general population.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
08:00–12:00
AN UPDATE ON THE MANAGEMENT OF HEPATOCELLULAR CARCINOMA - ROOM G

OP013 APLN PROMOTES TUMORIGENICITY IN HEPATOCELLULAR CARCINOMA THROUGH ACTIVATING PI3K-AKT PATHWAY AND ITS EXPRESSION IS ASSOCIATED WITH POOR SURVIVAL IN PATIENTS

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Introduction: We have recently identified that Apelin (APLN) was highly expressed in 18 pairs of hepatocellular carcinoma (HCC) tumor tissues compared to adjacent normal liver specimen by transcriptome sequencing. APLN is an endogenous ligand for the G-protein-coupled AJR receptor. In this study, we aim to investigate its function, mechanism of action and clinical implication in HCC.

Aims & Methods: APLN expression was examined in paired human HCC tissues, HCC cell lines, and mouse models of liver cancer. Biological function of APLN was determined using cell viability, colony formation, cell cycle, apoptosis and senescence induction. APLN expression was observed in a normal liver cell line (MIHA) and human normal liver tissue of patients with hepatocellular carcinoma confirmed the expression of APLN in 18 paired hepatocellular carcinoma (HCC) tumor tissues, expressed in eight HCC cell lines (7404, HepG2, Huh6, Huh7, PLC5, SKHEP1, Hep3B, Hep2). APLN was ubiquitously expressed in 18 paired hepatocellular carcinoma (HCC) tumor tissues compared to adjacent non-tumor tissues. APLN was also overexpressed in human HCC tissues as compared with adjacent normal tissues at mRNA level (28 pairs of non-alcoholic steato-hepatitis [NASH]-HCC and 26 pairs of HBV-HCC patients). APLN protein level (9 pairs of NASH-HCC patients). APLN was ubiquitously expressed in eight HCC cell lines (7404, HepG2, HuH6, HuH7, PLC5, SKHEP1 and two NASH-HCC cell lines HJK2-1 and HJK1-10), whilst no or very low expression was observed in a normal liver cell line (MIA) and human normal liver tissues. Ectopic expression of APLN (in HuH7, Miha, HJK1-2 and HJK1-10) induced senescent hepatocytes, preventing malignant transformation and tumor initiation; a process termed ‘senescence surveillance’ (1). However, APLN was also able to promote liver cancer growth in vivo. Moreover, luciferase reporter assay revealed that APLN promotes the PI3K-AKT pathway. Ectopic expression of APLN or exogenous addition of APLN peptide induced the phosphorylation of AKT and glioblastoma multiforme 2 (Gli3) proteins in HCC cells. Promoter luciferase reporter assay revealed that APLN promotes the PI3K-AKT pathway. Ectopic expression of APLN or exogenous addition of APLN peptide induced the phosphorylation of AKT and glioblastoma multiforme 2 (Gli3) proteins in HCC cells. Promoter luciferase reporter assay revealed that APLN promotes the PI3K-AKT pathway.

Conclusion: Current infection of H. pylori increased the risk of gastric cancer about 2.4-fold in a large general population.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
**MONDAY, OCTOBER 17, 2016**

**10:30–12:00**

**IMPROVEMENTS OF ENDOSCOPIC RESECTION TECHNIQUES IN THE COLON**

**R0060 K**

**OP015 COLD FORCEPS AVULSION (CFA) WITH ADJUVANT SNARE TIP SOFT COAGULATION (STSC) IS AN EFFECTIVE AND SAFE STRATEGY FOR THE MANAGEMENT OF NON-LIFTING LARGE LATERALLY SPREADING COLORECTAL LESIONS (NL-LSLs)**

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**Introduction:** Non-lifting (NL) large laterally spreading and colorectal lesions (NL-LSLs) are challenging to resect endoscopically and often necessitate surgery. Conventional endoscopic resection, pre-resection biopsy and sub-lesion carbon particle suspension are common reasons for NL. Conventional endoscopic mucosal resection (EMR) is often ineffective due to extensive submucosal fibrosis. Simple methods for safe and effective endoscopic management of NL-LSL have not been described.

**Aims & Methods:** The study aimed to evaluate the characteristics of NL-LSL and the safety and efficacy of endoscopic treatment by Cold Forceps Avulsion (CFA) followed by thermal ablation of the avulsion site by Snare Tip Soft Coagulation (STSC). Amongst a prospective observational study of patients referred for wide field EMR of LSL > 20 mm, LSLs which could not be completely resected by snare due to NL were labelled NL-LSL. These were divided into previously attempted non-lifting LSLs (PANL-LSL) and naïve, non-lifting LSLs (NNL-LSL). [MB] Such lesions had completion of resection using a standardized approach with CFA and STSC. The NL area was isolated by circumferential snare excision of all adjacent tissue including adenoma and/or normal mucosa to free the lateral margins. This then allowed effective CFA of NL adenoma. Systematic CFA was then performed to remove all visible NL adenoma. The exposed submucosa of the avulsion site and its margins were treated with control thermal ablation using STSC (ERIE effect 4, 80W). Scheduled surveillance colonoscopy was performed at 5 months (SC1) and 18 months (SC2) post the index procedure. The primary outcome was endoscopic and histological evidence of adenoma clearance. The secondary outcome was safety. Statistical analyses were performed to compare standard LSL with NL-LSL.

**Results:** From January 2012 to April 2016, 677 patients (mean age 69 years, 50.6% male) with 780 lesions (median size 35 mm (IQR 25–45 mm), 65.4% proximal colon) were referred for WF-EMR. 33 lesions were excluded due to suspicion for submucosal invasive cancer and the patients referred for surgery. EMR was performed on 83 NL-LSL and 664 standard LSL. 14 lesions were excluded at initial EMR as a two-stage procedure was required for their resection. Key comparisons between NL-LSL and standard LSL are presented in table 1. PANL-LSL (n = 33) were smaller and more likely to be non-granular (62.5 versus 33.9%, p = .003) than standard LSL. NNL (n = 50) were also more likely to be non-granular (46 versus 33.9%, p = .12) and were associated with previous biopsy (32 vs 13.8%, p = .001) and carbon particle suspension injection within 10 mm of the lesion (26 vs 3.8%, p < .001). Neither intra-procedural bleeding nor deep injury were more common in NL-LSL treated with CFA and STSC. The technique was technically successful in all cases. One perforation was recognised secondary to CFA in a previously attempted lesion and was successfully closed with endoscopic clips with no sequelae. Endoscopic recurrence at SC1 was not significantly different for PANL-LSL treated with CFA and STSC than LSLs treated with complete snare excision, whereas NNL-LSL recurred more frequently (16.0 vs 12.2%, p = .578 and 28.2 vs 12.2%, p = .005 respectively).

**Conclusion:** CFA and adjuvant STSC is a safe, effective and surgery-sparing therapy for the majority of NL-LSL. It is easy to use, inexpensive and does not require additional equipment. Early recurrence rates at SC1 are comparable between PANL-LSL and standard LSL. NL-LSL recur more frequently. Non-granular LSLs were over-represented in both groups. They may be more susceptible to developing fibrosis after biopsy and therefore care should be taken to avoid significant tampering with these lesions prior to referral for definitive endoscopic treatment.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Table 1:** lesions where cold forceps avulsion and snare tip soft coagulation (CFA and STSC) was used in the resection of PANL or NNL. p values represent comparison to LSL. Two stage procedures were excluded. SD – standard deviation, IQR – interquartile range, SC1 – surveillance colonoscopy 1, IVC – ileocaecal valve, PANL – previously attempted non lifting lesion, NNL – naïve non lifting lesion.

<table>
<thead>
<tr>
<th>Patient</th>
<th>PANL n = 33</th>
<th>p</th>
<th>NNL n = 50</th>
<th>p</th>
<th>LSL n = 650</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>70.2 (8.6)</td>
<td>.121</td>
<td>73.0 (9.5)</td>
<td>&lt;.001</td>
<td>66.9 (12.1)</td>
</tr>
<tr>
<td>Male, (%)</td>
<td>59.3</td>
<td>.598</td>
<td>29 (58.0)</td>
<td>.266</td>
<td>324 (49.8)</td>
</tr>
<tr>
<td>Lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median size (IQR)</td>
<td>25 (20–30)</td>
<td>&lt; .001</td>
<td>37.5 (25–50)</td>
<td>.424</td>
<td>35 (25–45)</td>
</tr>
<tr>
<td>Morphology (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granular</td>
<td>8 (25.0)</td>
<td>.003</td>
<td>22 (44.0)</td>
<td>.012</td>
<td>323 (52.4)</td>
</tr>
<tr>
<td>Non granular</td>
<td>20 (62.5)</td>
<td></td>
<td>23 (46.0)</td>
<td></td>
<td>209 (33.9)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>4 (12.5)</td>
<td></td>
<td>5 (10.0)</td>
<td></td>
<td>85 (13.8%)</td>
</tr>
<tr>
<td>Location (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>11 (34.4)</td>
<td>.121</td>
<td>6 (13.0)</td>
<td>.091</td>
<td>121 (18.8)</td>
</tr>
<tr>
<td>Splenic to sigmoid</td>
<td>6 (18.8)</td>
<td></td>
<td>11 (23.9)</td>
<td></td>
<td>98 (15.2)</td>
</tr>
<tr>
<td>Transverse</td>
<td>5 (15.6)</td>
<td></td>
<td>14 (30.4)</td>
<td></td>
<td>132 (20.5)</td>
</tr>
<tr>
<td>Ascending and caecum (+ICV)</td>
<td>10 (31.3)</td>
<td></td>
<td>15 (32.6)</td>
<td></td>
<td>294 (45.6)</td>
</tr>
<tr>
<td>Submucosal fibrosis</td>
<td>33 (100)</td>
<td>&lt; .001</td>
<td>50 (100)</td>
<td>&lt;.001</td>
<td>179 (27.6)</td>
</tr>
<tr>
<td>Previous attempt at resection (%)</td>
<td>33 (100)</td>
<td>&lt;.001</td>
<td>0 (0)</td>
<td>.030</td>
<td>56 (8.7)</td>
</tr>
<tr>
<td>Previous biopsy (%)</td>
<td>na</td>
<td></td>
<td>16 (32.0)</td>
<td>.001</td>
<td>90 (13.8)</td>
</tr>
<tr>
<td>SPOT mark within 10 mm of lesion (%)</td>
<td>na</td>
<td></td>
<td>13 (26)</td>
<td>&lt; .001</td>
<td>25 (3.8)</td>
</tr>
<tr>
<td>Histopathology (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional adenoma</td>
<td>25 (92.6)</td>
<td>.324</td>
<td>44 (90.0)</td>
<td>.147</td>
<td>482 (77.5)</td>
</tr>
<tr>
<td>Serrated adenoma</td>
<td>2 (7.4)</td>
<td></td>
<td>4 (10.0)</td>
<td></td>
<td>135 (21.7)</td>
</tr>
<tr>
<td>Cancer</td>
<td>0 (0)</td>
<td></td>
<td>0 (0)</td>
<td></td>
<td>4 (0.6)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0)</td>
<td></td>
<td>0 (0)</td>
<td></td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration, minutes, median (IQR range)</td>
<td>35 (18–45)</td>
<td>.004</td>
<td>25 (15–40)</td>
<td>.003</td>
<td>20 (10–30)</td>
</tr>
<tr>
<td>Intraprocedural bleeding requiring endoscopic control (%)</td>
<td>2 (7.7)</td>
<td>.078</td>
<td>11 (22.4)</td>
<td>.966</td>
<td>144 (22.2)</td>
</tr>
<tr>
<td>Deep injury</td>
<td>6 (18.2)</td>
<td>.181</td>
<td>1 (2.0)</td>
<td>.049</td>
<td>66 (10.7)</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endoscopic Recurrence at SC1 (%)</td>
<td>4 (16.0)</td>
<td>.578</td>
<td>11 (28.2)</td>
<td>.005</td>
<td>59 (12.2)</td>
</tr>
</tbody>
</table>
challenge to endoscopic resection due to the narrow lumen, rich venous/hemor-
Recal polyps extending to the dentate line (RPDL) pose a technical

Lesion characteristics and histology

Table 1: Lesion characteristics and histology

<table>
<thead>
<tr>
<th>Lesion size, median (range), mm</th>
<th>50 (12-150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphology, n (%)</td>
<td>LST – G, 29 (72.5) 2 (5) 2 (5) 7 (17.5) nodular mixed LST – G, 13 (32.5) homogenous LST – NG Is, 30 (75) 6 (15) 3 (7.5) 1 (2.5)</td>
</tr>
<tr>
<td>Scarring, n (%)</td>
<td>13 (32.5)</td>
</tr>
<tr>
<td>Histology, n (%)</td>
<td>Adenoma with LGD Adenoma with HGD Cancer Other – Condyloma acuminatum</td>
</tr>
</tbody>
</table>

Conclusion: This is the largest reported series of KAR for RPDLs. Our data demonstrates that for Western endoscopists, KAR is a very safe and effective technique in the treatment of RPDLs. As KAR is a viable alternative to full ESD, TEMS and TAR, it will play an increasingly significant role in the management of RPDLs.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP018 THERMAL ABLATION OF THE MARGIN OF THE POST ENDOSCOPIC MUCOSAL RESECTION (EMR) MUCOSAL DEFECT STSC AT 80m EFFECT 4, or no additional treatment. SC1 was performed at 5-6 months, with standardized photo documentation and biopsies of the scar.

Results: Over 32 months to January 2015, 768 lesions > 20 mm were referred for EMR at 4 centers (407 were enrolled, 48 were later excluded, 359 were randomized (null arm n = 178, active arm n = 181)). Patient, procedure and lesion characteristics were similar between the two groups. 267 (74.3%) patients have completed SC1. Endoscopic, and histologic recurrences at SC1 were significantly lower in the active arm (8/138 (5.8%) versus 26/129 (20.2%), p < .001, relative risk (RR) = 0.29 (95% CI 0.14-0.61) and 6/104 (5.8%) versus 20/97 (20.6%), p = 0.002, RR = 0.28 (95% CI 0.12-0.67) respectively (Table 1). Endoscopic assessment of the post EMR scar had a sensitivity of 100%, a specificity of 98% and a negative predictive value of 100% for correctly identifying recurrence when compared to histology results. There was no difference in the rate of delayed bleeding between the active and null groups (8/124 (6.5%) versus 9/136 (6.6%), p = .957) and no difference in delayed perforation (0/124 (0%) vs 1/136 (0.7%), p = .341).

Table 1: Endoscopic and histological recurrence in patients randomised to null versus active arm of the SCAR study. Relative risk (RR); Confidence interval (CI)

<table>
<thead>
<tr>
<th>Tumour characteristics</th>
<th>Null arm</th>
<th>Active arm</th>
<th>RR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopic recurrence (95% CI)</td>
<td>26/129 20.2% (14.1-27.9%)</td>
<td>8/138 5.8% (2.9-11.0%)</td>
<td>0.29 (95% CI 0.14-0.61)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Histological recurrence (95% CI)</td>
<td>20/97 20.6% (13.8-29.7%)</td>
<td>6/104 5.8% (2.7-12.0%)</td>
<td>0.28 (95% CI 0.12-0.67)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Conclusion: Thermal ablation of the margin of the post EMR mucosal defect with STSC, results in significantly lower adenoma recurrence rates at first surveillance colonoscopy. Routine implementation of this simple and safe technique may enhance EMR efficacy and reduce surveillance requirements with fewer procedures and extended intervals.

Disclosure of Interest: All authors have declared no conflicts of interest.
In the twin-grasper group, the mean number of hemoclips used per case and total closure time were significantly lower than in the hemoclip group.

Conclusion: The twin-grasper technique seems to reduce the use of hemoclips and to result in more effective and rapid closure than does the conventional technique in large perforations of the sigmoid colon.

References
**Aims & Methods:** We aimed to evaluate the safety and efficacy of hybrid-APC in naïve or refractory GAVE patients. Methods: This is a prospective, longitudinal study of hybrid-APC in naïve or refractory GAVE patients. Results: Of the 14 patients included, 12 (86%) achieved complete response and 2 (14%) partial response. No major complications were observed. Conclusion: Hybrid-APC is safe and effective for the treatment of naïve or refractory GAVE, achieving complete response in most cases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References:**

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Disclosure of Interest: This indicates an important, previously under-estimated macrophage-intestinal inflammation, macrophage-specific loss of PTPN2 promotes metaplasia.

Conclusion: This effect was mediated by increased phos- 
phorylation of the inflammasome adaptor apoptosis associated speck-like protein containing CARD (ASC), a mechanism recently shown to promote inflammasome activation in vivo.

Aims & Methods: In this study, we aimed to address whether loss of PTPN2 in macro- 
phages is an additional mechanism underlying the exacerbation of acute colitis, which this affects colitis severity and susceptibility for colorectal cancer. To specifically delete PTPN2 in macrophages, mice with a floxed PTPN2 gene were crossed with mice expressing Cre-recombinase under the Lysozyme promoter (PTPN2-LysMCre mice). Acute colitis was induced in 10-12 week old female mice by administration of 2% DSS for 7 days, chronic colitis by administration of four cycles of 1.5% DSS for 7 days, followed by 10 days normal drinking water each. For tumour induction, mice were injected with AOM at day 1 and day 10 of each DSS cycle during chronic colitis induction.

Results: PTPN2-deficient macrophages show enhanced levels of cleaved caspase-1 and IL-1β upon in vitro activation of the NOD-like receptor protein 3 (Nlrp3) and absent in melanoma 2 (AIM2) inflammasomes, finally resulting in enhanced secretion of active IL-1β and IL-18. This effect was mediated by increased phosphorylation of the inflammasome adaptor apoptosis associated speck-like protein containing CARD (ASC), a mechanism recently shown to promote inflammasome activation in vivo.

Conclusion: PTPN2 is an important regulator of inflammasome activation, and loss of PTPN2 in macrophages enhances acute colitis. Further, chronic intestinal inflammation, macrophage-specific loss of PTPN2 promotes metaplasia but at the same time protects from tumour formation.

Disclosure of Interest: All authors have declared no conflicts of interest.

Contact E-Mail Address: Marianne.Spalinger@usz.ch

Introduction: Variants in the gene locus encoding protein tyrosine phosphatase 293T-Rex cells induced the activation of the NOD-like receptor protein 3 (Nlrp3) inflammasome.

Results: Using mice colonoscopy. Histology confirmed by an experienced pathologist was successful in all 32 included patients, an algorithm for EUS-tissue acquisition (EUS- 
FNB) can result in a greater chance to reach a diagnosis than a typical EUS-FNA sample. Based on a previous study (2), which reported a 19-gauge flexible needle to be able to sample transduodenal lesions and be diagnos- 

Aims & Methods: To test the validity of this recommendation we performed a prospective multicenter study aimed at evaluating the technical feasibility, pro- 

contact E-mail address: mribas@gmail.com

Disclosure of Interest: This indicates an important, previously under-estimated macrophage-intestinal inflammation, macrophage-specific loss of PTPN2 promotes metaplasia.

Conclusion: This effect was mediated by increased phos- 
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Contact E-Mail Address: mribas@gmail.com

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Comparison of procedure outcomes according to needle size and use of suction

<table>
<thead>
<tr>
<th></th>
<th>22G No Suction (n = 88)</th>
<th>22G Suction (n = 88)</th>
<th>25G No Suction (n = 85)</th>
<th>25G Suction (n = 91)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROSE-Diagnostic adequacy: n (%)</td>
<td>88 (100)</td>
<td>86 (97.7)</td>
<td>85 (100)</td>
<td>91 (100)</td>
<td>0.182</td>
</tr>
<tr>
<td>Total no. of passes for onsite diagnostic adequacy Mean (SD)</td>
<td>1.8 (1.9)</td>
<td>2.8 (2.7)</td>
<td>1.7 (1.1)</td>
<td>2.0 (2.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Specimen bloodiness: n (%)</td>
<td>1 (1-2)</td>
<td>2 (1-3)</td>
<td>1 (1-1)</td>
<td>1 (1-2)</td>
<td>-</td>
</tr>
<tr>
<td>Diagnostic cell block: n (%)</td>
<td>52 (59.1)</td>
<td>32 (36.4)</td>
<td>55 (64.7)</td>
<td>43 (47.3)</td>
<td>0.089</td>
</tr>
<tr>
<td>ROSE-Diagnostic performance: % (95% CI)</td>
<td>98.9 (93.8–100)</td>
<td>92.6 (83.7–97.6)</td>
<td>98.8 (92.2–100)</td>
<td>98.8 (93.2–100)</td>
<td>-</td>
</tr>
<tr>
<td>Specificity</td>
<td>93.3 (68.1–99.9)</td>
<td>95.0 (75.1–99.9)</td>
<td>100 (79.4–100)</td>
<td>90.9 (58.7–99.8)</td>
<td>-</td>
</tr>
<tr>
<td>PPV</td>
<td>98.6 (92.7–100)</td>
<td>98.4 (91.6–100)</td>
<td>100 (94.6–100)</td>
<td>98.8 (93.2–100)</td>
<td>-</td>
</tr>
<tr>
<td>NPV</td>
<td>100 (78.6–100)</td>
<td>79.2 (78.7–92.9)</td>
<td>88.9 (65.3–96.6)</td>
<td>90.9 (58.7–99.8)</td>
<td>-</td>
</tr>
<tr>
<td>Diagnostic cell block: n (%)</td>
<td>71 (80.7)</td>
<td>63 (71.6)</td>
<td>56 (65.9)</td>
<td>37 (40.1)</td>
<td>0.177</td>
</tr>
<tr>
<td>EUS-FNA-Diagnostic performance: % (95% CI)</td>
<td>98.9 (93.8–100)</td>
<td>98.8 (93.8–100)</td>
<td>98.9 (93.8–100)</td>
<td>98.9 (93.8–100)</td>
<td>-</td>
</tr>
<tr>
<td>Specificity</td>
<td>93.3 (68.1–99.9)</td>
<td>95.0 (75.1–99.9)</td>
<td>100 (79.4–100)</td>
<td>90.9 (58.7–99.8)</td>
<td>-</td>
</tr>
<tr>
<td>PPV</td>
<td>98.6 (92.7–100)</td>
<td>98.4 (91.6–100)</td>
<td>100 (94.6–100)</td>
<td>98.8 (93.2–100)</td>
<td>-</td>
</tr>
<tr>
<td>NPV</td>
<td>100 (78.6–100)</td>
<td>79.2 (78.7–92.9)</td>
<td>88.9 (65.3–96.6)</td>
<td>90.9 (58.7–99.8)</td>
<td>-</td>
</tr>
<tr>
<td>Technical failure: n (%)</td>
<td>0 (0%)</td>
<td>5 (5.7)</td>
<td>1 (1.2)</td>
<td>7 (7.7)</td>
<td>0.179</td>
</tr>
<tr>
<td>Adverse events: n (%)</td>
<td>4 (4.5)</td>
<td>3 (3.4)</td>
<td>5 (5.7)</td>
<td>10 (11.0)</td>
<td>-</td>
</tr>
</tbody>
</table>

that the use of the 19-gauge flexible needle for transduodenal FNB cannot be widely suggested and its implementation should receive a local validation, with careful evaluation of both the local technical success rates and diagnostic yields.

Disclosure of Interest: L. Palazzo: Laureno Palazzo has received educational funds from Boston Scientific Corp.

A. Larghi: Alberto Larghi is a consultant for Boston Scientific Corp.

All other authors have declared no conflicts of interest.

References

Aim & Methods: We aimed to compare the 22 and 25G needles and evaluate the role of suction in EUS-FNA of pancreatic masses. Methods: Consecutive patients with solid pancreatic masses were randomized to 1 of 4 cohorts: 22G needle with suction, 22G needle without suction, 25G needle with suction and 25G needle without suction. After two dedicated passess at 8 gauages, diagnostic accuracy of the flexible 19-gauge EUS-FNA needle. Gastrointest Endosc 2012; 76: 336-43.

Aim: The primary endpoint was the diagnostic accuracy of ROSE by final pathology interpreted by a second independent pathologist. Diagnostic accuracy of ROSE was confirmed by final pathology interpreted by a second independent pathologist.

Final diagnosis was established by surgical histology or patient follow-up at 12 months. Main outcome measures were to compare diagnostic accuracy and adequacy of ROSE, number of passes to establish onsite diagnostic adequacy, specimen bloodiness, diagnostic accuracy of cell block and operating characteristics between cohorts. To detect a 1.5% difference in diagnostic accuracy and cell block yield between the type of needles and use of suction at 80% power and type I error of 0.05, the total sample size was estimated at 352 patients.

Results: The median age of 352 patients was 69 years, 54.3% male, median size of mass was 3cm with vascular invasion in 55.4% and FNA passes were transduodenal in 68.5%. The final diagnosis was adenocarcinoma or other malignancy in 290 (82.4%) and benign or chronic pancreatitis in 62 (17.6%) patients. Interim analysis pending completion of 12-month follow-up is shown in the Table. Conclusion: While there was no overall difference in operating characteristics between the 22 and 25G needles, the use of suction must be avoided in centers using ROSE as it increases specimen bloodiness and number of passes needed to achieve diagnostic adequacy, particularly with 22G needles.

Disclosure of Interest: R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc.

S. Varadarajulu: Consultant for Boston Scientific Corporation and Olympus America Inc.

All other authors have declared no conflicts of interest.

OP027 EUS-GUIDED BILIARY DRAINAGE VERSUS PERCUTANEOUS BILIARY DRAINAGE: RESULTS OF A MULTICENTER RANDOMIZED PHASE II STUDY

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Introduction: For 10 years, EUS-guided biliary drainage has been an option as EUS guided choledocho-ductenochoemomy or hepatico-gastrostomy. Two small randomized studies showed no difference between EUS guided BD vs Percutaneous drainage. The aim of this work was to evaluate in a multicenter randomized study the percutaneous biliary drainage (PBD) vs EUS-guided biliary drainage (EBD) in patients with an obstructive jaundice when ERCP failed or impossible due to duodenal involvement or previous Surgery. Aims & Methods: Inclusion criteria were: benign or malignant obstructive jaundice with failure of ERCP. Exclusion criteria were: ascites, blood coagulation defects with failure of EUS-guided drainage. The main endpoint was the decrease of the morbidity rate in the EGD arm (A=30%), B= 5% (Amarettog) trandispillary stenting, choledoco-duodenostomy, hepatico-gastrostomy). The main goal was to evaluate the specific morbidity and mortality during the 30 days following the biliary drainage in each arm. To prove a decrease of 50% of the morbidity rate in the EGD arm (A=30%), B= 15%, 55 patients should be included in the EGD arm (B) as a Simon plan in 2 steps with an intermediate analysis to exclude severe adverse events in the EGD arm.

Intermediate analysis was performed after inclusion of 47 patients showed and significantly higher morbidity rate in the PTB arm. Then, PTB arm was stopped and inclusions were made only in the EGD arm.

Result: Sixty-five patients from 4 centers were screened between 2011 to 2015. Eight patients were excluded (ascites, EUS-TBD finally feasible). Fifty-six patients were randomized (Arm A = 21/Arm B = 35). The 2 groups were similar except the sex ratio (Female: Arm A = n = 11; Arm B, n = 7; p = 0.012). The biliary access was successful in 100% in the Arm A and in 94% in the Arm B. However, technical success was respectively 17/21 (85%) in the Arm A and 33/36 (94%) in the Arm B. No difference was showed regarding the decrease of the biliusum level after the drainage in the two arms. Median hospitalization duration was shorter in the Arm B (6 days range 3–30 days) than the Arm A (12 days range 2–32 days). Ten patients died 30 days following the biliary drainage, 7 deaths were reliable to biliary drainage process (Arm A = 3, Arm B = 4). One specific complication occurred in twelve patients (62%) in the Arm A as 7 (31%) in the Arm B p = 0.0276: Bleding (A=5[24%], B=3[20%]; ns), Cholangitis (A=3 [14%], B = 1[3%]), Sep;is not related to cholangitis (A = 7 [35%], B = 5 [25%]), Peritonitis (A = [5%], B=1[3%]; ns), external biliary fistula (A = [5%], B = [5%]).
Conclusion: This randomized prospective study showed similar high technical and clinical success rates in PTB and EUS-guided biliary approach. Specific complication rate was higher in the PTB arm than in the EUS-guided biliary drainage. EUS-guided biliary drainage should be the first therapeutic approach after failure of ERCP, in selected patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP028 EUS-GUIDED GASTROENTEROSTOMY IS COMPARABLE TO ENTERAL STENTING IN TERMS OF TECHNICAL FEASIBILITY AND SUCCESS WITH LOWER RATES OF LUMEN OBLITERATION: AN INTERNATIONAL MULTICENTER COMPARATIVE STUDY

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Introduction: Endoscopic enteral stenting (ES) in malignant gastric outlet obstruction (GOO) is limited by high rates of stent obstruction. EUS-guided gastroenterostomy (EUS-GE) is a novel procedure that potentially offers sustan-tiability and tumor ingrowth/overgrowth.

Aims & Methods: The aim of this study is to compare EUS-GE with ES in terms of 1) need for re-intervention, 2) technical success (proper stent positioning as de-signed) and endoscopic necrosis (technical need to trephine oral intake without vomiting), and 3) procedure-related adverse events (AEs).

This is a multicenter retrospective study of all consecutive patients who underwent either EUS-GE at 4 centers between 2013 and 2015 or ES at one center between 2008 and 2013.

Results: A total of 82 patients (mean age 66.5 years ± 13.0 and 40.2% female) were identified: 30 in EUS-GE and 52 in ES. Technical and clinical success were not significantly different: EUS-GE vs. ES (p = 0.02) and 83.3% vs. 69.2% ES (p = 0.2) respectively. Need for re-intervention, however, was significantly lower in EUS-GE 3.3% vs. 46.2% ES (p < 0.001). Post-procedure medical success failure was comparable at 13.3 days ± 6.6 for EUS-GE vs. 9.5 days ± 8.3 for ES (p = 0.3). Rates and severity of AEs (as per the ASGE lexicon) were also similar occurring in 16.7% EUS-GE vs. 11.5% ES (p = 0.5). On multivariable analysis, EUS-GE was independently associated with fewer needs for re-intervention (OR 0.03, p < 0.002).

Conclusion: EUS-GE may be ideal for malignant GOO with comparable effectiveness and safety to ES while being associated with fewer requirements for re-intervention.

Disclosure of Interest: M. Khashab: Consultant for Boston Scientific. All other authors have declared no conflicts of interest.

OP029 DEDICATED BI-FLANGED METAL STENT WITH ENDOSCOPIC “STEP-UP APPROACH” REDUCES THE NEED FOR DIRECT NECTORECTOMY IN WON - LARGE EXPERIENCE FROM A SINGLE TERTIARY CARE CENTRE

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Introduction: EUS-guided trans-mural drainage using plastic stents may be inadequate for pancreatic fluid collections (PFC) having solid debris, i.e. “Walled Off Necrosis (WON)”. Recent publications have reported variable outcome using covered metal stents for PFC drainage, using either conventional or dedicated metal stents. Few reports on dedicated metal stent for EUS-guided drainage of only WON. Treatment strategy using a “step-up approach” by endoscopic methods has not been systematically addressed.

Aims & Methods: To evaluate the efficacy of a dedicated covered bi-flanged metal stent (BFMS) using a “step-up approach” in drainage of symptomatic WON. Consecutive patients with symptomatic WON undergoing EUS-guided drainage using BFMS were included from January 2013 to December 2015. Patients were reassessed at 4 weeks for symptom improvement and reduction in size of collection. The endoscopic interventions were approached in a step-up manner to manage patients who did not have expected clinical improvement after index drainage of WON with BFMS. Declogging of blocked lumen of BFMS was the first step. Second step involved a nasc granularity (NTC) placement through BFMS followed by intermittent irrigation with saline and hydrogen peroxide. Third step involved direct endoscopic necrosectomy (DEN), which was performed through BFMS in patients with persistent symptomatic WON. Patients were reassessed between 4 to 8 weeks and BFMS were removed after documenting radiological resolution of collection. The main outcome measures included technical success, clinical success, adverse events and the need for various endoscopic reinterventions, using step-up approach.

Disclosure of Interest: All authors have declared no conflicts of interest.

Results: A total of 205 patients (mean age 34.8 ± 12.5 years, 181 males) underwent EUS-guided drainage with BFMS. Technical success was achieved in 203 patients (99%). Peri-procedure adverse events occurred in 8 (3.9%) patients (bleeding in 6 and perforation in 2). WON resolved with BFMS in 158 (77%) patients. Endoscopic re-intervention was required in 49 (23.9%) patients, for persistent or new onset symptoms, was approached in step-up manner. At first, declogging of BFMS alone succeeded in 10 out of 21. Second step of nacao- cystic placement through BFMS followed by irrigation with saline and hydrogen peroxide improved 16 out of 29. At final step, DEN improved outcome in 19 out of 23. BFMS migrated in 5 (2.9%) patients (2 internal, 3 external). Four patients failed to achieve clinical success, requiring surgery (n = 2) or additional percuta-neous drainage (n = 2). Overall, clinical success was achieved in 198 (96.5%) patients.

Conclusion: EUS-guided drainage with BFMS is safe and effective in WON. BFMS substantially reduces the requirement of DEN. Success rate incrementally improves with endoscopic step-up approach.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP030 CLINICAL OUTCOME AFTER BILIARY DRAINAGE FOR METASTATIC COLORECTAL CANCER: SURVIVAL ANALYSIS


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Introduction: Biliary obstruction secondary to colorectal cancer liver metastases is associated with a poor prognosis with the drainage being the cornerstone of chemotherapy care or re. However, little information is known about the benefits of such endoscopic and radiological interventions, as well as the impact of chemotherapy achievement. The aim of this study was to determine survival after biliary drainage and look for prognostic factors.

Aims & Methods: This retrospective study analyzed patients from two expert French centers between 2005 and 2014. Patients were included after first biliary endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC) drainage for biliary obstruction secondary to liver metastases of colorectal cancer occurring during chemotherapy. Demographical, biochemical, and outcome data were registered. We used Kaplan-Meier analysis to assess survival after first biliary stenting and cox models for univariate and multivariate analysis.

Results: The final analysis included 69 patients. Sixty patients underwent ERCP, 2 underwent PTC drainage, and 7 underwent both techniques. Overall median survival was 115 days (5-1876). In univariate analysis, a previous liver surgery, a technical and a functional success of drainage and restated chemotherapy were significantly associated with an improved survival. Chemotherapy was restarted after a median of 27 days. When drainage was efficient survival improved from 33 days to 262 days (p = 0.001). In multivariate analysis, protective factors for survival included a previous hepatectomy (hazard ratio (HR) 0.41, 95% CI [0.22-0.75], p = 0.004), functional success drainage (HR 0.29, 95% CI [0.15-0.56], p = 0.0002), Predictive factors for death included increased lines of chemotherapy (HR 1.66, 95% CI [1.36-2.06], p < 0.001), and fever before drainage (HR 2.97, 95% CI [1.39-6.36], p = 0.005).

Conclusion: This is the first study concerning benefits of biliary drainage during the course of chemotherapy of colorectal cancer with malignant biliary obstruction. A successful biliary drainage leads to improved survival and allows achievement of chemotherapy for 50% of patients.

Disclosure of Interest: All authors have declared no conflicts of interest.
Bile calprotectin in relation to variables of PSC activity

S-AST, U/L 231.0 [59.1–286.8] 1100 5.3 [0.9–22.9] 1

S-CA19–9 kU/l dysplasia.

Individual risk stratification for PSC patients for disease progression and bile duct inflammation based on BC-neutrophils (BC-Neurophil 1–2 vs 0, OR 8.2 0.0001 or UC [7.6%, p < 0.001]. Distribution of the two types of PABs was equal and one-third of the positive cases showed double positivity. Anti-GP2 antibody positivity was exclusively IgA type, while anti-CUZD1 antibodies were of both IgA and IgG isotypes. No difference was found in the frequency of PABs according to the baseline disease characteristics. Positivity for the IgA subtype of anti-GP2, but not for the classical serologic markers, predicted a faster progression of the disease. In Kaplan-Meier analysis, anti-GP2 IgA by ELISA). A previously reported inflammatory test [IFT] system with GP2 and CUZD1 expressing transfected HEK 293 cells [anti-rPAg2 and rPAg1 IgA/IgG]. Classical serologic markers of IBD [anti-OMP PlusTM IgA/IgG].

Conclusion: S-ALP, U/l 105 1.2 [0.9–2.6] 0.0001

S-AgG, g/l 15 2.8 [0.2–27.0] 0.008

S-AgG, g/l 15 2.8 [0.2–27.0] 0.008

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Aims & Methods: We aimed to evaluate the grade of bile duct inflammation as a risk factor for dysplasia and cholangiocarcinoma in PSC patients. In total, 210 patients with confirmed PSC referred for ERC for disease surveillance were included. Female patients (59 males), mean comulination of the common bile duct in the bile sample was aspirated using balloon catheter and immediately in liquid nitrogen (<190°C) and then stored in −20°C. Brush cytology (BC) was collected both from extra- and intrahepatic bile ducts for Papanicolaou staining for grading dysplasia and inflammation. Neutrophilic inflammation in BC was evaluated semiquantitatively (0 = neutrophils/epithelial cells < 0.05, 1 = neutrophils/epithelial cells 0.05–0.4, 2 = neutrophils/epithelial cells > 0.4). Bile concentrations of calprotectin were analyzed using ELISA method. Liver function tests were taken at the time of ERC. ERC findings were scored according to modified Amsterdam score, [Helsinki score] (9). Results: Bile duct inflammation assessed by biliary calprotectin correlated significantly with neutrophils in BC, with S-CA19–9, S-ALP and S-AST levels and interestingly with S-IgG. Patients with dysplasia or CCA had markedly elevated B-calprotectin, as compared to those without dysplasia (34.7 vs 4.0 mg/l, respectively), see table. The risk of dysplasia was associated with advanced bile duct dysplasia (8). Chronic inflammation has been regarded as risk factor for dysplasia and malignancy. Because CCA is generally a contraindication for liver transplantation (LT) and the prognosis of CCA is dismal, it would be feasible to screen the dysplastic changes of the biliary epithelium to treat patients with LT before development of advanced malignancy, detected based on imaging methods or symptoms.

Aims & Methods: To evaluate the grade of bile duct inflammation as a risk factor for dysplasia and cholangiocarcinoma in PSC patients. In total, 210 patients with confirmed PSC referred for ERC for disease surveillance were included. Female patients (59 males), mean comulination of the common bile duct in the bile sample was aspirated using balloon catheter and immediately in liquid nitrogen (<190°C) and then stored in −20°C. Brush cytology (BC) was collected both from extra- and intrahepatic bile ducts for Papanicolaou staining for grading dysplasia and inflammation. Neutrophilic inflammation in BC was evaluated semiquantitatively (0 = neutrophils/epithelial cells < 0.05, 1 = neutrophils/epithelial cells 0.05–0.4, 2 = neutrophils/epithelial cells > 0.4). Bile concentrations of calprotectin were analyzed using ELISA method. Liver function tests were taken at the time of ERC. ERC findings were scored according to modified Amsterdam score, [Helsinki score] (9). Results: Bile duct inflammation assessed by biliary calprotectin correlated significantly with neutrophils in BC, with S-CA19–9, S-ALP and S-AST levels and interestingly with S-IgG. Patients with dysplasia or CCA had markedly elevated B-calprotectin, as compared to those without dysplasia (34.7 vs 4.0 mg/l, respectively), see table. The risk of dysplasia was associated with advanced bile duct dysplasia (8). Chronic inflammation has been regarded as risk factor for dysplasia and malignancy. Because CCA is generally a contraindication for liver transplantation (LT) and the prognosis of CCA is dismal, it would be feasible to screen the dysplastic changes of the biliary epithelium to treat patients with LT before development of advanced malignancy, detected based on imaging methods or symptoms.
**OP035 GUT BARRIER FAILURE BIOMARKERS ARE ASSOCIATED WITH PREDICTIVE OUTCOME IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS**

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**Introduction:** Gut liver interaction is a prominent feature of primary sclerosing cholangitis (PSC), however the effect of this cross-talk on the disease course has not been fully elucidated. A panel of serological markers that reflect either mucosal or gut barrier dysfunction were assessor for a cohort of patients with PSC. Association of these markers with disease specific characteristics and the long-term disease course was evaluated.

**Aim & Methods:** Sera of 69 PSC patients (median age [range]: 32 [5–79] years, concomitant IBD: 67% and cirrhosis: 20%) were assayed for intestinal fatty acid-binding protein (I-FABP) and various immunoglobulin A (IgA) molecules (IgA1, IgA2 and secretory[s]IgA, anti-F-actin[AAA IgA] and anti-gliadin[AGA IgA and IgG], respectively. Frequencies of AAA IgA and AGA IgA and AGA IgG, respectively. Frequencies of AAA IgA (p < 0.01, for both) and AGA IgG (p < 0.01, for both) not but AGA IgA were significantly higher compared to either the HCONT or the UC group respectively, which were in line with the previous reports.

**Results:** In PSC, median I-FABP level was similar to that in HCONT (216 vs. 244 pg/mL) but higher than in UC (176 pg/mL, p < 0.05). sIgA level (95.7 pg/mL) was two- and three-fold higher compared to either the HCONT or the UC group respectively, which were in line with the previous reports.

**Conclusion:** In our small-scale study, gut-related IgA type antibodies identified these markers further enhanced their predictive potential (HR[95%CI]: 2.57–20.86 for AAA IgA and 5.07–21.54 for AGA IgA). Combined these markers further enhanced their predicative potential (HR[95%CI]: 11.30–84.44 for IgA positivity). Those patients progressed with severe disease, further highlighting the importance of the gut-liver interaction in PSC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP036 SELECTIVE TARGETING OF FXRA ISOFORMS BY NOVEL BILE ACID DERIVATIVES IS ASSOCIATED WITH INHIBITION OF LIPTOXICITY IN LIVER CELLS**

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6Faculty Of Pharmacy, University Of Lisboa, Lisboa/Portugal
7Research Institute of Medicines, Faculdade de Farmácia, Universidade de Lisboa, Lisboa/Portugal
8Faculty Of Pharmacy, University Of Lisboa, Lisboa/Portugal
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**Introduction:** Farnesoid X receptor (FXR), a bile acid (BA)-activated nuclear receptor, plays a critical role in maintaining lipid, glucose and BA homeostasis. Farnesoid X receptor (FXR), a bile acid (BA)-activated nuclear receptor, plays a critical role in maintaining lipid, glucose and BA homeostasis.

**Aim & Methods:** Our aim was to screen potential BA-derived FXR agonists for their ability to selectively activate different FXR isoforms and protect liver cells against free fatty acid (FFA)-induced steatosis and cytotoxicity. Nineteen novel BA derivatives, synthesized based on the cholic (CA), deoxycholic (DCA), chenodeoxycholic (CDCA) and ursodeoxycholic (UDCA) acid scaffolds were incubated with HepG2 cells for 24 h. Inhibition of cell death, cell death and hepatocellular injury, respectively.

**Results:** Ten FXR derivatives, synthesized based on the cholic (CA), deoxycholic (DCA), chenodeoxycholic (CDCA) and ursodeoxycholic (UDCA) acid scaffolds were incubated with HepG2 cells for 24 h. Inhibition of cell death, cell death and hepatocellular injury, respectively.

**Conclusion:** These derivatives were among the stronger inducers of SHP, VLDLR and PPAR-β/δ receptors, respectively.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP037 COMPARISONS OF IMAGING AND BILIARY BIOPSY BETWEEN IGG4-RELATED SCLEROSING CHOLANGITIS AND EXTRAHEPATIC CHOLANGIOCARCINOMA**

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**Introduction:** IgG4-related sclerosing cholangitis (IgG4-SC) often presents similar medical images to extrahepatic cholangiocarcinoma (ECC). However, the differentiation is crucial for further treatment.

**Aim & Methods:** Among the characteristics of medical images of IgG4-SC and ECC, we retrospectively analyzed images of multi-detector computed tomography (MDCT) and intraductal ultrasonography (IDUS). Biopsy-based diagnoses from both methods were also compared. From April 2013 to March 2018, 48 IgG4-SC patients and 50 ECC patients who underwent an initial ERCP at our institution were analyzed. Diagnosis of IgG4-SC was made based on the Japanese diagnostic criteria (2012), and autoimmune pancreatitis (AIP) based on the Japan Consensus Diagnostic Criteria (JCCD). The pathological criteria consist of four items: (1) marked lymphocytic and plasma cell infiltration and fibrosis, (2) infiltration of IgG4-positive plasma cells: > 10 IgG4-positive plasma cell/HPE, (3) storiform fibrosis, and (4) obliterative phlebitis. In all cases of ECC, pathological evidence of carcinoma was obtained from biliary biopsy, cytology or surgical material. On MDCT, bile duct when the enhanced, biliary wall thickness was recognized at more than 10 mm upstream of the stenosis.

**Results:** Autoimmune pancreatitis (AIP) was accompanied in 88% (42/48) of IgG4-SC patients at the initial diagnosis. On MDCT imaging, the long thickened bile ducts rate was higher in IgG4-SC cases (76±2 mm in SC, 15±4 mm in ECC, respectively). By IDUS, a continuous circular-symmetric wall thickness more than 10 mm upstream from stenosis was recognized in 84% of IgG4-SC cases and in 36% of ECC cases. In IgG4-SC cases, biliary biopsy revealed one or more positive pathological diagnostic criteria in only 13% of cases. In ECC cases, the sensitivity of biopsy was 92%, and brush cytology increased this by 6%. Among three out of six IgG4-SC patients without AIP, pancreaticoduodenectomy was performed without positive conclusion. The remaining three underwent steroid trial after negative work up for malignancy.

**Conclusion:** A longitudinal biliary wall-thickness, upstream of the stenosis, was characteristic for imaging of IgG4-SC. Endobiliary forceps biopsy is effective for discriminating IgG4-SC from ECC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References:**


OP036 THE IMPACT OF PNPLA3 (rs738409 C>G) POLYMORPHISM ON PRIMARY SCLEROSING CHOLANGITIS (PSC)

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Introduction: PNPLA3 (pataxin-like phospholipase domain containing 3) encodes carbohydrate-regulated lipogenic and/or lipolytic enzymes in liver. The mutation of isoleucine to methionine at position 148 (I148M) causes a loss of function effect leading to increased triglyceride synthesis and accumulation in liver (1). The PNPLA3 rs738409 C>G on liver damage has a strong environmental interaction and is usually associated with concomitant liver insult. PSC is a chronic inflammatory disease of bile duct epithelium leading to strictures and may secondarily cause liver cirrhosis. PSC is also associated with inflammatory bowel disease and markedly increased risk of cholangiocarcinoma (3,4). PLPN3 variant has been associated with elevations of liver enzymes in IBD (5) and in increased risk of bile duct stenosis in male PSC patients (6). Survival free of liver transplantation is reduced in male PSC patients with dominant striations in carriers of PNPLA3 I148M variant (5).

Aims & Methods: To evaluate the allele dose effect of PNPLA3 variant on the clinical manifestations, disease severity, progression and prognosis of PSC in a large patient population from single center.

Results: Of the 563 patients 334 (59.3%) had the wild type (CC), 197 (35%) were with CC, in 6 (3.1%) of CG and in none of GG, (p for linearity 0.42; adjusted for sex, age and IBD). 40 patients underwent liver transplantation during 5 years mean follow up: 2.5% (95% CI: 1.2 to 5.1) in CC, 3.1% (95% CI: 1.3 to 7.3) in CG and 7.1% (95% CI: 1.8 to 24.4) in GG, (p for linearity 0.12; adjusted for sex, age and IBD).

PNPLA3 rs738409 in PSC

Variable, mean(SD)  

<table>
<thead>
<tr>
<th></th>
<th>n=334</th>
<th>n=197</th>
<th>n=32</th>
<th>p for linearity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n (%)</td>
<td>193(58)</td>
<td>124(63)</td>
<td>17(53)</td>
<td>0.75</td>
</tr>
<tr>
<td>Age at diagnosis of PSC, y</td>
<td>38(14)</td>
<td>36(13)</td>
<td>35(13)</td>
<td>0.10</td>
</tr>
<tr>
<td>Weight, kg, males</td>
<td>82(14)</td>
<td>80(15)</td>
<td>81(14)</td>
<td>0.37</td>
</tr>
<tr>
<td>Weight, kg, females</td>
<td>69(7)</td>
<td>70(17)</td>
<td>71(13)</td>
<td>0.62</td>
</tr>
<tr>
<td>IBD, n (%)</td>
<td>263(71)</td>
<td>152(77)</td>
<td>9(65)</td>
<td>0.49</td>
</tr>
<tr>
<td>Age at diagnosis of PSC, y</td>
<td>26(11)</td>
<td>26(11)</td>
<td>29(12)</td>
<td>0.74</td>
</tr>
<tr>
<td>ERC-score (0–16)</td>
<td>5.8(3.5)</td>
<td>5.3(3.3)</td>
<td>5.7(3.7)</td>
<td>0.88</td>
</tr>
<tr>
<td>Dominant strictures, n (%)</td>
<td>128(38)</td>
<td>61(31)</td>
<td>9(28)</td>
<td>0.061</td>
</tr>
<tr>
<td>Progression of ERC score/month*</td>
<td>0.014</td>
<td>0.002</td>
<td>0.004</td>
<td>0.44</td>
</tr>
<tr>
<td>Advanced fibrosis F3/4, (%)*</td>
<td>8.8</td>
<td>15.1</td>
<td>12.5</td>
<td>0.25</td>
</tr>
<tr>
<td>S-ALP, U/l &lt; 105</td>
<td>183(148)</td>
<td>194(170)</td>
<td>182(135)</td>
<td>0.60</td>
</tr>
<tr>
<td>S-GT, U/l &lt; 60</td>
<td>191(249)</td>
<td>236(289)</td>
<td>189(154)</td>
<td>0.94</td>
</tr>
<tr>
<td>S-AST, U/l &lt; 45</td>
<td>74(125)</td>
<td>78(96)</td>
<td>63(50)</td>
<td>0.35</td>
</tr>
<tr>
<td>S-AST, U/l &lt; 45</td>
<td>55(73)</td>
<td>54(63)</td>
<td>59(41)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

*Adjusted for sex, age and IBD Cholangiocarcinoma was diagnosed in 12 (3.6%) patients with CC in 6 (3.1%) of CG an in none of GG, (p for linearity=0.42; adjusted for sex, age and IBD). 40 patients underwent liver transplantation during 5 years mean follow up: 2.5% (95% CI: 1.2 to 5.1) in CC, 3.1% (95% CI: 1.3 to 7.3) in CG and 7.1% (95% CI: 1.8 to 24.4) in GG, (p for linearity=0.12; adjusted for sex, age and IBD).

Conclusion: The PNPLA3 I148M variant did not have any significant impact on clinical manifestation, disease progression, development of dominant strictures, on risk of cholangiocarcinoma or liver transplantation in PSC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
OP038 CELL-SPECIFIC ROLES OF CALCINEURIN IN INTESTINAL TUMOR DEVELOPMENT


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13Kings College London - ISS on November 25, 2016

Introduction: Colorectal cancer (CRC) development is characterized by the sequential accumulation of somatic mutations, which promotes epithelial proliferation and subsequently tumor invasion. Calcineurin is a phosphatase, which contributes to innate and adaptive immunity through the activation of transcription factors of the family of nuclear factor of activated T cells (NFAT). Systemic contributions of calcineurin are described in the development as well as in the AOM/DSS model of colitis-associated cancer. In contrast, intestinal epithelial cell-specific deletion of calcineurin is associated with reduced intestinal tumor formation and growth in the Apcfl/wt and ApcMin/+ mice, which is consistent with an increased CRC incidence observed in patients receiving calcineurin inhibitors. In contrast, intestinal epithelial cell-specific deletion of calcineurin is associated with reduced intestinal tumour formation and growth in the Apcfl/wt and ApcMin/+ model. Antibiotic treatment of mice as well as backcrossing to a Myd88-deficient background revealed that the activation of oncogenic epithelial calcineurin promotes tumor development in a cell-intrinsic manner.

Aims & Methods: To investigate the role of calcineurin and NFAT in intestinal tumor development, we generated mice with intestinal epithelial cell (IEC)-specific deletion of the regulatory B1 subunit of calcineurin and analyzed these mice in the Apcfl/wt and ApcMin/+ models of genetically induced intestinal tumor development as well as in the AOM/DSS model of colitis-associated cancer. For mechanistic studies, organoid cultures, immortalized IECs and CRC cell lines as well as samples of more than 700 CRC patients were studied.

Results: We demonstrate that systemic inhibition of calcineurin with cyclosporine leads to increased intestinal tumor growth in Apcfl/+ mice, which is consistent with an increased CRC incidence observed in patients receiving calcineurin inhibitors. In contrast, intestinal epithelial cell-specific deletion of calcineurin is associated with reduced intestinal tumour formation and growth in the Apcfl/wt and ApcMin/+ model. Antibiotic treatment of mice as well as backcrossing to a Myd88-deficient background revealed that the activation of oncogenic epithelial calcineurin is dependent on the intestinal microbiota and results from tumor-associated alterations in microbial composition and stratification as well as from increased tumor-associated toll-like receptor expression. Tumor-promoting effects of epithelial calcineurin are elicited through NFAT-dependent transcriptional regulation of Lgr5-positive tumor stem cells as shown by chromatin immunoprecipitation (ChIP), gene expression analysis and functional studies together leading to control of tumor stem cell apoptosis and proliferation as shown by FACS and immunofluorescence staining. Moreover, somatic mutations identified in human CRC are associated with constitutive activation of calcineurin, while nuclear translocation of NFAT correlates with reduced survival in a large cohort of CRC patients.

Conclusion: These results support the concept of cell-specific roles of calcineurin in the regulation of colorectal carcinogenesis and reveal novel potential targets for the prevention and treatment of CRC.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP039 ALIX POSITIVE EXOSOMES IN COLORECTAL ADENOMA-CARCINOMA SEQUENCE

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Introduction: During colorectal carcinoma (CRC) formation exosomes play important roles as intercellular regulators in conveying complex signals between epithelial/carcinoma cells and their abnormal microenvironment.

Aims & Methods: Our aim was to characterize changes in exosome-based communication in the colorectal adenoma-carcinoma sequence by determining ALIX 2-interacting protein X (ALIX) exosome marker production on mRNA and protein level. mRNA expression was analyzed using Affymetrix HGU133 Plus2.0 whole transcriptome data of healthy (n=49), adenoma (n=49) and CRC (n=49) samples. Immunohistochemistry was performed on healthy (n=27), adenoma (n=42), CRC (n=37) patients and stained for ALIX exosome, cytoskeleton (CK) epithelial, podoplanin (PDPN) lymphatic vessel, Ki-67 proliferative and Musashi-1 (MSI1) stem cell markers. Slides were digitalized and analyzed with digital microscopy.

Results: We found significantly decreased (p<0.05) ALIX mRNA expression both in adenoma and CRC samples compared to normal samples. Similarly, significantly reduced (p<0.05) ALIX protein levels were detectable in adenoma and CRC samples compared to normal ones. The reduced protein expression was accompanied by gradual transition from diffuse cytoplasmic (in normal epithelium) expression to granular signals (in adenoma and CRC samples) with 0.6–2 µm diameter size range of multivesicular bodies. The granular ALIX expression was not limited to the proliferative and stem cells, but was also observed in budding CK+ and MSI1+ stromal cells, as well as in the lumen of PDPN+ lymphatic vessels in invasive CRCs.

Conclusion: The altered ALIX expression pattern in pre-neoplastic lesions suggests that abnormal exosome transport may play an important role in the adenoma to carcinoma transformation. Furthermore, the increased frequency of exosome marker expression in stromal and budding cancer cells, and also in the lumen of lymphatic vessels suggests that the exosome based information flow may be fundamental in the development of local and distant pre-metastatic microenvironments in CRC patients. This study was funded by the Research and Technology Innovation Fund, Hungary, KMR_12-1-2012-0216 and Hungarian Scientific Research Fund (OTKA-K111743 grant).

Disclosure of Interest: All authors have declared no conflicts of interest.
OP040 NHERF2 REGULATES COLON CANCER PROGRESS VIA STAT3

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Scaffold proteins mediate protein-protein interaction to bring together key members of signaling pathways that drive cell division and growth. The Na+/H+ exchanger regulatory factor (NHERF) family of proteins is crucial for this orchestration of organelle and cellular protein interactions. Among the NHERF proteins, NHERF1 and NHERF2 share most similarities with tandem PDZ domains and an ERM interacting motif in the carboxyl domain that enables anchoring to the actin cytoskeleton. One major function of NHERF1/2 is to recruit and spatially organize signaling proteins that either alters protein functions or downstream signaling pathways originating from receptor. NHERF1 is reported to be a tumor suppressor. However, the role of NHERF2 in cancer progression has not been reported.

Aims & Methods: We investigated the role of NHERF2 in colon tumor progression. We first determined NHERF2 expression in human colorectal cancer (CRC) using a tissue microarray. Next, the role of NHERF2 on colon cancer growth and invasion was assessed by a loss-of-function approach (shRNA) and a small peptide which blocked the PDZ domain of NHERF2 to bind using colon cancer cell lines (HCT116, SW480, and HT-29). We validated tumor growth effects in part by regulation of Stat3 and CD24. This study provides NHERF2 as a new potential target for cancer treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP041 THE EXTRACELLULAR MATRIX PROTEIN EMILIN2 AS A TARGET OF THE MYOELD DIFFERENTIATION FACTOR-2-INDUCED COLON CARCINOGENESIS

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Introduction: EMILIN2 is an extracellular matrix molecule belonging to the EMI Domain ENdowed (EDEN) protein family that exerts pleiotropic effects in the tumor microenvironment, including a tumor suppressive role in colorectal cancer (1). Our preliminary results highlight a possible new function for EMILIN2 in the control of CRC incidence. In particular these findings indicate that EMILIN2 seems to modulate the myeloid response and to profoundly affect the inflammatory microenvironment associated with CRC.

Aims & Methods: Given its involvement in the regulation of Wnt signaling, a crucial pathway in colon carcinogenesis, and its altered expression in colorectal cancer, we took advantage of the EMILIN2 null mouse model to assess its role in colorectal cancer (CRC) development, subjecting the mice to the inflammation-related AOM/DSS protocol. Colorectal tumors were induced using the mouse to a AOM/DSS treatment. Tumor development was assessed by colonoscopy. Histopathological and IHC analyses were performed on colon samples from treated mice. β-catenin activation was assessed by Western blot and qPCR. Multiplex serum cytokine analyses from the two mouse models were performed through Luminex Screening and peripheral blood cells were counted. The inflammatory infiltrate was analysed by flow cytometry.

Results: The EMILIN2 KO mice developed a significantly higher number of tumors compared to wt mice. Tumors from EMILIN2 KO mice were more undifferentiated and at an advanced stage compared to the tumors from control mice. Interestingly, and contrary to our expectations, tumors from EMILIN2 KO mice did not display any changes in the activation of the Wnt/β-catenin pathway compared to the controls. Accordingly, the β-catenin target genes cyclin D1 and c-Myc were not altered in the tumors and in the normal mucosa of the two mouse models. Histopathological and IHC analyses were performed on colon samples from treated mice. In particular these findings indicate that EMILIN2 KO mice where characterized by a higher number of macrophages and granulocytes than those from WT mice. Similar alterations in the KO model results highlight a possible new function for EMILIN2 in the control of CRC incidence.

Conclusions: Our results let us suggest that EMILIN2 may affect colon carcinogenesis by impinging on the recruitment and/or the activation of myeloid cells. By altering the inflammatory microenvironment, EMILIN2 may significantly influence colon cancer development.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
Disclosure of Interest: renewal of colon spheres and differentiation ability of HCT116 colon spheres.


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Aims & Methods: CSCs (CCSCs) to self-renew and differentiate.

in this context, we hypothesise that miR-145 may play a role in the ability of colon CSCs (CCSCs) to self-renew and differentiate.

Aims & Methods: miR-145 overexpression in maintaining CSCs-like properties. We produced miR-145 overexpressing and empty vector control cells using HCT116, HT29, SW480 and SW620 colon cancer cell lines, and examined their ability to form colon spheres in ultralow-attachment plates and specific CSCs media. Colon spheres were dissociated to single cells and reseeded to yield the second and third generation of colon spheres.

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Introduction: H. pylori rescue therapy is still a major concern for clinicians treating this infection. Although several rescue treatments have been proposed and tested, the selection of resilient strains or acquisition of resistance after failed eradication hinders the success rate of most proposed regimens. Traditionally rescue treatments in Europe have been divided in bismuth quadruple therapy or levofloxacin triple. Some authors have recently proposed a combination of both strategies in order to return back to the traditional quadruple as a rescue therapy. Aims & Methods: To evaluate the outcomes and quadruple therapy containing a proton pump inhibitor, bismuth, levofloxacin and amoxicillin in the European Registry on H. pylori Management (Hp-EuReg). Methods: Systematic prospective registry of the clinical practice of European gastroenterologists regarding H. pylori infection and treatment.

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Introduction: Cancer stem cells (CSCs) are thought to be responsible for tumour initiation, metastasis and relapse through their unlimited self-renewal and differentiation. This feature has recently emerged as promising candidates to target CSCs. miR-145 is a tumour suppressor miRNA, downregulated in colon cancer adenomas and carcinomas. It has been shown to be involved in tumour growth, angiogenesis and chemoresistance to chemotherapy targeted agents, as well as in modulation of CSC-like properties in prostate cancer and lung adenocarcinoma.

Results: CD44 and CD133 expression levels and aldehyde dehydrogenase 1 (ALDH1) activity were evaluated by flow cytometry. We showed that forced miR-145 expression reduced colon sphere diameter and number of cells per sphere in HCT116, HT29, SW480 and SW620 cells.

Conclusions: miR-145 significantly reduced the proportion of CD44+/CD133+ cells and ALDH1 activity (p < 0.05). The mature colonocytic marker, CK20, was increased in HCT116 spheres overexpressing miR-145 (p < 0.01).

Conclusion: miR-145 appears to be involved in colon sphere formation, self-renewal of colon spheres and differentiation ability of HCT116 colon spheres. miR-145 may contribute to the induction of CSCs differentiation to cells that are sensitive to chemotherapy and targeted agents.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
10:30-12:00
GASTRODUODENAL DAMAGE: H.PYLORI, ACID AND BILE - ROOM 1.86

OP043 PAN-EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): INTERIM ANALYSIS OF THE RESCUE TREATMENT WITH BISMUTH, LEVOFLOXACIN AND AMOXICILLIN

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United European Gastroenterology Journal 4(5S)
A19

Results: Up to now, 16,025 patients have been included, and 12,921 have finished follow up (93% females, 87% Caucasian). Mean age was 55 years. The bismuth- containing quadruple therapy was prescribed to 327 patients (2% of all patients registered): 7% in first-line, 76% in second, 12% in third, and 5% in following rescues. Overall efficacy was 84% (95% CI: 75–93%) by ITT and 92% (95% – 95%) by PP. First-line data is insufficient for analysis. Second-line eradication rate was 85% (80–91%) by ITT and 92% (89–94%) by PP. Treatment was generally prescribed with esomeprazole (95%) and as a 14 day regimen (98%). Compliance with treatment was 95%. Adverse events were reported in 38% of cases and caused treatment discontinuation in 7 (2.1%) patients.

Conclusion: A 14-day regimen combining bismuth salts with levofloxacin triple therapy as second-line treatment for H. pylori eradication achieves near 90% eradication rates.

Disclosure of Interest: A.G. McNicholl: Speaker for allreglan
M. Castro: Teaching activities for allreglan
J.P. Gisbert: Scientific Advisory for Casen Recordati
Teaching activities for Almirall, allreglan
AstraZeneca, Casen Recordati, Nycomed.

All other authors have declared no conflicts of interest.

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Introduction: A proton pump inhibitor (PPI)-based triple regimen containing two antibiotics (amoxicillin, PAMC, and clarithromycin, CAM) was considered the gold standard for the eradication of Helicobacter pylori for more than a decade. However, low eradication rates have been reported recently, which has been attributed in part to increased prevalence of clarithromycin-resistant H. pylori. Insufficient acid inhibitory effect during treatment also causes eradication failure. This is because the antimicrobial agents are unstable and degraded in the stomach. Esomeprazole (EPZ) is a relatively new PPI available in Japan since September 2011. EPZ has an improved pharmacokinetic profile as regards CYP2C19 genotype; therefore, it shows less individual variability. Vonoprazan (VPZ) is a potassium-competitive acid blocker (K-ACB). P-ACBs are a new class of gastric acid suppressants available since February 2015 in Japan. VPZ has a potent and long-lasting anti-secretory effect on H+K+/ATPase due to its high accumulation in, and slow clearance from the parietal cell. Therefore, VPZ may be considered in combination with conventional PPIs. The aim of this study was to compare H. pylori eradication rates with EPZ-based and VPZ-based triple therapies with CAM and AMPC.

Aims & Methods: A total of 807 patients who had undergone upper gastrointestinal endoscopy and diagnosis with H. pylori infection from November 2013 to March 2016 were enrolled. From December 2013 to September 2014, 431 patients were treated with EPZ-based triple therapy, while 376 patients were treated with VPZ-based triple therapy from April 2015 to March 2016. At baseline, demographic and clinical characteristics including gender, age, body mass index (BMI), smoking status, and consumption of alcohol were checked. The first-line eradication regimen was CAM 200 mg, AMPC 750 mg, and either EPZ 20 mg or VPZ 20 mg, each twice daily for 7 days. The second-line eradication regimen was metronidazole 250 mg, AMPC 750 mg, and either EPZ 20 mg or VPZ 20 mg, each twice daily for 7 days. The eradication of H. pylori infection was diagnosed using urease breath tests at 4-8 weeks after each of therapy.

Results: The overall first-line eradication rate was 79.1% (341/431) for the EPZ regimen and 84.6% (318/376) for the VPZ regimen based on Intention to treat (ITT) analysis. The eradication rate was 87.6% (341/390) for the EPZ regimen and 87.8% (318/363) for the VPZ regimen based on PP analysis. Significant differences were found both in ITT analysis (p = 0.045) and in PP analysis (p = 0.046). The overall second-line eradication rate was 72.6% (45/62) for the EPZ regimen and 85.3% (29/34) for the VPZ regimen based on ITT analysis. Using PP analysis, the eradication rate was 88.2% (45/51) for the EPZ regimen and 87.9% (29/33) for the VPZ regimen. There were no statistically significant differences between the two regimens in both the ITT and PP analyses.

Conclusion: In conclusion, VPZ has a rapid, sustained, and possibly more potent acid-inhibitory effect than EPZ, irrespective of CYP2C19 genotype. The rate of second-line recruiting investigators). A local coordinator was selected from each country. Each coordinator selected a representative group of recruiting investigators from his/her country. An electronic clinical research file (Ce-CRF) was created on AEG-REDCap to systematically register all adult patients infected with H. pylori. Variables included: Previous eradication attempts, prescribed eradication treatments, adverse events, and outcomes (cure rates, compliance, follow up, etc.). Patients with both eradication confirmation test and with less than one year follow-up have been considered ongoing cases and were excluded from the analysis.

All other authors have declared no conflicts of interest.
OP045 STROMAL MYOFIBROBLASTS ORCHESTRATE GASTRIC EPITHELIAL WNT-SIGNALING AND STEM CELL KINETICS IN GASTRITIS AND DISEASE

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Introduction: The gastric epithelium is characterized by constant, rapid self-renewal, which in the antrum is driven by long-lived stem cells situated at the base of the glands. Infection with the gastric pathogen Helicobacter pylori is the main risk factor for gastric cancer and increases stem cell and the turnover kinetics of the glands. Wnt signaling is known to be crucial for stem cell homeostasis in several tissues and for long-term organoid culture of stomach epithelium, but it is not clear how Wnt signaling is spatially organized in the stomach in vivo. Whether it modulates stem cell kinetics and glandular turnover.

Aims & Methods: The aim of the present study was to characterize the cellular and molecular Wnt-network in the stomach and to explore its function in physiological epithelial turnover, as well as upon infection with H. pylori. Using in single molecule situ hybridization, different stem cell- and WNT-signaling reporter mice and the murne and as well as human 3Dorganoid system we addressed these questions.

Results: We found that Wnt-responsive cells are limited to the base of the antral glands where stem cells reside. However, in addition to previously described Lgr5-positive cells, we found another Wnt-dependent population of highly proliferative Lgr5-negative stem cells in the gland base. We show that the positional identity of these different stem cells relies on R-spondin 3, which is produced by stromal myofibroblasts. Wnt signaling stimulated by exogenous R-spondin induces an expansion and increased proliferation of Axin2-positive stem cells in the stomach antrum while the Lgr5-positive cells remain silent. Infection of mice with H. pylori increases expression of R-spondin 3, which also expands the induction of Axin2-positive cells and results in gland hyperplasia. By increasing gland turnover following infection, R-spondin counterbalances bacterial gland colonization through increased shedding of cell-attached bacteria.

Conclusion: Thus, stromal R-spondin hierarchically organizes the stem cell compartment producing two Wnt-responsive populations that differ in position within the gland, proliferation kinetics and sensitivity to R-spondin. In addition to its role in physiological gland homeostasis R-spondin driven regeneration is increased by infection with H. pylori, limiting glandular colonization. This establishes a new link between infection, stem cell signaling and epithelial homeostasis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

Aims & Methods: Using gastric tissue from humans, rats treated with proton pump inhibitors and/or a cholera type B receptor (CCK-BR) agonist (CCKB), and two cell lines expressing either CCK-BR or R-spondin, we investigated the expression pattern and gastrin-mediated regulation of CLU. Using parallel reaction monitoring mass spectrometry, in situ hybridization and immunohistochemistry. Human gastric cancer cell lines were used to study the gastrin-mediated regulation and biological function of secretory CLU in vitro.

Results: CLU was highly expressed in neuroendocrine cells and normal oxyntic mucosa of humans, rats and mice. In response to hypergastrinemia, expression of CLU was significantly increased and localized shift from neuroendocrine cells to basal groups of proliferating intragastric acidity. To exert such a protective effect the reduced acidity would need to be evident in the majority of H. pylori-infected subjects. To investigate this we have examined the acid secretory capacity of H. pylori-positive volunteers in the stomach following a standardised meal. The position of the squamocolumnar junction (SCJ) was determined by radio-opaque clips and visualised using high-resolution pHmetry (12 sensors at 11 mm intervals) and manometry (36 sensors at 7.5 mm intervals) was performed for 20 minutes fasted and then for 90 minutes following a standardised meal. The position of the squamocolumnar junction (SCJ), marked with two endoscopically placed radio-opaque clips, was visualised radiologically close to the probes. Biopsy specimens were scored quantitatively for inflammation and stained with monoclonal antibody to H+/K+ATPase and immunogen I for calculating parietal cell and chief cell densities respectively.

Results: The mean age of the H. pylori-positive group was 55 years (38–78 years) compared to 56 years (24–74y) for the H. pylori-negative group. Under fasting conditions, the H. pylori-positive subjects had less intragastric acidity compared to the H. pylori-negative subjects at all sensors more than 1.1cm distal to the peak lower oesophageal sphincter (LOS) pressure (p < 0.01). Throughout the three 30-minute postprandial periods, intragastric acidity was significantly less in H. pylori-positive subjects at the sensors 2.2, 3.3 and 4.4cm distal to the peak LOS pressure (p < 0.05), but there was no significant difference in the sensors 5.5 and 6.6cm distal to peak LOS pressure (Table 1). The postprandial acid pocket was thus attenuated in H. pylori positive subjects compared to negatives. The H. pylori positives had a significant reduction in density of both parietal and chief cells compared to H. pylori negatives, and this was seen in 10 of the 11 gastric locations (p < 0.01 for 9 locations). The degree of reduction was similar for the two cell types. The cardia mucosal length was longer in H. pylori positives (1.5mm vs 0.7mm; p = 0.013). 17/31 (54.8%) of the H. pylori positives were also CagA seropositive and they showed more a more marked reduction in intragastric acidity and increased mucosal inflammation compared to the CagA negative subjects.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Table 1: Median pH (IQR) detected by sensors relative to the peak LOS pressure during the 30-60 minute postprandial period. NOTE: *p < 0.05, **p = 0.01

<table>
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<tr>
<th>Sensor location</th>
<th>H. pylori negative</th>
<th>Median pH (IQR)</th>
<th>H. pylori positive</th>
<th>Median pH (IQR)</th>
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<tr>
<td>1.1cm proximal</td>
<td>7.06 (1.42)</td>
<td>7.00 (0.75)</td>
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<tr>
<td>1.1cm distal</td>
<td>6.76 (1.02)</td>
<td>6.88 (0.48)</td>
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<tr>
<td>1.1cm distal</td>
<td>5.25 (4.19)</td>
<td>6.40 (1.72)</td>
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<tr>
<td>2.2cm distal</td>
<td>6.15 (5.49)</td>
<td>3.21 (4.46**)</td>
<td></td>
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<tr>
<td>3.3cm distal</td>
<td>5.99 (2.29)</td>
<td>2.07 (2.29**)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.4cm distal</td>
<td>1.81 (2.09)</td>
<td>2.93 (3.25*)</td>
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</tr>
<tr>
<td>5.5 cm distal</td>
<td>2.13 (2.02)</td>
<td>3.48 (2.89)</td>
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<tr>
<td>6.6cm distal</td>
<td>3.39 (2.19)</td>
<td>4.10 (2.23)</td>
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</table>
**Result:** The majority of *H. pylori-*infected subjects have reduced intragastric acidity compared to the uninfected population and this is most marked close to the gastroesophageal junction. The density of parietal cells and chief cells is reduced in *H. pylori*-infected subjects throughout the gastric mucosa. These findings may provide negative associations between *H. pylori* infection and both gastroesophageal reflux disease and oesophageal adenocarcinoma.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References:**

**Contact Email Address:**
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**Disclosure of Interest:**
We aimed to investigate the location of distal and proximal gastroesophageal reflux disease (GERD) in patients with non-erosive reflux disease. We investigated mucosa from 10 patients with typical heartburn symptoms, normal macroscopic oesophageal appearances, and all had non-erosive oesophageal acid exposure on reflux testing (oesophageal pH exposure > 4.2%). In each patient, endoscopic mucosal biopsies were taken from 3 cm above the gastrooesophageal junction (distal) and at 20 cm from the incisors (proximal). Biopsies were fixed in 4% paraformaldehyde, cryoprotected, and 10 μm sections were cut on a cryostat and prepared on slides. Slides were examined immunohistochemically for presence and location of calcitonin gene-related peptide (CGRP) and protein gene product (PGP) 9.5 - immunoreactive nerve fibres. Where fibres were identified their location in the mucosa was recorded in terms of cell layers from luminal surface. In the distal oesophagus in the patients with NERD, afferent nerves were found a mean of 7.7 ± 1.3 cell layers from the surface. In the distal oesophagus nerves were found a mean of 8.9 ± 2 cell layers from the surface. In contrast, in healthy volunteers proximal nerves were found 12.3 ± 0.9 cell layers from the lumen in the proximal oesophagus, and 22.2 ± 2.7 cell layers from the lumen in the distal oesophagus. On ANOVA, the more superficial location of distal oesophageal nerves in patients versus healthy controls was statistically significant (p < 0.001) and this was a non-significant trend to more superficial proximal nerves in NERD patients versus healthy volunteers.

**Disclosure of Interest:**

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**Disclosure of Interest:**
Reflux episodes that extend to the proximal esophagus are more likely to be perceived. Our hypothesis is that the enhanced sensitivity of the proximal esophagus is related to more pronounced impairment of mucosal integrity in this part of the esophagus.

**Aims & Methods:** We aimed to assess acid sensitivity and mucosal integrity of the proximal and distal esophageal segments separately in patients with gastroesophageal reflux disease (GERD) and to investigate the relationship between these parameters. We included patients with heartburn and evidence of GERD on ambulatory pH-impedance measurement. After PPI washout, an esophageal hydrochloric acid perfusion test measuring segmental acid sensitivity proximally and distally in the esophagus (3 and 18 cm above the Z-line) and an upper endoscopy with biopsies at both levels were performed. During endoscopy, electrical tissue impedance spectroscopy was performed at the two levels and biopsies were taken from macroscopically unaffected mucosa. Biopsies were used to measure dilution of intercellular spaces with transmission electron microscopy to investigate a morphological measure of impaired integrity and to investigate transmucosal electrical resistance and transepithelial fluorescein permeability in Ussing Chambers as a functional measure of mucosal integrity.

**Reference:**

**Disclosure of Interest:**
All authors have declared no conflicts of interest.
Resistance were not statistically significant between the proximal and distal esophageal segments.

Conclusion: The proximal segment of the esophagus in GERD patients off PPI is more rapidly sensitive to acid perfusion, while the distal esophagus shows a more pronounced impairment of acid sensitivity. The marker of GERD in the patients. Recently, a low-cost, non-invasive saliva pH monitoring test (PeptestTM, RB Biomed Limited, UK) was found able to measure pH in the saliva/sputum and to test the correlation between samples from individuals with GERD and normal controls.

Disclosure of Interest: A.J. Bredenoord: Received research funding from Endosimt, Medical Measurement Systems, Danone and Given and received speaker and/or consulting fees from MMS, Astellas, AstraZeneca and Almirall. All other authors have declared no conflicts of interest.

OP051 LARYNGOPHARYNGEAL SYMPTOMS IN PRIMARY CARE: USEFULNESS OF SALIVARY PEP SIN MEASUREMENT IN PREDICTING GERD

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3Division of Gastroenterology, Department Of Surgery, Oncology and Gastroenterology, University of Padua, Padua/Italy
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Introduction: Incidence of chronic laryngeal symptoms in primary care is about 25% and, gastroesophageal reflux disease (GERD) is considered by far the main disorder associated to them, leading to a specific syndrome called Laryngopharyngeal Reflux (LPR). Several studies demonstrated that pepsin measurement offers a specific tool to identify patients with chronic laryngeal symptoms as an indication to perform diagnostic evaluations of upper gastrointestinal disease. In this pilot study, PeptestTM was not able to discriminate among primary care patients with LPR from those without and therefore cannot be recommended for daily use.

Methods: B200 consecutive patient responses were collected within one year. Patients suffering from GERD (LPOP) had an average of 9.7 years and prescribed PPI therapy for an average duration of 8.2 years. 74% were dissatisfied or very dissatisfied on their current PPI therapy (score of 1 or 2), 89% reported heartburn or regurgitation at least twice per week (57% 4-7 days), 53% reported additional medication other than their prescribed PPI at least 2 days per week (77% 2-4 times per week). In patients diagnosed with PPI, the most cited insufficient symptom control (91%) as a reason for dissatisfaction. In addition, 26% cited concern with long-term use of drugs and 23% the need for daily medication. 92% of patients had received an upper endoscopy, 6% had a prior pH-metry, 5% manometry, and 7% received prior surgical consultation for GERD. The rate of “Lost Patients” in this study was 63%.

Conclusion: Chronic GERD patients who are dissatisfied with their PPI therapy are rarely referred to specialized GERD diagnostic procedures or treatment alternatives. Half of the patients took medication in addition to PPI to control their reflux. In addition to persistent symptoms, concerns of long-term PPI use and burden of daily medication play a role in patient dissatisfaction with PPI therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP053 EFFICACY OF ACOXITAMIDE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE UNRESPONSIVE TO PROTON PUMP INHIBITOR THERAPY

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Introduction: Acid suppression is the mainstay of gastroesophageal reflux disease (GERD) therapy, and proton pump inhibitors (PPIs) are the first choice of drug therapy. In addition to persistent symptoms, concerns of long-term PPI use and burden of daily medication play a role in patient dissatisfaction with PPI therapy.

Methods: 200 consecutive patient responses were collected within one year. Patients suffering from GERD (LPOP) had an average of 9.7 years and prescribed PPI therapy for an average duration of 8.2 years. 74% were dissatisfied or very dissatisfied on their current PPI therapy (score of 1 or 2), 89% reported heartburn or regurgitation at least twice per week (57% 4-7 days), 53% reported additional medication other than their prescribed PPI at least 2 days per week (77% 2-4 times per week). In patients diagnosed with PPI, the most cited insufficient symptom control (91%) as a reason for dissatisfaction. In addition, 26% cited concern with long-term use of drugs and 23% the need for daily medication. 92% of patients had received an upper endoscopy, 6% had a prior pH-metry, 5% manometry, and 7% received prior surgical consultation for GERD. The rate of “Lost Patients” in this study was 63%.

Conclusion: Chronic GERD patients who are dissatisfied with their PPI therapy are rarely referred to specialized GERD diagnostic procedures or treatment alternatives. Half of the patients took medication in addition to PPI to control their reflux. In addition to persistent symptoms, concerns of long-term PPI use and burden of daily medication play a role in patient dissatisfaction with PPI therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.
showed no significant change. In patients with a symptom index > 30% or total reflux events > 40, the effective rate was significantly different (p = 0.038) at 60 and 33% for the aci
ught and placebo groups, respectively. These results suggest that aci
ught may be effective in patients with associated reflux events. Conclusions: The symptom score was reduced in reflux events and improved reflux symptoms in patients whose symptoms were associated with reflux events. Co-administration of aci
ught and PPIs may be a new strategy for PPI-refractory GERD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. Pauleau A, et al. The gastric accommodation response to meal intake deter-

OP054 A RANDOMIZED CONTROLLED TRIAL TO ASSESS THE CLINICAL EFFICACY OF ESOMEPRAZOLE VS. VONOPRAZAN FOR RESOLUTION OF GASTRO-ESOPHAGEAL REFLUX DISEASE SYMPTOMS IN NEWLY DIAGNOSED PATIENTS

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Introduction: Esomeprazole (EPZ) 20 mg once daily vs. VPZ 20 mg once daily for the resolu-
tion of GORD symptoms in newly diagnosed patients. Patients > 20 years of age with upper gastrointestinal symptoms of at least mod-
erate severity (Global Overall Symptom score [GOS] ≥ 4 on a 7-point Likert scale) were randomized to treatment with EPZ or VPZ.

The primary endpoint was the proportion of patients with sufficient relief of upper gastrointestinal symptoms (GOS ≤ 2) after 4 weeks of treatment. Secondary endpoints were the proportion of patients with complete overall symptom relief (GOS = 0) after 4 weeks of treatment.

Results: 88 patients were entered and randomly assigned to the EPZ group and the VPZ group.

After 4 weeks, proportion of patients with sufficient relief was achieved by 88.6% in the EPZ group, compared to 58.1% in the VPZ group (p < 0.01).

The worsened provability in FSSG Functional Dyspepsia (FD) score were sig-
ificant lower in the EPZ group, compared to 58.1% in the VPZ group (p < 0.01).

After 4 weeks, proportion of patients with sufficient relief was achieved by 88.6% in the EPZ group, compared to 58.1% in the VPZ group (p < 0.01).

The result observed in this study was considered to be caused by the multifactorial pathophysiology of GORD. Various mechanisms may contribute to dyspeptic symptoms, for example, finding that patients with gastric achlorhydria or hypergastrinemia showed impaired gastric motility may be supportive of this point (2).

These findings can suggest that increasing the degree of acid inhibition beyond that afforded by treatment with VPZ 20 mg once daily. In addition, the probability of worsened FD symptoms were significantly lower in the EPZ group than the VPZ group.

The result observed in this study was considered to be caused by the multifactorial pathophysiology of GORD. Various mechanisms may contribute to dyspeptic symptoms, for example, finding that patients with gastric achlorhydria or hypergastrinemia showed impaired gastric motility may be supportive of this point (2).

These findings can suggest that increasing the degree of acid inhibition beyond that already achieved by EPZ 20 mg does not translate into increased clinical efficacy for the resolution of GORD symptoms in newly diagnosed patients. Conclusion: EPZ 20 mg once daily was more effective than VPZ 20 mg once daily for the resolution of GORD symptoms in newly diagnosed patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
3. Endoscopic band ligation is a safe, well tolerated and cost-effective therapeutic option for refractory GERD. 20 patients were enrolled in the study after informed consent was taken. They were treated with rubber band ligation and the cap used for ligation had a diameter of 11 mm and loaded with 6 rings. The main outcome is reduction of reflux symptoms measured by GERD health related quality of life Questionnaire. Patients were included if they were 18 years of age or older with typical symptoms of heartburn or regurgitation refractory or less responsive to maximally optimized dose of PPI therapy (given twice, 30 min before food) and even after adding H2 receptor blocker before bedtime and baco 10 mg twice daily to the unresponsive patients. Patients excluded if they had lower esophageal ulcers, pregnancy, red flag signs as loss of weight, fever, dysphagia, odynophagia, bleeding. Large hiatal hernia more than 2 cm, paraesophageal hernia, active Helicobacter pylori infection, eosinophilic esophagitis were also excluded. Band ligation was performed in the four quadrants 5 mm distal to the Z-line which is measured before and after the sessions were completed. Results: 13 males and 7 females were enrolled in the study. Their mean age 39.5 ± 6.2 with a range (31–49 years). The pre-endoscopic intervention character-
istics were mean hemoglobin 10.6 ± 0.9 gm/dl, median GERD related quality of life questionnaire (GERD-QOL) score was 35.4 ± 6.9, depth of Z-line 34 ± 1.1cm, frequency of the sessions needed 1.6 ± 0.6 times over 4 months. After 6 months of follow-up, GERD-QOL score had dramatically improved 15.4 ± 4.6 (t = 11.85, p < 0.000), depth of Z line became 35 ± 0.9 cm (t = −3.2, p = 0.005), hemoglobin level showed non-significant increase (10.9 ± 0.8 gm/dl, p = 0.008). 5 patients experienced mild dysphagia, dysphagia improved after 6 ± 2.2 days. 8 patients (40%) experienced transient epigastric pain which disappeared within 5.4 ± 1.5 days. 13 patients stopped PPI use (65%), 6 patients were on demand therapy (30%), and only one patient needed continuous low dose PPI which was significantly reduced when compared to pre-endoscopic PPI intake. Conclusion: Endoluminal band ligation is a safe, well tolerated and cost-effective therapeutic option for refractory GERD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Introduction: LSG is the most commonly performed bariatric procedure in the US, Canada and the Asia-Pacific region. However, LSG can result in new GERD and may worsen pre-existing GERD.1 LSG patients with GERD not well controlled with PPI do not have good treatment options except for more invasive, anatomy-altering gastric bypass surgery. LES electrical stimulation therapy has shown to improve outcomes in GERD patients.ii-iii

Aims & Methods: To evaluate the safety and efficacy of LES stimulation in LSG patients with GERD not controlled with maximum dose PPI therapy. Patients with severe esophagitis or bothersome symptoms on maximum PPI therapy underwent LES stimulator implant procedure and were enrolled in an international patient registry prospectively tracking outcomes in GERD patients treated with LES electrical stimulation. Electrical stimulation was delivered at 5mA, 220uSec pulse in 12, 30 minute sessions daily. GERD outcomes pre and post-stimulation were evaluated.

Results: 12 patients, 66% (8/12) women at 8 centers have been treated. Median age was 46 (IQR 42–55) years. All (12/12) were on daily double-dose PPIs. At their last follow-up (median = 12 months), 75% (9/12) were off-PPI and one each was using PPIs on < 50% of days and standard dose once a day. The latest 12-hour pH testing showed chronic GERD in 2/12 patients. GERD-HRQL scores at baseline was 25 (IQR 18–31) which improved to 4 (IQR 3–10) at last follow-up (n = 6, p = 0.01). All patients improved esophageal acid exposure, 83% (5/6) patients had normalized acid exposure and 1/6 patient had > 40% improvement in distal esophageal acid exposure. Median GERD-HRQL scores at baseline was 25 (IQR 18–31) which improved to 4 (IQR 3–10) at last follow-up (n = 6, p = 0.01). All patients improved esophageal acid exposure, 83% (5/6) patients had normalized acid exposure and 1/6 patient had > 40% improvement in distal esophageal acid exposure. Median GERD-HRQL scores at baseline was 25 (IQR 18–31) which improved to 4 (IQR 3–10) at last follow-up (n = 6, p = 0.01). No adverse events related to the device or procedure were reported.

Conclusion: Preliminary results on patients with LSG and GERD with bothersome symptoms on maximum PPI therapy, revealed that LES stimulation is safe and results in a significant improvement in GERD symptoms and esophageal acid exposure. Most patients were off their PPI therapy with remaining taking PPI at a reduced dose. Data from a larger patient experience for this indication is being collected using the international registry trial.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.
Abstract No: OP058

Anatomomas overall, N

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Proximal colon adenomas, N

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Conclusion: The overall accuracy of ECV-CAD was comparable to that of experts and significantly better than that of novices. Thus, ECV-CAD could be a powerful decision tool for less-experienced endoscopists.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Monday, October 17, 2016 14:00–15:30

OP060 LYMPHOMA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A FRENCH NATIONWIDE OBSERVATIONAL COHORT STUDY

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2Institut Pierre Louis D’Épidémiologie Et De Santé Publique (unité Mixte De Recherche En Santé 1136), INSERM, Paris/ France
3Gastroenterology Unit, CHU de Bicêtre, APHP-Université Paris Sud, Le Kremlin Bicêtre/ France

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Introduction: Thiopurines are associated with an increased risk of lymphoma. The risk of lymphoma associated with anti-TNFs is uncertain.

Aims & Methods: The aim of this study was to assess the risk of lymphoma in patients with inflammatory bowel disease (IBD) treated with thiopurines, anti-TNFs or the combination of both treatments (combi-therapy). Every patient affiliated to the French national health insurance with a diagnosis of IBD, based on listed long-term diseases and/or hospital discharge diagnosis, was included from 1st July 2009 through 31st December 2013, and followed up until December 31st, 2014. A propensity score was built, using a multinomial logistic regression conditional of multiple covariates, to predict the probability to receive thiopurines, anti-TNFs or combitherapy at baseline. Hazard ratios for lymphoma were estimated using Cox proportional hazards regression in which each treatment was introduced as a time dependent covariate.

Results: The cohort included 173,190 patients with IBD, followed for a median of 4.9 years, accounting for 522,487 persons-years (PY) exposed to thiopurines or anti-TNFs, 111,113 PY exposed to thiopurines, 60,736 PY exposed to anti-TNFs and 11,514 PY exposed to combitherapy. Among them, 166, 56, 31 and 13 patients developed lymphoma, respectively. In multivariate analysis, patients exposed to thiopurines or anti-TNFs monotherapy had an increased risk of lymphoma as compared to unexposed patients (Hazard ratio and 95% confidence interval (HR95%): 1.64 (1.08–2.6) and HR95%: 1.87 (1.15–3.03), respectively). Patients exposed to combi-therapy had a more than four-fold increased risk of lymphoma as compared to unexposed patients (HR95%; 4.83 (2.5–9.6)).

Conclusion: The risk of lymphoma associated with combitherapy is more than two-fold higher than that associated with thiopurines and anti-TNFs monotherapy. This risk should be taken into consideration and weighed against potential benefits of combitherapy.

Disclosure of Interest: F. Carbonnel: Franck Carbonnel had consulting fees from Genentech, Otsuka, Vifor, and lecture fees from Hospira. All other authors have declared no conflicts of interest.
Table: Hazard ratio for lymphoma in thiopurines, anti-TNFs monotherapy and comotherapy exposed patients compared to unexposed patients

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<td>Thiopurines</td>
<td>60 736 PY</td>
<td>Crude</td>
<td>60 736 PY</td>
<td>Crude</td>
</tr>
<tr>
<td>anti-TNFs monotherapy</td>
<td></td>
<td>Adjusted</td>
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<td>Comotherapy</td>
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Person-years

<table>
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<tr>
<th>CD-K</th>
<th>CD-C</th>
<th>UC-K</th>
<th>UC-C</th>
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<tbody>
<tr>
<td>12</td>
<td>166</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>1.19 (0.85–1.68)</td>
<td>1.56 (0.98–2.04)</td>
<td>21.0 (1.07–7.10)</td>
<td>1.94 (1.05–3.05)</td>
</tr>
<tr>
<td>1.10 (0.71–1.70)</td>
<td>1.94 (1.05–3.05)</td>
<td>21.0 (1.07–7.10)</td>
<td>1.94 (1.05–3.05)</td>
</tr>
</tbody>
</table>

IS and anti-TNFs occurred only in CD. In CD, risk factors included perianal disease and 2.47 [1.06–5.73] and UC-related surgery (OR 3.07 [1.15–8.02] for extracolonic cancers. The same risk factors (extensive UC, penetrating CD, IS and anti-TNFs use) were at limit of the statistical significance for urinary tract and skin cancers.

Disclosure of Interest: L. Biancone: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Astra Zeneca, Chiesi, Ferring, MSD, Otsuka, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar; A. Arumzui: The author declares no conflicts of interest specifically related to the study. Financial support for research not related to the present study from MSD, lecture fees from Abbvie, MSD, Hospira, Mundipharma, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar; M.L. Scribano: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Astra Zeneca, Chiesi, Ferring, MSD, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar; D. Parner: No conflicts of interest specifically related to the study. Financial support for research not related to the present study from MSD, lecture fees from Abbvie, MSD, Hospira, Mundipharma, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar; C. Papi: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Consultant for Abbvie, Abbvie, MSD, Sofar, Chiesi, Ferring; L. Guidi: No conflicts of interest related to the study. Lecture fees from Abbvie, Abbvie, Takeda, Zambon, financial support for research not related to the study from Abbvie, Chiesi, Ferring; A. Kohn: Financial support for research not related to the study from Merck and others; W. Fries: The study was not sponsored. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, MSD, Hospira, Ferring.

G. Riegler: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, MSD, Ferring.

Introduction: Conventional immunosuppressants (thiopurines or methotrexate) and anti-TNF agents (IMMs) can influence the immunologic control of cancer. And they might ease cancer spread and recurrence. Therefore, a past history of cancer and anti-TNF agents (IMMs) can influence the immunologic control of cancer.

Method: A retrospective cohort study was performed in patients with IBD and a past history of cancer, treated with IMMs, compared with patients without a past history of cancer.

Results: Of the initially 756 included patients with confirmed IBD, 599 (79%) patients further treated with IMMs and 97%, 96% and 92% at 1, 2, and 5 years in controls, respectively (p<0.013). Cancer-free survival was 99%, 98% and 97% at 1, 2, and 5 years (hazard ratio and confidence interval 95% 1.31 (1.14–1.51), HR95%: 2.12 (1.49–3.00), respectively), while exposure to anti-TNFs was associated with an increased risk of serious and opportunistic infections compared to anti-TNFs exposure in patients aged 18–64 years (hazard ratio and confidence interval 95% (HR95%) 1.74 (1.20–2.52)). Similar results were observed in a sensitivity analysis conducted in incident patients.

Conclusion: Thiopurines, anti-TNFs monotherapy and combotherapy were associated with an increased risk of serious and opportunistic infections, compared to unexposed patients. Combotherapy was associated with a higher risk of serious and opportunistic infections compared to anti-TNFs exposure in patients aged 18–64 years (hazard ratio and confidence interval 95% (HR95%) 1.82 (1.67–1.99) and 1.83 (1.43–2.35), respectively). Exposure to thiopurines was associated with an increased risk of serious infections compared to anti-TNFs monotherapy in patients aged 18–64 years (HR95%: 1.74 (1.20–2.52)). Among them, a total of 4926, 1144, 1096 and 252 serious infections and 245, 183, 147 and 40 opportunistic infections occurred, respectively. After adjustment (based on propensity score, age, time-consuming to the development of cancer in both cancer patients and IBD patients, the risk of serious and opportunistic infections might be taken into consideration and weighed against potential benefits of anti-TNFs.

Disclosure of interest: F. Carbonnel: Franck Carbonnel had consulting fees from Tenebenth, Osuka, Vífor, and lecture fees from Hospira. All other authors have declared no conflicts of interest.

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Introduction: Serious and opportunistic infections are a major concern in patients with inflammatory bowel disease (IBD) treated with immunosuppressive agents and biotherapies.

Aims and methods: The aim of this study was to assess the risk of serious and opportunistic infections associated with thiopurines monotherapy, anti-TNFs monotherapy and the combination of both treatments (combotherapy).

Results: Of the initially 756 included patients with confirmed IBD, 599 (79%) patients further treated with IMMs and 97%, 96% and 92% at 1, 2, and 5 years in controls, respectively (p<0.013). Cancer-free survival was 99%, 98% and 97% at 1, 2, and 5 years (hazard ratio and confidence interval 95% 1.31 (1.14–1.51), HR95%: 2.12 (1.49–3.00), respectively), while exposure to anti-TNFs was associated with an increased risk of serious and opportunistic infections compared to anti-TNFs exposure in patients aged 18–64 years (hazard ratio and confidence interval 95% (HR95%) 1.74 (1.20–2.52)). Similar results were observed in a sensitivity analysis conducted in incident patients.

Conclusion: Thiopurines, anti-TNFs monotherapy and combotherapy were all associated with an increased risk of serious infections in IBD patients compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs than with thiopurines and the risk of serious and opportunistic infections is higher with combotherapy than with anti-TNFs. The risk of serious and opportunistic infections should be taken into consideration and weighed against potential benefits of anti-TNFs.

Disclosure of interest: F. Carbonnel: Franck Carbonnel had consulting fees from Tenebenth, Osuka, Vífor, and lecture fees from Hospira. All other authors have declared no conflicts of interest.

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Disclosure of interest: All authors have declared no conflicts of interest.

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Disclosure of interest: All authors have declared no conflicts of interest.

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Disclosure of interest: All authors have declared no conflicts of interest.

Contact E-mail Address: julienn.kirchgesner@gmx.com

Disclosure of interest: All authors have declared no conflicts of interest.
Table: Hazard ratios for any serious or opportunistic infections according to medication exposure

<table>
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<tr>
<th>Follow-up year</th>
<th>UC Men</th>
<th>UC Women</th>
<th>CD Men</th>
<th>CD Women</th>
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<tr>
<td>5</td>
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<td>10</td>
<td>5</td>
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<td>20</td>
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</tr>
</tbody>
</table>

**Serious infections, all**

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>N (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–64 years</td>
<td>361</td>
<td>1.87 (1.00–3.47)</td>
<td>1.17 (0.46–2.97)</td>
</tr>
<tr>
<td>65 years</td>
<td>184</td>
<td>4.18 (1.98–8.84)</td>
<td>2.82 (1.07–7.44)</td>
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**Serious infections, excluding GI infections**

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>N (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–64 years</td>
<td>184</td>
<td>5.30 (4.13–6.81)</td>
<td>4.31 (3.48–5.36)</td>
</tr>
<tr>
<td>65 years</td>
<td>133</td>
<td>0.94 (0.81–1.10)</td>
<td>0.89 (0.74–1.06)</td>
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**Opportunistic infections, all**

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>N (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
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<tr>
<td>18–64 years</td>
<td>133</td>
<td>4.00 (3.48–4.53)</td>
<td>3.57 (3.08–4.11)</td>
</tr>
<tr>
<td>65 years</td>
<td>60</td>
<td>1.31 (1.20–1.42)</td>
<td>1.09 (0.87–1.38)</td>
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**Opportunistic infections, excluding mycobacterial infections**

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>N (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
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</thead>
<tbody>
<tr>
<td>18–64 years</td>
<td>133</td>
<td>2.50 (2.12–3.00)</td>
<td>2.12 (1.49–2.80)</td>
</tr>
<tr>
<td>65 years</td>
<td>60</td>
<td>0.73 (0.62–0.87)</td>
<td>0.74 (0.61–0.91)</td>
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**Serious infections, all**

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>N (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–64 years</td>
<td>361</td>
<td>1.29 (1.20–1.39)</td>
<td>1.27 (1.15–1.59)</td>
</tr>
<tr>
<td>65 years</td>
<td>184</td>
<td>3.02 (2.65–3.54)</td>
<td>2.62 (2.30–3.02)</td>
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**Serious infections, excluding GI infections**

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>N (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
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</thead>
<tbody>
<tr>
<td>18–64 years</td>
<td>184</td>
<td>3.20 (2.93–3.54)</td>
<td>2.94 (2.59–3.31)</td>
</tr>
<tr>
<td>65 years</td>
<td>133</td>
<td>3.32 (3.12–3.53)</td>
<td>2.97 (2.73–3.23)</td>
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**Opportunistic infections, all**

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>N (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–64 years</td>
<td>133</td>
<td>3.20 (3.00–3.42)</td>
<td>2.85 (2.63–3.11)</td>
</tr>
<tr>
<td>65 years</td>
<td>60</td>
<td>3.13 (2.96–3.30)</td>
<td>2.78 (2.60–3.00)</td>
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</tbody>
</table>

**Opportunistic infections, excluding mycobacterial infections**

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>N (%)</th>
<th>Crude Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
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<tbody>
<tr>
<td>18–64 years</td>
<td>133</td>
<td>2.40 (2.12–3.00)</td>
<td>2.40 (2.12–3.00)</td>
</tr>
<tr>
<td>65 years</td>
<td>60</td>
<td>1.64 (1.40–2.00)</td>
<td>1.52 (1.28–1.80)</td>
</tr>
</tbody>
</table>

**Table 1: N-IBDQ total scores and General Health dimensional scores**

<table>
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<th>Follow-up year</th>
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<th>CD</th>
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</thead>
<tbody>
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<td>20</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

**N-IBDQ: Inflammatory Bowel Disease Questionnaire (Norwegian version). SF-36: Short Form 36. GH: General Health dimension. SD: standard deviation, N: number of participants.**

**Introduction:** The aim of this study was to identify patient- and disease-related factors influencing the real-life long-term response of infliximab in CD patients. The inclusion criteria were patients who responded to an induction dose (5 mg/kg on week 0, 2 and 6), followed by scheduled IFX maintenance treatment were included. Exclusion criteria were prior infliximab use, ever episodic treatment, drug interval (>14 weeks), CD-related surgery during induction therapy and extra-intestinal manifestations as main indication. IFX failure was the primary endpoint, defined as stopping IFX due to one of the following reasons: 1) loss of response (LOR) despite treatment optimization, 2) presence of persistent antibodies towards infliximab (ATI), and 3) the need for IBD related surgery. Since 2010–2011, IFX and ATI serum concentrations at trough were measured in the majority of patients with an in-house-developed and clinically validated drug sensitive bridging enzyme-linked immunosorbent assay (ELISA). Therapeutic drug monitoring (TDM) was used as the tool for the use of serum IFX concentrations to support treatment decisions and optimization. Patient- and disease-related factors were used to identify independent predictors of IFX failure-free survival using Cox proportional hazards model and Kaplan-Meier analysis. Internal validation of the Cox regression analysis was performed with bootstrapping with 1000 replications. The c-statistic was used to assess the predictive accuracy of the regression model.

**Results:** A total of 261 CD patients were included in the final analysis. Median time on IFX was 2.4 [IQR 1.4–4.7] years, and 65 (24.9%) patients experienced IFX failure. Median age at start of IFX was 32.8 [22.6–44] years, after a median disease duration of 3.4 [0.7–13.6] years. In total, 59 (14.9%) patients received anti-TNF prior to IFX start (adalimumab or certolizumab pegol). TDM was used in 202 (77.4%) patients. Estimated 1, 5, and 10 year IFX failure-free survival was 93.7% (95% CI 90.7–96.7), 65.9% (58.3–73.5) and 58.2% (45.6–70.9), respectively. When combining all available IFX measurements during the follow-up of the study, median IFX concentrations were lower in patients who experienced IFX failure (3.1 [0.3–7.5] µg/mL) compared to patients who did not fail IFX (5.3 [3.1–8.4] µg/mL), t < 0.0001. Multivariate Cox regression analysis identified disease duration < 1 year (hazard ratio (HR) 2.5 (95% CI 1.2–5.2), p = 0.02), isolated L1 disease location (HR 2.0 (1.1–3.5), p = 0.002), and first IFX dose opted too low (HR 2.0 (1.1–3.9), p = 0.002) as independent predictors of IFX failure-free survival. These factors remained significant after internal validation with bootstrapping. This final model had a c-statistic of 0.80 which is considered as a well discriminating model. Stratifying patients into risk groups resulted in estimated 5 year IFX failure-free survival rates of 93.5% (95% CI 92.4–94.6) for the low risk group (0 or 1 risk factor), 79.3% (78.4–80.2) for the medium risk group (2–3 risk factors), and 26.3% (8.6–44.0) for the high risk group (4 or more risk factors) (p = 8x10⁻¹⁵). IFX concentrations at
week 14 were available in 199 (76.2%) patients, and in this subgroup of patients, IFX concentration at week 14 was also a significant predictor of IFX failure-free survival (HR 0.87 (0.80–0.94), p = 0.001).

Conclusion: This study identified several predictors of clinically relevant IFX failure. Stratifying patients according to the amount of risk factors can identify patients at high risk for IFX failure. Initiating IFX sooner rather than later and using TDM in this group to proactively strive for adequate drug concentrations may ensure optimal disease outcome.

Disclosure of Interest: T. Billiet: Lecture Fee: Ferring

M. Ferrante: - Research grant: Takeda - Speakers fee: Abbvie, Boehringer-Ingelheim, Chiesi, Falk, Ferring, Janssen, Mitsubishi Tanabe, MSD, Takeda, Tillots, Zeria - Consultancy: Abbvie, Boehringer-Ingelheim, Ferring, Janssen, MSD

G. Van Assche: - Financial support for research: Abbvie, MSD - Lecture fees: Abbvie, Ferring, MSD, Janssen

A. Giel: - Financial support for research: FWO grant G061712, Pfizer Hr grants - Speakers fee: MSD, Abbvie, Janssen Biologicals, Pfizer - Consultancy: UCB

S. Vermeire: - Grant support: Abbvie, MSD, Takeda - Lectures: Abbvie, MSD, Takeda, Ferring, Falk Pharma, Hospira, Tillots - Consultancy: Abbvie, MSD, Takeda, Ferring, Genentech/Roche, Shire, Pfizer, Galapagos, Mundipharma, Hospita, Celgene

All other authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016

14:00-15:30

MICROBIOTA AND DIET: FROM BENCH TO BEDSIDE – ROOM K

OP066 CYCLIC ENTERAL NUTRITION FOR THE MAINTENANCE OF REMISSION IN PEDIATRIC CROHN'S DISEASE PATIENTS

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2Hospital Domus Estefania, Lisbon/Portugal

3Paris-cite Hospital, Universite Sorbonne, Paris/Paris

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Introduction: Enteral nutrition (EN) is a well-established treatment in pediatric Crohn's disease (CD) for induction of remission. Stratifing patient findings, according to intestinal sampling site, the analysis revealed that only Ruminococcaceae resulted statistically increased in the colon. Tackling in account only colon biopsy samples, a significant reduc- tion of Prevotellaceae was observed in patients and an increment of Enterobacteriaceae was observed in CTRLs. Finally, stratifying patient findings, according to intestinal sampling site, the analysis revealed that only Ruminococcaceae resulted statistically increased in the colon. Tackling in account only colon biopsy samples, a significant reduc- tion of Prevotellaceae was observed in patients and an increment of Enterobacteriaceae was observed in CTRLs. Finally, stratifying patient findings, according to intestinal sampling site, the analysis revealed that only Ruminococcaceae resulted statistically increased in the colon. Tackling in account only colon biopsy samples, a significant reduc- tion of Prevotellaceae was observed in patients and an increment of Enterobacteriaceae was observed in CTRLs. Finally, stratifying patient findings, according to intestinal sampling site, the analysis revealed that only Ruminococcaceae resulted statistically increased in the colon. Tackling in account only colon biopsy samples, a significant reduc- tion of Prevotellaceae was observed in patients and an increment of Enterobacteriaceae was observed in CTRLs. Finally, stratifying patient findings, according to intestinal sampling site, the analysis revealed that only Ruminococcaceae resulted statistically increased in the colon. Tackling in account only colon biopsy samples, a significant reduc-

Disclosure of Interest: All authors have declared no conflicts of interest.

OP067 CHANGES IN MUCOSAL-ASSOCIATED INTESTINAL MICROBIOTA AND FECAL BACTERIA IN INFILMATING OR BOWEL DISEASE PATIENTS AND HEALTHY SUBJECTS: A PILOT STUDY

M. P.L. Guarino1, L. Puignedi1, A. Altomare2, F. Del Chierico2, S. Cocea1, M. Emerenziani1, B. Dalla Piccola1, M. Cicalà1, C. Crisci1

1Gastroenterology Unit, Campus Bio Medico University, Rome/Italy

2Parasitology and Metagenomics Unit, Bambino Gesù Children’s Hospital and Research Institute, Rome/Italy

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Introduction: The existing literature on the intestinal microbiota in inflammatory bowel diseases (IBD) reveals conflicting changes in microbiota composition in all patients, having most of studies been conducted only on fecal microbiota. Microbiota adherence to the gut mucosa might affect epithelial and mucosal function to a greater degree than fecal bacteria.

Aims & Methods: The aim of the present study was to evaluate the mucosal and fecal microbiota composition in healthy controls (CTRLs) and IBD patients, in a case-control study exploited by 16S rRNA targeted metagenomics-based approach (phylotyping, PH). Fecal specimens were collected from 14 IBD patients [10 Crohn’s disease (CD), 4 ulcerative colitis (UC)], and from 11 healthy subjects [7 CTRLs]. The study did not change the bacterial species obtained during colonoscopy from the terminal ileum, and descending colon. PH was assessed by pyrosequencing as follows. All patients were in wash-out from antibiotics, probiotics and corticosteroids. Genomic DNA was isolated from the entire set of samples. The VI-V3 region of 16S rRNA was amplified on a 454-Junior Genome Sequencer. Reads were analyzed by Quantitative Insights into Microbial Ecology (QIIME, v.1.8.0), grouped into operational taxonomic units (OTUs) at a similarity level of 0.97% by PyNAST for taxonomic assignement, and aligned by UCLUST for OTUs matching against Greengenes database (v. 13.8).

Results: In adult IBD patients colonic biopsies showed a statistically significant increase of Proteobacteria and decrease of Firmicutes and Actinobacteria, compared to CTRLs. The microbiota analysis of stool samples from IBD patient showed an increment of Proteobacteria and decrease of Bacteroidetes, the difference was not significant compared to CTRLs. Particularly, a predomi-

nent presence of Enterobacteriaceae in IBD and a prevalent presence of Ruminococcaceae, Rikenellaceae and Prevotellaceae in CTRLs were prevalent (P < 0.05). The study did not change the bacterial species obtained during colonoscopy from the terminal ileum, and descending colon. PH was assessed by pyrosequencing as follows. All patients were in wash-out from antibiotics, probiotics and corticosteroids. Genomic DNA was isolated from the entire set of samples. The VI-V3 region of 16S rRNA was amplified on a 454-Junior Genome Sequencer. Reads were analyzed by Quantitative Insights into Microbial Ecology (QIIME, v.1.8.0), grouped into operational taxonomic units (OTUs) at a similarity level of 0.97% by PyNAST for taxonomic assignement, and aligned by UCLUST for OTUs matching against Greengenes database (v. 13.8).

Disclosure of Interest: All authors have declared no conflicts of interest.

OP068 BACTERIOPHAGE THERAPY: A NEW STRATEGY TO TARGET ADHERENT-INVASIVE ESCHERICHIA COLI BACTERIA IN THE GI TRACT OF CROHN’S DISEASE PATIENTS

M. Galitri1, L. De Sordi2, A. Sivignon2, A. De Vallerie2, D. Maura3, C. Neuf3, O. Rahmoun4, K. Wannerberger5, P. Desreumaux5, N. Barnich6, E. Debarboux7

1Dept Of Microbiology, Institut Pasteur, Molecular Biology of the Gene in Extremebipiles Unit, Paris/France

2Institut d’Anevrage Inserm U921, Clermont-Ferrand/France

3Universite Lille Nord De France, Division of Bacteriology, Lille/France

4Univ. Lille, Inserm, LIRIC, UMR965, Lille/France

5Feering Pharmaceuticals, Saint-Prey/Switzerland

6Universite Lille, Chü Lille, LIRIC UMR965, Claude Huriez hospital, Lille/ France

Contact E-mail Address: adelina.sivignon@u-clermont1.fr

Introduction: Adherent-invasive Enterichia coli (AIEC) are abnormally predomi-

nant on Crohn’s disease (CD) ileal mucosa. AIEC are pathobiont bacteria able to induce inflammatory responses that could initiate or perpetuate the chronic gut inflammation. Antimicrobial treatments, such as bacteriophages (viruses infecting bacteria) represent a way to eliminate these bacteria from the GI tract without disturbing the microbiota homeostasis. Here, we aimed to evaluate the therapeutic potential of bacteriophages to reduce AIEC colonization associated to intestinal diseases. Antibacterial treatments, such as bacteriophages (viruses infecting bacteria) represent a way to eliminate these bacteria from the GI tract without disturbing the microbiota homeostasis. Here, we aimed to evaluate the therapeutic potential of bacteriophages to reduce AIEC colonization associated to intestinal diseases.

Aims & Methods: Three bacteriophages were selected to efficiently target AIEC isolated from CD patient. Efficacy of this bacteriophage cocktail was investigated using two in vivo experimental models: transgenic mice expressing CEACAM6 colonized by AIEC strain LF82 and the DSS chemically-induced colitis model infected with AIEC strain LF82.

Results: In LF82-colonized CEACAM6-expressing mice, 24h after the oral administration of AIEC, lesion index increased in the colon. This study demonstrates for the first time prolonged clinical, biologi-

cal remission and improved growth in pediatric CD patients treated only with cyclic enteral nutrition. Cyclic EN can be an efficacious non pharmacological treatment of Crohn’s disease patients potentially acting ahead of the inflamma-
tory cascade in the intestinal mucosa. A sufficiently power randomized controlled trials is currently conducted by the GETAID pediatrique to confirm this pilot study.

Disclosure of Interest: F. Ruemmele: Nestle Nutrition Institute, Nestle Health Science

All other authors have declared no conflicts of interest.

"Microbiota and Diet: From Bench to Bedside – Room K" is an event that occurred on Monday, October 17, 2016, from 14:00 to 15:30. The discussions centered around the role of microbiota and diet in the maintenance of remission in pediatric Crohn’s disease patients and its implications for patients with inflammatory bowel disease (IBD). The presentations included studies on the impact of cyclic enteral nutrition on remission, the microbiota changes associated with IBD, and the potential use of bacteriophages to target adherent-invasive Escherichia coli (AIEC) bacteria in the gut of Crohn’s disease patients. The studies highlighted the importance of understanding the microbiome’s role in disease management and the need for further research in these areas.
concentration of LF82 bacteria has significantly dropped by two log in the bacteriophage group and stays significantly lower than in control group four days post-treatment, without any additional bacteriophage administration demonstrating the benefit of self-amplification of bacteriophages over time. Furthermore, we found that administration of the cocktail during the first day reduces progressively over a period of five days the colonization level of LF82 bacteria through the entire gut. In addition, bacteriophage treatment reduced colitis symptoms in the DSS-induced model, with a reduction of LF82 bacteria levels in feces, compared to the control group. Then, we showed that bacterio-

phages were driving a long-term digestive tract decolonization of AIEC LF82 bacteria which in turns reduces colitis symptoms.

Conclusion: Bacteriophages targeting AIEC bacteria with high efficacy in murine models suggest that such a treatment could reduce AIEC-associated symptoms in CD patients, providing an incentive to initiate clinical studies. The use of bacterio-

phages proves for the first time a new “microbiota friendly” way to efficiently target gut pathogens.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP009 CIPROFLOXACIN RESISTANCE IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH ESBL-PRODUCING ENTEROBACTERIACEAE COLONIZATION

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Introduction: Ciprofloxacin is one of the most frequently used antibiotics in hospitalized inflammatory bowel disease (IBD) patients. In the last few years an emerging resistance to ciprofloxacin, ranging from 43% to 82%, has been described in extended-spectrum beta-lactamase (ESBL)-producing bacteria colo-

nizing the gut [1, 2]. The objective of this study was to evaluate the gut colonization with ESBL-producing Enterobacteriaceae in IBD patients, resistance to ciprofloxacin and bacterial plasmid genes associated with that.

Aims & Methods: All consecutive IBD outpatients and IBD inpatients with confirmed ulcerative colitis (UC) and Crohn’s disease (CD) hospitalized in Riga East Clinical University Hospital 2012–2015 were collected, Enterobacteriaceae were cultured and analyzed for ESBL presence according to EUCAST guidelines, resistance to ciprofloxacin and bacterial plasmid genes CTX-M, TEM and SHV were detected.

Results: A total of 86 patients with confirmed IBD diagnosis were included in the study – 65 (75%) with UC, 21 (24%) with CD. We found that 7 (11%) of the UC patients and 2 (10%) of the CD patients were colonized with ESBL producing Enterobacteriaceae. The isolated ESBL producing strains from UC patients included Escherichia coli (n = 5), Klebsiella oxytoca (n = 1) and Escherichia her-

manii (n = 1). The isolated ESBL-producing Enterobacteriaceae from CD patients included Escherichia coli (n = 2). The isolated bacterial plasmid genes associated with ESBL production in 1 UC were CTX-M and TEM (n = 7) and 100% TEM (n = 2; 29%), SHV (n = 1; 14%), in CD – TEM (n = 2; 100%), TEM (n = 1; 50%). In UC 4 (57%) of the isolated ESBL-producing Enterobacteriaceae were resistant to ciprofloxacin. In CD all of the ESBL producing Enterobacteriaceae were sensitive to ciprofloxacin. In 1 case of ESBL resistance CTX-M, TEM and SHV gene combination was observed, in 1 case CXT-M and TEM gene combination was observed and in 2 cases only CXT-M gene was present.

Conclusion: 1. High gut colonization rate (11%) with ESBL-producing bacteria in UC patients, mostly E. coli, expressing CXT-M gene. 2. High resistance to cipro-

floxacin (57%) in UC patients. 3. CXT-M gene associated with resistance to ciprofloxacin.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

1. Lübbert, Christoph, et al. “Colonization with Extended-Spectrum Beta-


OP070 CARD9 IMPACTS COLITIS BY ALTERING GUT MICROBIOA METABOLISM OF TRYPOTHIOPAN INTO ARYL HYDROCARBON RECEPTOR LIGANDS

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Introduction: Inflammatory bowel diseases (IBD) develop as a result of combination of genetic predisposition, dysbiosis of the gut microbiota, and environ-

mental influences. Caspase recruitment domain 9 (CARD9), one of the numerous IBD susceptibility genes, encodes an adenylate receptor for innate immunity toward a wide range of microorganisms. Card9−/− mice are more susceptible to colitis as a result of impaired of the IL-22 pathway1. Our aim was to explore the role of the gut microbiota in the susceptibility of Card9−/− mice to colitis.

Aims & Methods: Germ-free (GF) C57BL/6 wild-type (WT) mice were inoculated by oral gavage with fresh stools from conventional WT (WT→GF) or Card9−/− (Card9−/−→GF) mice. Colitis was induced by DSS. AHK activity in intestinal content was determined using a reporter cell line. Immune response was assessed at transcripts level, at the protein level and at the cellular level using flow cyto-

metry. Patients with IBD were genotyped for the major IBD-associated SNPs including CARD9. Statistical analysis was performed using parametric or non-

parametric tests as appropriate.

Results: Bacterial and fungal gut microbiota of Card9−/− mice (assessed by 16s and ITS2 sequencing) were altered compared to WT mice. Card9−/−→GF mice were more susceptible to colitis than WT→GF with impaired recovery. Moreover, IL-22 defect was observed in Card9−/−→GF mice at the gene expres-

sion and protein levels in the colon and in MNLs. IL-22 production by T helper 2 cells, dendritic cells, lymphoid tissue inducer cells, and CD3+CD4+ NKp46+ innate lymphoid cells was decreased in stools of Card9−/−→GF and Card9−/− mice. Moreover, feces from Card9−/− and Card9−/−→GF mice were defective in their ability to activate AHR. In Card9→GF mice, susceptibility of colitis, and IL-22 defect were rescued after treatment with AHR agonist (6-formylindolo[3,2-b]carbazole), or inoculation with three Lactobacillus strains with strong AHR activity. These effects were abrogated in the presence of AHR antagonist (CH223191). Reduced production of AHR ligands was also observed in the microbiota from patients with IBD, particularly in those with CARD9 risk alleles.

Conclusion: Card9 deletion has an effect on the gut microbiota in mice and its transfer to WT GF recipient is sufficient to recapitulate the defective IL-22 activation and increased sensitivity to colitis observed in Card9−/− mice. These alterations were due to an impaired ability of the microbiota of Card9−/− mice to catabolise tryptophan into AHR ligands. Our results are relevant to humans, as impaired microbial production of AHR ligands was observed in patients with IBD. Thus, defects in expression of factors involved in innate immunity, such as CARD9, can shape an altered microbiota, which can then modify the host gut microbiota functions, such as ability to produce AHR ligands, is an attractive strategy in IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


OP071 FAECAL MICROBIOTA TRANSPLANTATION (FMT) IN ULCERATIVE COLITIS (UC) IS ASSOCIATED WITH SPECIFIC BACTERIAL CHANGES: STOOL AND COLONIC MUCOSA 16S MICROBIOTA ANALYSIS FROM THE RANDOMISED CONTROLLED STUDY FOCUS


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Introduction: In a randomised placebo-controlled trial, intensive FMT therapy for active ulcerative colitis (UC) was significantly superior to placebo, producing a clinical response in > 50% and clinical remission with endoscopic remission or response in 27% of patients (ECCO 2016 & DDW 2016)1. This part of the FOCUS study aimed to characterise the microbial changes underlying FMT in UC, and identify those predictive of, and associated with, response and lack of response.

Aims & Methods: Active UC patients were randomised to intensive FMT or placebo enemas 5 days/week for 8 weeks, with placebo-treated patients subse-

quently offered 8 weeks of open label FMT. Each FMT enema was derived from randomised mixed stool samples were collected from patients at week 0, 4

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RLN-MNP showed specific binding and uptake to TGF-β. On the other hand, unconjugated RLN induced systemic side effects by inducing gated RLN, increased Nitric oxide release by significant up-regulation of iNOS. ECM production and angiogenesis. Importantly, RLN-MNP, but not unconjugated RLN and RLN-MNP strongly attenuated fibrosis by inhibiting HSC activation, and RLN has very poor pharmacokinetics and administration of high or frequent doses to the liver function. Relaxin (RLN) has been shown to inhibit HSC activation and PEGylated magnetic nanoparticles (RLN-MNP) and characterized the size, and colonic mucosal microbiota. These findings may be important in both understanding the pathophysiology of the microbiota in UC and shaping future bacterial therapy.

Disclosure of Interest: T.J. Borody: Thomas J. Borody has an interest in the material therapy.

Reference

MONDAY, OCTOBER 17, 2016 14:00–15:30
FREE PAPER SESSION: THE FUTURE OF DIAGNOSTIC IN HBV AND UPPER GI – ROOM N3

OP073 A QUANTITATIVE IMAGING PLATFORM TO REAL-TIME MEASURE SPECIFIC ROS LEVELS IN LIVER DISEASES
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Introduction: Reactive oxygen species (ROS) are chemically reactive molecules containing oxygen, including the peroxide (H₂O₂), hypochlorous acid (HOCl), singlet oxygen (¹O₂), and superoxide (O₂⁻). ROS have been reported to play an important role in the development of liver diseases. For example, H₂O₂ can activate hepatic stellate cells in liver fibrosis. During hepatic ischemia-reperfusion injury, HOCl is generated by neutrophils and diffuses into hepatocytes, causing oxidant stress-mediated injury. O₂⁻ can react with nitric oxide to form peroxynitrite to modify the cell structure and function of proteins in diseased liver. Various methods have been developed to monitor ROS generation in the liver, but the presence of different cellular sources for ROS as well as the distinct chemical properties of specific ROS may lead to conflicting results. Most developed ROS-detection probes were difficult to be distinguished from endogenous fluorophores and only can be employed under one-photon microscopy. Thus, an optimal strategy for precise real-time ROS detection is highly required to rapidly and accurately reveal the cellular microenvironment in liver diseases in clinic.

Aims & Methods: Four different two-photon fluorescent probes were designed and synthesized for selective detection of chemically reactive molecules of thiol and ROS including glutathione (GSH), H₂O₂, HOCl, and O₂⁻. Mouse models of hepatic steatosis, fibrosis, and ischemia-reperfusion injury were developed to mimic human liver diseases. After sacrificing the animals, unfixed live liver tissues were collected and incubated with each probe at the final concentration of 50 to 100 μmol for 10 min, and then imaged using multiphoton microscopy (JenLab GmbH, Jena, Germany).

Results: Each probe exhibited a strong positive fluorescent response only in the presence of its specific chemically reactive molecule, whereas negligible fluorescent signals were observed upon the additions of other reactive oxygen/nitrogen species and metal ions. There was a good linear relationship between the probe response and ROS concentration and the control. The concentration of each specific ROS was first calculated based on the intensity of images at the cellular level.

Conclusion: We developed a quantitative imaging platform to real-time measure specific ROS changes in liver diseases at the cellular level. This technique can be used to investigate ROS-mediated liver injury and predict treatment response in human liver biopsy, and can be readily extended to examination of diseases and injury of other organs. We anticipate that in the near future this quantitative imaging platform will be evaluated from bench to bedside, leading to real-time monitoring of cellular microenvironment in human diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
OP074 RANDOMIZED CONTROLLED TRIAL (RCT) OF DOPPLER ENDOSCOPIC PROBE (DEP) FOR BLOOD FLOW DETECTION IN SEVERE NON-VARICEAL UGI HEMORRHAGE (NVUGH)

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Introduction: For decades, stigmata of recent hemorrhage (SRH) in ulcers & NVUGH have been used to guide endoscopic hemostasis. Arterial blood flow underlying SRH is rarely monitored, yet determines rebleed risk after treatments. Aims & Methods: In a RCT, our primary aim was to compare 30-day rebleed rates of index lesions for patients treated with Standard vs. DEP guided endoscopic hemostasis. Patients with severe inpatient or outpatient start of UGHI (clinical signs, hemo-globin – Hgb - drop of > 2 gms from baseline, & RBC transfusions) were randomized at urgent endoscopy if they had benign appearing ulcers & some SRH (active arterial bleed, non-bleeding visible vessel - NBV, or adherent clot, oozing without other SRH, or flat spot) or Dieulafoy’s lesions or Mallory Weiss tears- MWT (with active bleeding or NBV). For Standard treatment, hemoclip-ping &/or multipolar probe electrocoagulation (MPEC-large probe) with or without dilute epinephrine injection was used without DEP & visual end points were control of bleeding, flattening VVs, & a foot-print at the SRH. For the DEP group, SRH & lesion base were interrogated for underlying blood flow at < 4 mm deep settings with an FDA approved control unit & disposable DEP probe (Vascular Technology, Nashua, NH). Then Standard RX was applied on & out from the SRH, where the artery was traced. DEP was used to recheck if & residual blood flow was detected. Standard group patients with flat spots were not treated endoscopically, but DEP patients were if they had blood flow detected. All patients with ulcers & Dieulafoy’s lesions received high dose PPI infusion X 72 hours & then BID for 30 days. MWT patients were treated with anti-emetics & BID PPI. Rebleeding was determined by a > 2 gm decrease of Hgb, with clinical signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients were followed prospectively by research coordinators who recorded routine 30 day outcomes.

Results: All blood flow detected by DEP was reproducible & arterial. For 148 patients randomized, see the Table for 30 day rebleed rates by SRH. There was a significant difference in rebleed rates (15.2% higher) in Standard group vs. DEP group (p = 0.02138) & surgery (4/76 vs. 8/72; p = 0.0484). 1 perforation occurred in the Standard group & none in the DEP group.

Non-Variceal UGIB Doppler Probe RCT - Primary Outcome of 30 day Rebleeds from the Same Lesion

<table>
<thead>
<tr>
<th>Stigmata</th>
<th>Standard</th>
<th>DEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Arterial</td>
<td>5/10 (50.0%)</td>
<td>4/14 (28.6%)</td>
</tr>
<tr>
<td>NBV</td>
<td>7/27 (25.9%)</td>
<td>4/26 (15.4%)</td>
</tr>
<tr>
<td>Adherent Clot</td>
<td>4/16 (25%)</td>
<td>0/13 (0%)</td>
</tr>
<tr>
<td>Flat Spots</td>
<td>3/16 (18.8%)</td>
<td>0/15 (0%)</td>
</tr>
<tr>
<td>Oozing bleeding</td>
<td>1/7 (14.3%)</td>
<td>0/4 (0%)</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td>20/76 (26.3%)</td>
<td>8/72 (11.1%)*</td>
</tr>
</tbody>
</table>

*p = 0.02138 by Fisher Exact test

Conclusion: In a RCT of patients with severe NVUGIH, use of Doppler probe as a guide to endoscopic hemostasis significantly reduced 30 day rebleed & surgery rates compared to Standard, visually guided hemostasis. We now recommend DEP (along with SRH) as a new guide for risk stratification & definitive endoscopic hemostasis in patients with severe NVUGIH. RCT was supported by a VA Caregiver Research Grant in part by NIH-NIDDK. AM 41301 CURE DRRC-Human Studies Core. Registered with ClinicalTrials.gov as Project CLIN-013-07F.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. Fox et al., DDW 2014.
Aims & Methods: This was a prospective observational study performed at a single tertiary referral center. The subjects are 72 lesions of 67 patients with gastric neoplasm. We are indicated of the endoscopic submucosal dissection (ESD), and were given pre-ESD endoscopy in our hospital from September 2014 to February 2016. Firstly we observed the lesions by magnifying endoscopy with LCI+AIM method and diagnosed using VS classification system1). Secondly we observed the lesions by magnifying endoscopy with LCI+AIM method and diagnosed using VS classification system. Furthermore, we classified the visualization ability of the surface fine structure in Clear, Visible, and Invisible and evaluated it. Finally, we carried out ESD and compared the image with the histopathology.

Results: By the pathology results, 60 lesions were gastric cancer and 12 lesions were gastric adenoma. The differentiation ability of a cancer and the non-cancer (adenoma) did not have the significant difference between the ESD and AIM. ESD and AIM were used and compared together. AIM and ESD were used together in 33 lesions, 34 lesions were visible, 5 lesions were invisible by AIM. Furthermore, we classified the visualization ability of the surface fine structure in Clear, Visible, and Invisible and evaluated it. Finally, we carried out ESD and compared the image with the histopathology.

Conclusion: We aimed to investigate whether cancer cell-derived exosomal miRNA could modulate cancer progression and metastasis and can be used as a diagnostic marker. In this study, we used miRNA microarray technology to identify exosomal miRNAs that were differentially expressed in GC patients and controls. We further examined the biological function of exosomal miR-21 on cell viability, apoptotic death and metastasis in human GC cells and explored the possible downstream mechanism. We also included another 100 GC patients and 100 controls to study whether exosomal miR-21 could be used as a potential biomarker.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Introduction: Recent material and technical development enables us to get many thousands of proteomes as a source for gastric cancer (GC). Accurate diagnosis is thus needed to choose an optimal treatment for GC, however, the current imaging diagnosis is not enough to identify incurable factors including peritoneal metastasis and local invasion. We have previously reported the usefulness of urinary biomarkers for diagnosis of GC. With the goal of discovering non-invasive biomarkers for progression and incurability of GC, we conducted this study using urine samples from GC patients and healthy control. Aim: The objective of this study was to find a potential biomarker for distinguishing operability of GC with an area under the curve (AUC) of more than 0.80.

Aims & Methods: We conducted a protease protein array analysis to identify potential candidate biomarkers, and three proteins were found to be elevated in the urine of advanced GC patients compared to early GC patients. Among them, urinary kallikrein-10 (KLK10) and proteinase 3 were positively associated with tumor stage progression. Moreover, urinary KLK10 was significantly elevated in the urine of inoperable GC patients compared to operable GC patients (uKLK10: median, 33.5 ng/ml vs. 10.8 ng/ml; P = 0.006), and disease-free survival (DFS) was significantly lower for GC patients with high uKLK10 compared to low uKLK10 (HR: 2.3 (95%CI, 1.23–5.21); P = 0.007).

Conclusion: Urinary KLK10 is a promising non-invasive biomarker for incurable GC.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Acknowledgement: This work was supported by JSPS KAKENHI grant number 15K09447.

Table: The table provides IBS prevalence rates (% by sex and age groups) in the US, UK and Canada survey samples (without census weighting).

Rome III IBS

<table>
<thead>
<tr>
<th>Age 18–34</th>
<th>Age 35–49</th>
<th>Age 50–64</th>
<th>Age 65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Females (n = 962)</td>
<td>15.6</td>
<td>16.6</td>
<td>13.7</td>
</tr>
<tr>
<td>US Males (n = 987)</td>
<td>7.2</td>
<td>9.3</td>
<td>8.4</td>
</tr>
<tr>
<td>UK Females (n = 976)</td>
<td>14.2</td>
<td>13.4</td>
<td>15.1</td>
</tr>
<tr>
<td>UK Males (n = 1018)</td>
<td>4.9</td>
<td>7.2</td>
<td>9.5</td>
</tr>
<tr>
<td>Canada Females (n = 980)</td>
<td>14.6</td>
<td>16.3</td>
<td>15.4</td>
</tr>
<tr>
<td>Canada Males (n = 1008)</td>
<td>6.3</td>
<td>10.3</td>
<td>8.2</td>
</tr>
</tbody>
</table>

Rome IV IBS

<table>
<thead>
<tr>
<th>Age 18–34</th>
<th>Age 35–49</th>
<th>Age 50–64</th>
<th>Age 65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Females (n = 962)</td>
<td>6.6</td>
<td>10.6</td>
<td>6.9</td>
</tr>
<tr>
<td>US Males (n = 987)</td>
<td>8.8</td>
<td>3.6</td>
<td>4.2</td>
</tr>
<tr>
<td>UK Females (n = 976)</td>
<td>6.7</td>
<td>10.2</td>
<td>8.6</td>
</tr>
<tr>
<td>UK Males (n = 1018)</td>
<td>1.8</td>
<td>5.1</td>
<td>5.5</td>
</tr>
<tr>
<td>Canada Females (n = 980)</td>
<td>7.1</td>
<td>9.8</td>
<td>8.1</td>
</tr>
<tr>
<td>Canada Males (n = 1008)</td>
<td>2.5</td>
<td>5.4</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Conclusion: These first-ever national population prevalence estimates for Rome IV IBS showed that IBS prevalence and demographic distribution is equivalent in the US, UK and Canada, and confirm that the disorder is female-prevalent and less common in older individuals. IBS prevalence is significantly lower when Rome IV criteria are used than with Rome III, and the new criteria also change IBS subtype distribution, markedly reducing the IBS-M proportion. [Support: The Rome Foundation.]


Introduction: Gastroesophageal reflux disease (GERD) and irritable bowel syndrome (IBS) are gastrointestinal (GI) disorders affecting a large part of the general population, with relevant impact on quality of life and health care costs. To date, population- and clinical-based studies have reported a certain degree of overlap between GERD and IBS, which cannot be explained solely by chance. By means of multichannel intraluminal impedance and pH (MII-pH) monitoring, patients with proton pump inhibitor (PPI)-refractory heartburn can be distinguished into PPI-refractory GERD and functional heartburn (FH), the latter to be considered a functional GI disorder separate from GERD. Symptoms of IBS have not yet been assessed in patients with reflux symptoms as distinguished into GERD and FH. Recently, it has been reported that patients with GERD as well as patients with IBS have increased levels of anxiety, in turn associated with increased perception of symptoms and reduced quality of life. Again, the prevalence of anxiety in patients with reflux symptoms as clearly evidenced by GERD and FH has not yet been assessed.
Introduction: Irritable bowel syndrome (IBS) is characterised by many comorbid symptoms as well as core symptoms, all of which are relevant for the clinical management of this group of patients. However, the evolution of these symptoms over time is not adequately understood.

Aims & Methods: The aim of this study was to determine the probability of IBS-related symptoms to persist or subside over time. The study consisted of three parts. First, we addressed the question which factors can determine the probability of FH versus GERD in patients presenting with heartburn was built. Second, we used the five factors in a Monte Carlo simulation, generating a reference-table of probabilities for symptoms to persist or subside. Third, we differentiated between patients with FH diagnosis and patients with GERD diagnosis and was quantified by calculating the area under the ROC curve (AUC). A calculator to help clinicians in automatically computing the predicted probability of FH versus GERD in patients with heartburn was built (URL: http://app.calculeisd.com/#/calculator/2012).

Conclusion: FH overlaps more frequently with FH than with GERD, suggesting common pathways and treatment. The score derived from ISAAH predictive model allows a high level of suspicion for FH and can be used in clinical practice.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Probabilities for IBS-related symptoms to persist or subside over a five-year period.

<table>
<thead>
<tr>
<th>Symptom persists</th>
<th>Symptom subsides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability</td>
<td>95% CI</td>
</tr>
<tr>
<td>Depression</td>
<td>22% - 18% - 26%</td>
</tr>
<tr>
<td>Sense of coherence</td>
<td>21% - 18% - 24%</td>
</tr>
<tr>
<td>Coping resources</td>
<td>19% - 18% - 21%</td>
</tr>
<tr>
<td>GI-specific anxiety</td>
<td>16% - 14% - 18%</td>
</tr>
<tr>
<td>Quality of life</td>
<td>16% - 14% - 18%</td>
</tr>
<tr>
<td>GI symptom severity</td>
<td>12% - 10% - 14%</td>
</tr>
</tbody>
</table>

Conclusion: For the first time, we show that IBS-related symptoms develop differentially over time. GI symptoms had a high likelihood of subsiding over time, in contrast to depression, sense of coherence, and coping resources. We suggest more attention needs to be paid to the management of depression, and to providing tools for better coping resources in IBS patients.


R. O. Curve: Consultant/Advisory Board member for Almirall, Danone and Shire. M. Simrén: Restricted research grants from Danone, and Ferring Pharmaceuticals Advisory Board; Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Albiros, Glycom and Shire; Speaker for Tillotis, Takeda, Shire and Almirall.

All other authors have declared no conflicts of interest.

OP082 SYMPTOMS COMPATIBLE WITH FUNCTIONAL BOWEL DISORDERS IN PATIENTS WITH ULCERATIVE COLITIS IN DEEP REMISSION

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4Sahlgrenska Academy, University of Gothenburg Sahlgrenska Academy Dept. of Internal Medicine & Clinical Nutrition, University of Gothenburg/Gothenburg/Sweden
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Introduction: Several studies have reported high prevalence of symptoms compatible with irritable bowel syndrome (IBS) in patients with ulcerative colitis (UC) who are in remission. However, previous studies have not determined how these changes are a cause of these symptoms, and nothing is known about the prevalence of symptoms compatible with other functional bowel disorders (FBD) than IBS in this group of patients and the burden of these symptoms.

Aims & Methods: In a cross-sectional study, patients with UC (n = 291) were divided into active disease or deep remission (a total Mayo score ≤ 2, physicians global assessment = 0, rectal bleeding = 0 and an endoscopic subscore = 0, with no relapse during the 3-6th period prior to no FBD and other FBD groups, respectively). Patients completed the Rome III FBD module to define presence of symptoms compatible with FBD, and questionnaires to measure psychological distress (Hospital Anxiety and Depression Scale; HADS), stress (Perceived stress scale; PSS), GI symptom severity (GI Symptom Rating Scale; GSRS), somatic symptoms (Patient Health Questionnaire-15; PHQ-15), disease-specific quality of life (Inflammatory Bowel Disease Questionnaire; IBDQ), and general fatigue (Multidimensional Fatigue Inventory; MFI).

Results: Active UC was present in 159 patients (55%). The 132 patients (45%) in deep remission were assessed by the Rome III diagnostic criteria and 37% fulfilled criteria for a FBD. 18% IBS (11% IBS-M, 4% IBS-C, 3% IBS-D), 21% functional bloating, 6% functional diarrhea, 4% functional abdominal pain, and 2% functional constipation. Additionally, among the UC patients in deep remission who did not meet diagnostic criteria for a FBD, patients who fulfilled diagnostic criteria for IBS reported more severe psychological distress (p < 0.001), somatic symptoms (p < 0.001), and general fatigue (p = 0.004), as well as reduced quality of life (p < 0.001), and they tended to have higher levels of perceived stress (p = 0.06). One of these factors differed between patients who met diagnostic criteria for a FBD other than IBS and patients who did not meet diagnostic criteria for FBD. Age, disease duration, fecal calprotectin levels or high-sensitivity CRP did not differ between the groups. Overall GI symptom severity (GSRS total score) was highest in patients with symptoms compatible with UC (p < 0.01) vs no FBD and other FBD groups and intermediate in patients who fulfilled one of the other FBDs (p < 0.05 vs no

Table 1: Prevalence of symptoms compatible with FBD in patients with UC in deep remission.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI symptom severity</td>
<td>18%</td>
</tr>
<tr>
<td>Functional bloating</td>
<td>21%</td>
</tr>
<tr>
<td>Functional diarrhea</td>
<td>6%</td>
</tr>
<tr>
<td>Functional abdominal pain</td>
<td>4%</td>
</tr>
<tr>
<td>Functional constipation</td>
<td>2%</td>
</tr>
</tbody>
</table>

Conclusion: The prevalence of FBD in patients with UC in deep remission is poorly understood.

Disclosure of Interest: No conflicts to declare.
Conclusion: Symptoms compatible with functional bowel disorders in general, and not only IBS, are common in patients with UC in deep remission. However, the overall disease burden seems to be greater in patients with symptoms compatible with IBS than with the other FBDs. These observations are of great importance when managing patients with IBD to avoid escalating anti-inflammatory treatment, and instead focus on other treatment options to help these patients to manage their symptoms.

Disclosure of Interest: M. Simren: Unrestricted research grants from Danone, and Ferring Pharmaceuticals; Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Alibieco, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall.

B. Jønfeldt: Speaker for Abbvie, MSD and MIDEA.

O. Palsson: Salary support from research grants from Salix Pharmaceuticals, Takeda Pharmaceuticals and Ironwood pharmaceuticals, as well as honoraria for participation in educational programs supported by these companies.

W.E. Whitehead: Unrestricted research grants from Takeda Pharmaceuticals; Unrestricted educational grants from Takeda and Ferring Pharmaceuticals; Consultant/Advisory Board member for Ono and Ferring Pharmaceuticals and from Merck USA.

H. Törnblom: Consultant/Advisory Board member for Almirall, Danone and Shire.

L. Ohman: Unrestricted research grant from AstraZeneca; Consultant/Advisory Board member for Genetic Analysis; Speaker for Takeda and Abbvie.

H. Strid: Consultant/Advisory Board member for Takeda, Abbvie, Ferring Pharmaceuticals, Tillotts, MSD Speaker for Takeda, Abbvie, Ferring Pharmaceuticals, Tillotts, MSD and Shire.

Aims & Methods: The objective of this study was to assess healthcare resource utilisation associated with IBS-D among a sample of adults in the EU5 (Spain, France, Italy, Germany, United Kingdom). Respondents were identified from the 2013 National Health and Wellness Survey, a self-administered, internet-based survey. Diagnosed IBS-D patients were defined as those respondents who reported a physician diagnosis of IBS-D; undiagnosed IBS-D patients included respondents who reported experiencing IBS-D symptoms but did not self-report a physician diagnosis. Controls included all respondents without IBS (diagnosed or undiagnosed) or inflammatory bowel disease. IBS-D severity was evaluated based on a single item assessing disease severity (mild, moderate, or severe).

Healthcare resource utilisation was evaluated based on the number of patient-reported healthcare provider visits (any healthcare provider, gastroenterologist, or general practitioner [GP]), emergency room (ER) visits, and hospitalisations in the past 6 months. Descriptive statistics were used to examine sample characteristics. Bivariate analyses were used to compare resource use by IBS-D severity. To further assess the burden of IBS-D specifically, multivariable generalised linear models compared resource use across groups, controlling for demographic and health characteristics, including age, gender, and comorbidities.

Results: A total of 58,161 respondents were included (859 diagnosed IBS-D: 370 undiagnosed IBS-D: 56,932 controls). Overall, the mean age was 47 years, and 52.6% of respondents were female. Unadjusted analyses revealed that patients (diagnosed and undiagnosed) with moderate (n = 499) or severe (n = 110) IBS-D had significantly greater healthcare resource utilisation compared with patients with mild IBS-D (n = 620), including more visits to any provider (8.65 and 10.10 vs. 6.22; both p < 0.05), a gastroenterologist (0.22 and 0.35 vs. 0.08; both p < 0.05), and the ER (0.37 and 0.46 vs. 0.19; both p < 0.05). After controlling for demographic and health characteristics, diagnosed IBS-D patients had a significantly greater mean number of visits to any provider, a gastroenterologist, a GP, and the ER, compared with both controls and undiagnosed IBS-D patients (Table).

Conclusion: IBS-D patients utilised significantly greater outpatient healthcare resources compared with controls, with diagnosed patients using more resources than those who are undiagnosed. In addition, patients with moderate or severe IBS-D have the greatest healthcare resource utilisation. The substantial burden imposed by IBS-D patients on healthcare systems highlights the need for treatments to more effectively treat and manage IBS-D symptoms.

Disclosure of Interest: C. Tucker: Catherine Tucker is an employee of Allergan plc.

R. Liebert: Ryan Liebert is an employee of Kantar Health, which was contracted by Allergan plc for work relating to this study.

A36 United European Gastroenterology Journal 4(5S)
### Table

<table>
<thead>
<tr>
<th></th>
<th>Diagnosed IBS-D</th>
<th>Undiagnosed IBS-D</th>
<th>Controls (n = 56,932)</th>
<th>p-value: Diagnosed vs. controls</th>
<th>p-value: Diagnosed vs. undiagnosed</th>
<th>p-value: Undiagnosed vs. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any provider visits</td>
<td>7.23 (0.31)</td>
<td>5.17 (0.35)</td>
<td>4.14 (0.02)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.018</td>
</tr>
<tr>
<td>Gastroenterologist visits</td>
<td>19 (0.62)</td>
<td>0.01 (0.01)</td>
<td>0.03 (0.00)</td>
<td>0.001</td>
<td>0.014</td>
<td>0.007</td>
</tr>
<tr>
<td>General practitioner visits</td>
<td>2.69 (0.12)</td>
<td>2.06 (0.15)</td>
<td>1.70 (0.01)</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.007</td>
</tr>
<tr>
<td>Emergency room visits</td>
<td>0.27 (0.04)</td>
<td>0.12 (0.03)</td>
<td>0.17 (0.0)</td>
<td>0.002</td>
<td>0.012</td>
<td>0.264</td>
</tr>
<tr>
<td>Hospitalisations</td>
<td>0.14 (0.03)</td>
<td>0.08 (0.03)</td>
<td>0.11 (0.0)</td>
<td>0.099</td>
<td>0.148</td>
<td>0.430</td>
</tr>
</tbody>
</table>

**Disclosure of Interest:**

**Introduction:**

Hospitalisations 0.14 (0.03) 0.08 (0.03) 0.11 (0) 0.099 0.148 0.430

Emergency room visits 0.27 (0.04) 0.12 (0.03) 0.17 (0)

**Aims & Methods:**

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**Conclusion:**

The derived models presented good discriminative power in the prediction of outcomes. Bayesian models and risk matrices can be used to predict individualized probabilities, which can improve the information transmitted to patient regarding a posteriori probabilities and can aid in the decision process regarding allocation for endoscopic or surgical treatment. Additionally, a posteriori probabilities of adverse events can guide management after gastric ESD, namely regarding the timing of discharge from hospital.

**Disclosure of Interest:**

All authors have declared no conflicts of interest.

**Reference**


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**MONDAY, OCTOBER 17, 2016 14:00–15:30**

**WHAT IS NEW IN GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) – ROOM L7**

**OP085 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) AND GASTRECTOMY BASED ON INDICATIONS FOR ESD**


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**Introduction:**

Endoscopic submucosal dissection (ESD) has been established as a standard treatment modality of early gastric cancer (EGC), however, long term outcomes between ESD and gastrectomy were rarely reported, especially in terms of ESD criteria.

**Aims & Methods:**

This study aimed to compare long term outcomes between ESD and gastrectomy, and according to the histopathologic ESD criteria; absolute criteria (AC), expanded criteria (EC) and beyond expanded criteria (BEC). Between 2006 and 2012, 925 EGC patients were enrolled; ESD was performed in 468 patients, and gastrectomy in 457 patients.

**Results:**

Recurrent rate was 1.9% in ESD patients, 0.7% in gastrectomy patients, nor was significantly different between three criteria groups among total patients. Thus, ESD with EC or even BEC might be an alternative option in EGC patients who refuse gastrectomy or with high operative risk.

**Disclosure of Interest:**

All authors have declared no conflicts of interest.

**OP086 PREDICTING CLINICAL OUTCOMES OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION USING A BAYESIAN APPROACH**

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2Health Information and Decision Sciences Department, Faculty Of Medicine Of Porto and Cintesi- Center For Health Technology and Services Research, Porto, Porto, Centro Hospitalar São João, Porto/Portugal
3Cintesi - Health Information and Decision Sciences Department, Faculty Of Medicine of Porto, Porto/Portugal

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**Introduction:**

In patients with gastric superficial neoplasms, the probabilities of success and of adverse events influence the decision process regarding treatment allocation. These probabilities can be predicted using a priori patients’ and lesions’ factors. However, the knowledge of risk factors alone is not readily and completely usable by patients and clinicians in the decision process since it is difficult to predict the additive effect of risk factors in the outcome, in a given patient. Bayesian networks are increasingly used for clinical decision support since Bayesian statistical methods allow taking into account prior knowledge when analyzing data and can aid in capturing and reasoning with uncertainty in medicine.

**Aims & Methods:**

The aim of this study was to develop a Bayesian model and a computerized tool that can be used in clinical practice to predict outcomes after ESD and aid in the decision-making process. Methods: Data from 245 ESDs performed in our institution was collected, including pre-resection patient factors (age, sex, ASA, antithrombotics) and lesion factors (morphology, pre-resection biopsies). The two main endpoints were curative resection and post-procedural bleeding.

We defined curative resection as a resection meeting the standard or expanded criteria of the Japanese Gastric Cancer Treatment guidelines. For the analysis and model construction, morphology was recoded into polypoid (0-Ia, 0-Ib, 0-Ip), depressed (0-IIa+c, 0-IIa+c, 0-IIa and 0-II) and non-polypoid non-depressed (0-IIa, 0-IIb, 0-IIa+b). Univariate analysis was conducted with chi-squared test to identify associations between pre-treatment factors and the two endpoints, for a significance level of 5%. Logistic regression and Bayesian networks were then built for each outcome. Stratified 10-fold cross-validation was performed to assess the predictive accuracy and discriminative power (ROC curves) of the models. Clinical decision support was then enabled by the definition of risk matrices, direct use of Bayesian inference software and through the use of an online platform.

**Results:**

In our sample, 85% were curative resections and PPB occurred in 8%. In the univariate analysis, age > 62 (p = 0.039), male sex (p = 0.027), ASA status (p = 0.008), carcinoma histology (p = 0.001), polypoid or depressed morphology (p = 0.015) and lesion size greater than 20 mm (p = 0.006) were associated with non-curative resection, while age > 70 (p = 0.041), ASA status (p = 0.017), antithrombotic medication (< 0.001) and lesion size greater than > 20 mm (p = 0.026) were associated with PPB. Logistic regression and Bayesian models presented AUCs above 80% (in-sample) and 75% (cross-validation) on both outcomes. Lesions with cancer at biopsies, > 20 mm, proximal and polypoid are more prone to non-curative resection (table 1). Risk matrices for PPB were also defined yielding a posteriori probabilities of PPB < 5% in lesions < 20 mm in the absence of antithrombotic medications while the risk of PPB increased in greater lesions and in the presence of antithrombotic medications. The Bayesian network can be interactively used in clinical practice to estimate individual probability of outcomes after ESD. Table 1: Risk (a posteriori probabilities) matrix for curative resection based on morphology, localization, size and pre-resection histology, using a Bayesian model (cross-validation AUC = 78%, 95%CI = [75%, 81%]).
Introduction: Endoscopic submucosal dissection (ESD) is an effective treatment for gastric superficial neoplasms, being curative in 80-85%. Identification of risk factors for a non-curative resection is of importance to improve patient selection. Furthermore, it is important to evaluate the management after an unsuccessful treatment in order to assess the clinical outcomes of each option: follow-up, surveillance or surgical treatment. Moreover, patients with an early neoplastic lesion are at risk of developing metachronous lesions and endoscopic surveillance will be needed after endoscopic resection. The identification of risk factors for metachronous development is also important to adequate surveillance.

Aims & Methods: The aims of this study were to identify risk factors for non-curative resection and metachronous development and to evaluate management and outcomes after non-curative resection. Methods: Single centre assessment of a cohort of consecutive patients submitted to gastric ESD, with a minimum follow-up of 18 months. The Japanese Gastric Cancer Treatment Guidelines criteria were used in clinical practice; resections were also classified using the recently published European Society of Gastrointestinal Endoscopy univariate analysis. The endoscopic Grasp-and-Loop closure method is feasible, effective and safe for closing the gastric defect after EFR in patients. All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
OP090 A CLINICAL STUDY OF ENDOSCOPIC FULL-THICKNESS RESECTION BY SEROsa SEALING METHOD FOR SUBmUCOSAL INVASIVE GASTRIC CANCER WITHOUT SENTINEL NODE METASTASIS

H. Kitakata1, T. Itoh, S. Kinami, S. Azukisawa1, R. Kobayashi1, K. Hamada1, K. Kawaura1, T. Kosaka2
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Introduction: Due to recent advances in endoscopic technology, endoscopic full-thickness resection (EFTR) and laparoscopic and endoscopic cooperative surgery (LECS) are useful procedures to avoid excessive resection of the gastric wall and postoperative complications, such as stenosis or deformity, because the location of tumor can be confirmed endoscopically to determine an appropriate resection line. However, these methods have some disadvantages, such as loss of endoscopic view caused by collapse of the stomach and peritoneal infection or tumor dissemination by outflow of gastric juice. Thus, we developed new technique of EFTR, we called sealed EFTR, for sealing the serosa of stomach with silicon sheet to prevent collapse of the stomach and outflow of gastric juice.

Aims & Methods: We introduce our sealed EFTR technique and describe a clinical study of EFTR in patients with submucosal invasive gastric cancer who were diagnosed as negative for lymph node metastasis by laparoscopic sentinel lymph node biopsy. Patients: Between December 2012 and April 2016, 9 patients with clinical T1 gastric cancer, who were outside of indication of ESD, were enrolled in this study. Before surgery, written informed consent was obtained from each patient. All procedures were conducted in accordance with the ethical standards of the institution’s Committee on Human Experimentation. Results: In all cases, serosal incision was performed endoscopically. All lesions were located at the anterior or posterior wall of the stomach. Total resection time was 120 minutes and total operative time for each case was 90 minutes. Endoscopic cooperative surgery (LECS) were performed in 2 cases, and postsurgical infection was observed in 1 case.

Conclusion: Our sealed EFTR technique is a new technique to prevent leakage of gastric juice. This technique could be useful in cases with potential risk of leakage such as large tumors.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

M. Di Stefano, B. Valvo, M. Bergonzi, I. Benedetti, M. De Amici, C. Torre, G. Testa, E. Pagani, G. Marseglia, G.R. Corazza
1Department Of Internal Medicine, IRCCS S. Matteo Hospital Foundation, University of Pavia, Pavia/Italy
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Disclosure: The Rome Rules Committee recognizes two distinct subgroups of functional dyspepsia (FD): the postprandial distress syndrome (PDS) and the epigastric pain syndrome (EPS). The underlying pathophysiological mechanisms of these disorders are partially known. Recently, the worsening of hypersensitivity in the postprandial period was shown in PDS (1–2) and an impairment of gastric compliance was detected in EPS (2). Moreover, in FD patients an altered permeability of intestinal mucosa, an altered expression of cell adhesion proteins and the presence of mucosal infiltration of mast cells and eosinophils were shown (1), suggesting a role for inflammation and permeability alterations in the pathogenesis of this condition.

Conclusion: Our results show that in PDS the ingestion of a standard meal induces an inflammatory response and a secondary activation of the endogenous inflammatory axis, strictly correlated with symptom occurrence. Further studies are needed to confirm the role of the intestinal systemic inflammatory response in a condition characterized by low-grade inflammatory alterations.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. Farre, Gastroenterology 2013.

OP094 INFLAMMATORY AND ANTIOXIDANT RESPONSE FOLLOWING STANDARD MEAL CONSUMPTION IN PATIENTS WITH FUNCTIONAL DYSPEPSIA AND HEALTHY VOLUNTEERS

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2Experimentel Oto-rhino-laryngology, KU Leuven, Leuven/Belgium
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Disclosure: The Rome Rules Committee recognizes two distinct subgroups of functional dyspepsia (FD): the postprandial distress syndrome (PDS) and the epigastric pain syndrome (EPS). The underlying pathophysiological mechanisms of these disorders are partially known. Recently, the worsening of hypersensitivity in the postprandial period was shown in PDS (1–2) and an impairment of gastric compliance was detected in EPS (2). Moreover, in FD patients an altered permeability of intestinal mucosa, an altered expression of cell adhesion proteins and the presence of mucosal infiltration of mast cells and eosinophils were shown (1), suggesting a role for inflammation and permeability alterations in the pathogenesis of this condition.

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Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. Farre, Gastroenterology 2013.

Results:
1. Farre, Gastroenterology 2013.

Conclusion: Acutely administered LG decreases both antral and duodenal motility during the interdigestive state and delays gastric emptying after a standard liquid meal. However, at this dose it does not seem to influence gastric accommodation or hunger and satiety feelings.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. Farre, Gastroenterology 2013.
An effective GES reduced significantly the frequency of refractory symptoms prospectively, patients were implanted with an ENTERRA (R) device with or without surgical, was eligible. After a screening period of 4 months to assess symptoms prospectively, patients were implanted with an ENTERRA (R) device without surgery. Then each subject was randomized in a masked fashion to one of two treatment arms: 1) a control arm with the device activated, or 2) a treatment arm with the device activated. The greater symptomatic effect with an OFF period (median score: 2 vs 1, p = 0.003) after baclofen compared to placebo. The number of postprandial regurgitation symptoms marked by the patient tended to be lower in the baclofen treatment arm (p = 0.09). OTE was superior after baclofen compared to placebo (1 (0–2) vs. 0 (1–1), p = 0.04).

Conclusion: This study confirms that baclofen is an effective treatment option for patients with rumination syndrome, probably through its effect on LOS pressure.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP096 GASTRIC ELECTRICAL STIMULATION (GES) FOR REFRACTORY RUMINATION: RESULTS OF A PROSPECTIVE MULTICENTER RANDOMIZED DOUBLE-BLIND CONTROLLED CROSS-OVER TRIAL


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3) Gastroenterology, Grenoble university hospital, Grenoble, France
4) Diabetology Unit, Lille University Hospital, Lille, France
5) Gastroenterology Department, Names university Hospital, Names, France
6) Hepato-gastroenterology, Hopital Saint Andre’ - CHU de Bordeaux, Bordeaux, France
7) Surgery, Lille University Hospital, Lille, France
8) Gastroenterology, Hopital Nord, Amiens, France
9) Digestive Physiology, Hospices Civils de Lyon, Lyon, France
10) Diabetology Unit, Poitiers University Hospital, Poitiers, France
11) Franche-Comté, CHRU Jean Minjoz, Besancon, France
12) Gastroenterology Department, Rennes University Hospital, Rennes, France
13) Caremeau Gastroenterologie, Nimes, France
14) Dept. De Medecine Digestive, CH Estang Medecine Digestive, Clermont Ferrand Cedex, France
15) Dept. De Gastroenterologie, Hopital Louis Mourier, Colomiers, France
16) Gastroenterology, Chu Nord Hepato-Gastroenterologie, Grenoble Cedex, France
17) Dept. De Medecine Digestive, CHU Rennes Hospital C. Nicolle, Dept. de Physiologie Digestive, Rouen Cedex, France
18) Diabetology Unit, nancy university hospital, nancy, France

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Introduction: Open trials have suggested that GES could be effective for the relief of refractory rumination symptoms. The aim of this study was to evaluate the efficacy of GES in patients with refractory rumination symptoms, compared to placebo, in a prospective, randomized, double-blind, cross-over trial.

Methods: Patients with refractory rumination symptoms were randomized to receive GES (active treatment) or sham GES (placebo treatment) for 12 months, followed by a 6-month washout period. The primary endpoint was the reduction in the number of rumination episodes per week, compared to the baseline period, during the ON period.

Results: A total of 20 patients (mean age 42 years, range 18–61) were enrolled. The mean number of rumination episodes per week was significantly lower during the ON period compared to the OFF period (median score: 2 vs 1, p = 0.003) after baclofen compared to placebo. The number of postprandial regurgitation symptoms marked by the patient tended to be lower in the baclofen treatment arm (p = 0.09). OTE was superior after baclofen compared to placebo (1 (0–2) vs. 0 (1–1), p = 0.04).

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Disclosure of Interest: All authors have declared no conflicts of interest.

OP097 BCL-3 ACTS AS A PROTO-ONCOGENE IN PANCREATIC TUMOR StromA

2) Leiden University Medical Centre, Enschede, Netherlands
3) Maastricht University, University of Twente, Enschede, Netherlands
4) University of Twente, Enschede
5) Oncology-pathology, Karolinska Institute, Stockholm, Sweden

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Introduction: Pancreatic cancer is the deadliest tumor type with less than 5% survival rate, characterized by the presence of abundant stroma. Pancreatic stellate cells (PSCs) are the main precursor of myofibroblasts (cancer-associated fibroblasts) in tumor stroma, and therefore become a key target in pancreatic cancer (1, 2). These cells secrete growth factors, exosomes, cell matrix (ECM) and thereby aggravate tumor growth and metastasis (2). It is of paramount importance to find out new targets in stromal myofibroblasts which could be used for developing novel prognostic, diagnostic and therapeutic strategies.

Aims & Methods: In this study, we investigated integrin α5 (ITGA5), a receptor expressed in pancreatic cancer, as a novel therapeutic target. We first investigated the expression of ITGA5 in pancreatic cancer tissues and cell lines obtained from humans and a mouse model of pancreatic cancer. We then investigated the behavior of PSCs as well as PSC-induced paracrine effects on tumor cells.

Results: The expression of ITGA5 was investigated using immunohistochemical staining on tissue microarray consist of 137 patient samples of pancreatic tumors. In vivo, Panc-1 and PSCs were co-injected subcutaneously into the flank of SCID mice and investigated the expression of ITGA5 versus Panc-1 tumor alone. To elucidate the role of ITGA5, we knocked down the expression of ITGA5 in PSCs using siRNA-ITGA5. We investigated the phenotypic changes in ITGA5-KD PSCs after TGFβ activation, using immunostainings, quantitative PCR and RT2 profiler human fibroblast array. We also examined the paracrine effect of TGFβ-activated ITGA5-KD PSCs on the proliferation of pancreatic tumor cells (Panc-1).

Related Keywords: Pancreatic cancer, integrin ITGA5, TGFβ, Panc-1, pancreatic tumor, Paracrine effects, TGFβ activation.

Conclusion: This study confirms that baclofen is an effective treatment option for patients with rumination syndrome, probably through its effect on LOS pressure.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
14:00–15:30
BASIC MECHANISMS IN PANCREATIC CANCER - ROOM 1.86

OP097 BCL-3 ACTS AS A PROTO-ONCOGENE IN PANCREATIC TUMOR STRUMA

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4) University of Twente, Enschede
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Aims & Methods: In this study, we investigated integrin α5 (ITGA5), a receptor expressed in pancreatic cancer, as a novel therapeutic target. We first investigated the expression of ITGA5 in pancreatic cancer tissues and cell lines obtained from humans and a mouse model of pancreatic cancer. We then investigated the behavior of PSCs as well as PSC-induced paracrine effects on tumor cells.

Results: The expression of ITGA5 was investigated using immunohistochemical staining on tissue microarray consist of 137 patient samples of pancreatic tumors. In vivo, Panc-1 and PSCs were co-injected subcutaneously into the flank of SCID mice and investigated the expression of ITGA5 versus Panc-1 tumor alone. To elucidate the role of ITGA5, we knocked down the expression of ITGA5 in PSCs using siRNA-ITGA5. We investigated the phenotypic changes in ITGA5-KD PSCs after TGFβ activation, using immunostainings, quantitative PCR and RT2 profiler human fibroblast array. We also examined the paracrine effect of TGFβ-activated ITGA5-KD PSCs on the proliferation of pancreatic tumor cells (Panc-1).

Related Keywords: Pancreatic cancer, integrin ITGA5, TGFβ, Panc-1, pancreatic tumor, Paracrine effects, TGFβ activation.

Conclusion: This study confirms that baclofen is an effective treatment option for patients with rumination syndrome, probably through its effect on LOS pressure.
Conclusion: In conclusion, the present study reveals ITGA5 as a novel prognostic and therapeutic target in pancreatic tumor stroma. These data make a strong base to utilize this target for developing novel diagnostic and therapeutic strategies against pancreatic tumor.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.

OP100 ESSENTIAL ROLE OF THE NON-RECEPTOR TYROSINE-PHOSPHATASE PTPN11/SHP-2 IN ORGAN DEVELOPMENT AND HOMEOSTASIS OF THE MURINE EXOCRINE PANCREAS

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Introduction: The Src-homology-2 (SH2) domain containing protein tyrosine phosphatase SHP-2 is expressed ubiquitously and is involved in an array of intracellular signal transduction processes (Ras-Raf-MAPK, JAK-STAT, PI3K-Akt-mTOR, NFκB...). Thus, for instance, SHP-2 plays a role in cellular proliferation, survival, differentiation, migration and metabolism. The role of SHP-2 in organ development and homeostasis of the pancreas has so far not been explored.

Aims & Methods: Mouse models with pancreas specific deletion of SHP-2 (Ptf1a-CrePtenFlox/Flox) or lineage tracing allele (ACTB-TdTomato-EGFP) were used for analysis.

Results: Early embryologic Deletion of SHP-2 in the pancreas via Ptf1a-Cre present a lethal phenotype. However, adequate expansion of the exocrine compartment in the growing pancreas is impaired. In adult mice, no organ weight is reduced by about 50%, compared to uncombined littermate-controls. In the organ growth phase, centro-(acinar) cells display enhanced cell death (necrosis and apoptosis) which is accompanied by markedly reduced proliferation. In aged SHP-2−/− mice acinar lobuli are consecutively replaced by adipocytes. Lineage-tracing experiments provide insight into the origin of this cell population (invasion vs. transdifferentiation) and will be presented. Interestingly, introduction of mutated Kras (LSL-KrasG12D) into the model fully compensates for the deletion of SHP-2. Finally, in the pancreas, we not only observe an essential role of SHP2 in adequate activation of the RTK-Ras-MEK-ERK-signaling axis but also in positive regulation of RTK-expression levels.

Conclusion: The central role of the non-receptor tyrosine phosphatase SHP-2 in organ development and homeostasis of the murine pancreas is linked to the RTK-Ras-MEK-ERK-signaling axis. SHP-2 is essential for adequate transmission of growth factor signals and thereby influences proliferation and survival of the acinar cell.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: Here we describe several applicable tools, using live cell and tissue microscopy, co-cultivation tumour cells or even to PDAC xenograft tissues with freshly isolated dorsal root ganglia (DRG), primary DRG neurons and F11 hybridoma neurons to investigate the reciprocal interaction at the tumour cell-nerve interface.

Results: To study the invasion of tumour cells along neurites we have combined 3D co-culture assays of dorsal root ganglia (DRG) and tumour cells with time-lapse microscopy and specifically track the unidirectional movement of individual tumour cells along neurites extending from DRGs. Quantification of the dynamic process revealed that neuronal scaffolds provide the infrastructure for an accelerated and consistent migration of tumour cells towards the DRG as the source of chemotactic gradients. In another approach, using explanted PDAC xenograft tissues instead of tumour cell colonies, it occurred that neurite outgrowth from DRG pathway lured towards the tumour tissue. Thus, neurites facing the tumour were more elongated than neurites at the opposite site of the DRG, suggesting that tumour gradients stimulate and/or attract neurite outgrowth and elongation. In support of a tumour-derived chemotactic effect, supernatants from tumour cell cultures supported varying amounts of neurite elongation and outgrowth of freshly isolated primary neurones in transwell assays. In order to gain a more dynamic representation on how neurites explore a chemotactic gradient, F11 hybridoma neurons were co-cultured with PDAC cell lines in separate patches divided by a 500 μm gap. These assays use time-lapse imaging and endpoint analysis in order to track the locomotion of individual neurite extensions, monitor their outgrowth from neurites and elongation towards the tumour cell front, and allow to quantitate length, velocity, forward migration index, and direction of each protruding trajectory in response to different PDAC cell lines. Moreover, the extent of growth cone formation and collapse can be scored by determining dynamic changes in circumferential size and area of the growth cone.

Conclusion: These in vitro and ex vivo models emulate several important aspects of nerve-tumour interactions and allow pharmacological or gain- and loss-of-function manipulations. In addition, semi- to fully-automated quantification for high-throughput screening can be offered offering reliable tools to test their candidate target genes or drugs.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
colonic of CDEIS responding patients. The molecular profile appears to be differ-
entiated from anti-TNF treatment.

Disclosure of Interest: S. Visvanathan: Sudha Visvanathan: Employee of
Boehringer Ingelheim. P. Baum: Patrick Baum: Employee of Boehringer Ingelheim
J. Panés: Julián Panés: Personal fees from Boehringer Ingelheim, during the con-
duct of the study, personal fees from Abbvie, Galapagos, Genentech Roche, Pfizer, Takeda, TiGenix and Topvert, outside the submitted work.

OP104 EFFICACY OF USTEKINUMAB FOR INDUCTION AND MAINTENANCE OF ENDOSCOPIC HEALING IN PATIENTS WITH CROHN’S DISEASE


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Introduction: Usteukinumab (UST) has been shown to induce & maintain clinical response & remission in 2 induction (UNITI-I&2) & 1 maintenance (IM-UNITI) trials in moderate-severe Crohn’s disease (CD). A substudy evaluated the efficacy of UST in the induction & maintenance of endoscopic healing.

Aims & Methods: Patients in the substudy had up to 3 colonoscopy evaluations (i.e. at UNITI-I or 2 baseline [BL] and Wk8, and IM-UNITI Wk44) in 5 ileocolonic segments (i.e. ileum, right colon, transverse colon, left colon, rectum) within the 52-Wk study period. A single central reader blindly scored all video endoscopies for ulcerations and simplified endoscopic activity score for CD (SES-CD). At induction Wk0, patients received a single IV dose (UST 130 mg, UST 60mg/kg, or PBO). At induction Wk3 (i.e. induction Wk8), UST induction responders [Primary randomized maintenance population] were re-randomized to subcutaneous (SC) PBO, UST 90 mg every 12 wks (q12w), or UST induction non-responders [Primary randomized maintenance population] were supported by the larger post-hoc randomized maintenance population were non-responders received UST IV 130 mg, then continued SC UST 90 mg if CDAI decreased ≥100 after 8wks; and [PBO induction non

Results: The substudy primary endpoint was met, as UST induced significantly greater reduction in SES-CD from BL at Week 8 vs PBO. Results were similar by induction study & UST dose. Other induction endoscopic endpoints also con-
sistently favored UST vs PBO (Table 1a). At IM-UNITI Wk44, trends for greater efficacy with UST vs PBO, maintenance, especially UST 90 mg q8w, was observed in the primary randomized maintenance population, but small sample sizes (UST n = 46; PBO n = 24) precluded definitive conclusions. In the larger post-hoc pooled maintenance population (Table 1b), consistent trends in support of UST maintenance, especially UST 90 mg q8w, were observed across endoscopic endpoints at Wk44.

Conclusion: The endoscopic substudy primary endpoint was met; a single IV dose of UST induced significantly greater reduction in endoscopic disease activity vs PBO, despite a relatively early evaluation at Wk6. Results in the small primary randomized maintenance population were supported by the larger post-hoc pooled maintenance population; greater proportions of subjects receiving UST maintenance, especially UST 90 mg q8w, achieved maintenance endoscopic end-
points vs PBO. Together, these data support the efficacy of UST in inducing & maintaining endoscopic healing of the mucosa in CD.

Disclosure of Interest: P. Rutgeerts: Investigator for Janssen Research and Development, LLC
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D. Chan: Employee of Janssen Research and Development, LLC
Y. Lang: Employee of Janssen Research and Development, LLC
P. Pollack: Employee of Janssen Research and Development, LLC
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W. Sandborn: Investigator for Janssen Research and Development, LLC

OP105 FILGOTINIB, A SELECTIVE JAK1 INHIBITOR, INDUCES CLINICAL REMISSION IN PATIENTS WITH MODERATE-TO-
SEVERE CROHN’S DISEASE: FINAL ANALYSIS OF THE PHASE 2 FILGOTINIB STUDY


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Introduction: Filgotinib is an oral, selective Janus kinase 1 (JAK1) inhibitor, which has demonstrated high efficacy in patients with rheumatoid arthritis. This 20-week Phase 2 study was designed to evaluate the efficacy and safety of filgotinib in patients with active Crohn’s disease (CD).

Aims & Methods: 174 patients with moderate-to-severe CD (CDAI > 220, 6 < CDAI < 450) at Week 10 were randomized to receive 200 mg FIL or placebo (PBO) QD for 10 weeks. Based on Week 10 clinical response, patients continued to receive filgotinib (200 mg or 100 mg QD) or placebo for an additional 10 weeks. Patients who demonstrated clinical response (CDAI < 150) underwent corticosteroid tapering after Week 10. Anti-TNF-naive as well as anti-TNF non-responders were included. Immunosuppressants were to be discontinued prior to treatment initiation. Final data for the primary endpoint of clinical remission (CDAI < 150) at Week 10 are presented.

Results: Baseline characteristics were comparable in both groups, including mean disease duration (8.3 yes), mean CDAI score (293), mean CRP (15.6 mg/L, 41% > 10 mg/L), oral corticosteroids (51%, mean daily dose 21.6 mg/day). Primary endpoint of the study was met: Filgotinib induced clinical remission in 47% of the patients, compared to placebo (p = 0.0077). Based on the assessment of PRO2 score, quality of life (IBQD changes from baseline) compared to placebo (table 1). Numerically more patients on filgotinib normalized CRP (FIL:27%, PBO:14%) and showed an improvement of at least 50% in CDAI compared to placebo (p = 0.05).

Table 1: Key efficacy parameters

<table>
<thead>
<tr>
<th>Variable/unit/population</th>
<th>Placebo</th>
<th>Filgotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value</td>
<td>0.0077</td>
<td>0.0321</td>
</tr>
</tbody>
</table>

Table 1: Key efficacy parameters

<table>
<thead>
<tr>
<th>Clinical remission (CDAI &lt; 150), %, ITT-NRI</th>
<th>Placebo</th>
<th>Filgotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRO2, mean change from baseline, ITT-LOCF</td>
<td>17.6</td>
<td>33.8</td>
</tr>
</tbody>
</table>

Filgotinib (FIL) or placebo (PBO) QD for 10 weeks. Based on Week 10 clinical response, patients continued to receive filgotinib (200 mg or 100 mg QD) or placebo for an additional 10 weeks. Patients who demonstrated clinical response (CDAI < 150) underwent corticosteroid tapering after Week 10. Anti-TNF-naïve as well as anti-TNF non-responders were included. Immunosuppressants were to be discontinued prior to treatment initiation. Final data for the primary endpoint of clinical remission (CDAI < 150) at Week 10 are presented.

Results: Baseline characteristics were comparable in both groups, including mean disease duration (8.3 years), mean CDAI score (293), mean CRP (15.6 mg/L, 41% > 10 mg/L), oral corticosteroids (51%, mean daily dose 21.6 mg/day). Primary endpoint of the study was met: Filgotinib induced clinical remission in 47% of the patients, compared to placebo (p = 0.0077). Based on the assessment of PRO2 score, quality of life (IBQD changes from baseline) compared to placebo (table 1). Numerically more patients on filgotinib normalized CRP (FIL: 27%, PBO: 14%) and showed an improvement of at least 50% in SES-CD endoscopy score (FIL: 25%, PBO: 13.6%), Histopathology overall total score (FIL: 27%, PBO: 14%) and showed an improvement of at least 50% in endoscopic response, endoscopic remission & mucosal healing; in both combined and individual treatment groups.

Results: The substudy primary endpoint was met, as UST induced significantly greater reduction in SES-CD from BL at Week 8 vs PBO. Results were similar by induction study & UST dose. Other induction endoscopic endpoints also consistently favored UST vs PBO (Table 1a). At IM-UNITI Wk44, trends for greater efficacy with UST vs PBO, maintenance, especially UST 90 mg q8w.
Table 1  Continued

<table>
<thead>
<tr>
<th>Variable/unit/population</th>
<th>Placebo</th>
<th>filgotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total IBDO score, mean change from baseline, ITT-LOCF</td>
<td>13.6</td>
<td>25</td>
</tr>
<tr>
<td>p-value</td>
<td>NS</td>
<td>0.059</td>
</tr>
<tr>
<td>SES-CD improvement by at least 50%, ITT-LOCF</td>
<td>-0.6</td>
<td>3.5</td>
</tr>
<tr>
<td>Overall total histopathology score, mean change from baseline, ITT-LOCF</td>
<td>-0.35</td>
<td>0.0359</td>
</tr>
</tbody>
</table>

CDAI: Crohn’s Disease Activity Index; ITT: Intent-to-treat; NRI: Non-responder imputation; LOCF: Last observation carried forward; PR2: Patient Reported Outcome = 7x (mean daily number of liquid or very soft stools) + 7x (mean daily abdominal pain score); IBDO: Inflammatory Bowel Disease Questionnaire; Simple Endoscopic Index for Crohn’s Disease; Histopathology score= Adaptation from histopathology score D’Haens; Overall, filgotinib was safe and well tolerated. Similar incidences in early discontinuations, SAEs and AEs including infections were observed, with the majority of the SAEs related to worsening of CA. An increase in mean haemoglobin concentration was observed, without difference between filgotinib and placebo. No clinically significant changes from baseline in mean neutrophil counts or liver function tests were observed. Filgotinib showed a favourable lipid profile with an increase in HDL and no change in LDL, resulting in an improved atherogenic index.

Conclusion: Inhibition of JAK1 with filgotinib induces clinical remission, supported by CRP, endoscopy and histopathology results, and improves quality of life in patients with moderate to severe CD. The efficacy and safety data of filgotinib support a risk/benefit profile, showing its potential as an oral treatment with a novel mechanism of action for the treatment of CD.

Disclosure of Interest: S. Vermeire: Grant support: Abbvie, MSD, Takeda; Lectures: Abbvie, MSD, Takeda, Ferring, Falk Pharma, Hospira, Tillotts Consultancy: Abbvie, MSD, Takeda, Ferring, Genentech/Roche, Shire, Pfizer, Galapagos, Mundipharma, Hospira, Celgene, Second Genome, J&J; S. Schreiber: Paid consultancies to Abbvie, Galapagos, Pfizer, Takeda; T. Kuehbach: Advising and/or speaking fees for Abbvie Takeda MSD Shire F. K. X. Hebuterne: Educational activities: ARARD, Abbvie, Ferring, MSD, Nutricia; Educational activities and consultancy: Takeda Member of: boards; Janssen, Fresenius-Kabi; X. Roblin: MSD, Abbvie, Takeda, Hospira, Janssen, Theradigm; M. Klopocka: Payment for lectures; Royalties: Abbvie, Aluvogen, Takeda, Polish Foundation for Gastroenterology Travel/accommodations/meeting expenses F. K. X. Roblin, Abbvie, Polish Foundation for Gastroenterology; K. Stoyanova: employee of PSi Pharma Support Ltd; C. Tasset: employee of Galapagos NV A. Van der Aa: employee of Galapagos NV; P. Harrison: employee of Galapagos NV All other authors have declared no conflicts of interest.

OP106 TOFACITINIB HAS INDUCTION EFFECT IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS, REGARDLESS OF PRIOR TNF INHIBITOR THERAPY


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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). Two Phase 3 randomised placebo (PBO)-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01459851) demonstrated efficacy of tofacitinib 10 mg twice daily (BID) vs PBO as induction therapy for patients (pts) with moderate to severe UC.

Aims & Methods: We investigated the effect of prior tumour necrosis factor inhibitor (TNFi) therapies or disease activity (baseline Mayo score) on clinical response at Week 8, stratified by study, prior treatment with tumour necrosis factor inhibitors, corticosteroid use at baseline and geographic region. As reasoning for TNFi failure (primary or secondary) or disease severity and the major-end point, the comparison of tofacitinib 10 mg BID vs PBO was assessed using the Cochran-Mantel-Haenszel (CMH) chi-square test stratified by study, prior TNFi treatment, corticosteroid use at baseline and geographic region. Within each subgroup, the CMH chi-square test stratified by study was used.

Results: At Wk 8, significantly more pts achieved remission, mucosal healing and clinical response with tofacitinib 10 mg BID vs PBO (all < p = 0.0001, Table). The difference generally remained significant regardless of prior TNFi exposure, prior TNFi failure reason for TNFi failure (primary or secondary) or disease severity (based on baseline Mayo score ≥9 or < 9; Table). For all three endpoints, greater effects were observed when comparing secondary vs primary TNFi failure subpopulations and baseline Mayo score <9 vs baseline Mayo score ≥9. IBDO remission and response were significantly greater with tofacitinib 10 mg BID vs PBO at Wk 8 regardless of prior TNFi exposure/prior TNFi failure.

Conclusion: Tofacitinib demonstrated efficacy vs PBO, regardless of prior TNFi therapy in pts with moderately to severely active UC. PRO results were similar in pts with/without prior TNFi exposure or failure.

Table: Summary of efficacy endpoints in OCTAVE Induction 1 and OCTAVE Induction 2 at Wk 8

<table>
<thead>
<tr>
<th>10 mg BID N = 905</th>
<th>Tofacitinib</th>
<th>Placebo</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission, n (%)</td>
<td>159 (17.6)</td>
<td>14 (6.0)</td>
<td>11.7 (7.5, 15.5)***</td>
</tr>
<tr>
<td>Prior TNFi exposure</td>
<td>99 (23.7)</td>
<td>13 (12.5)</td>
<td>11.2 (5.7, 18.8)**</td>
</tr>
<tr>
<td>Prior TNFi failure</td>
<td>53 (11.4)</td>
<td>1 (1.0)</td>
<td>10.6 (7.3, 13.9)**</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)</td>
<td>106 (24.1)</td>
<td>13 (11.8)</td>
<td>12.3 (5.0, 19.5)*</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)</td>
<td>17 (7.5)</td>
<td>1 (1.4)</td>
<td>6.2 (2.0, 10.3)</td>
</tr>
<tr>
<td>Baseline Mayo score &lt;9</td>
<td>91 (28.3)</td>
<td>6 (7.3)</td>
<td>21.0 (13.5, 28.5)**</td>
</tr>
<tr>
<td>Baseline Mayo score ≥9</td>
<td>68 (11.7)</td>
<td>5 (6.3)</td>
<td>6.4 (2.0, 10.8)</td>
</tr>
<tr>
<td>Mucosal healing, n (%)</td>
<td>271 (29.9)</td>
<td>32 (13.7)</td>
<td>16.3 (11.0, 21.6)***</td>
</tr>
<tr>
<td>Prior TNFi exposure</td>
<td>112 (23.0)</td>
<td>8 (6.2)</td>
<td>16.8 (11.2, 22.4)**</td>
</tr>
<tr>
<td>Prior TNFi failure</td>
<td>159 (38.1)</td>
<td>24 (23.1)</td>
<td>15.1 (5.7, 24.8)**</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)</td>
<td>103 (22.2)</td>
<td>8 (6.5)</td>
<td>15.7 (10.0, 21.4)***</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)</td>
<td>168 (38.2)</td>
<td>24 (21.8)</td>
<td>16.4 (7.4, 25.3)*</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)</td>
<td>38 (15.0)</td>
<td>5 (6.8)</td>
<td>8.3 (1.0, 15.5)NS</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)</td>
<td>57 (30.5)</td>
<td>2 (4.7)</td>
<td>25.8 (16.7, 34.9)**</td>
</tr>
<tr>
<td>Clinical response, n (%)</td>
<td>251 (57.6)</td>
<td>72 (30.8)</td>
<td>26.8 (20.1, 33.5)**</td>
</tr>
<tr>
<td>Prior TNFi exposure</td>
<td>254 (52.0)</td>
<td>29 (22.3)</td>
<td>22.7 (14.1, 31.0)**</td>
</tr>
<tr>
<td>Prior TNFi failure</td>
<td>267 (64.0)</td>
<td>43 (13.1)</td>
<td>22.2 (17.7, 26.7)**</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)</td>
<td>237 (51.0)</td>
<td>29 (23.4)</td>
<td>27.6 (18.9, 36.3)**</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)</td>
<td>284 (64.5)</td>
<td>43 (39.1)</td>
<td>25.5 (15.3, 35.6)**</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)</td>
<td>116 (45.8)</td>
<td>19 (25.7)</td>
<td>20.2 (8.5, 31.9)**</td>
</tr>
</tbody>
</table>

Full analysis set, non-responder imputation NS; Not significant; * p < 0.05; ** p < 0.01; *** p < 0.001 vs placebo; 95% confidence interval was based on normal approximation for the difference in binomial proportions. P = 0.488 for tofacitinib 10 mg BID and N = 130 for placebo; P = 0.417 for tofacitinib 10 mg BID and N = 104 for placebo; N = 465 for tofacitinib 10 mg BID and N = 124 for placebo; N = 440 for tofacitinib 10 mg BID and N = 110 for placebo; N = 253 for tofacitinib 10 mg BID and N = 74 for placebo; N = 187 for tofacitinib 10 mg BID and N = 43 for placebo; N = 321 for tofacitinib 10 mg BID and N = 82 for placebo; N = 582 for tofacitinib 10 mg BID and N = 151 for placebo; statistical significance based on the Cochran-Mantel-Haenszel chi-squared test stratified by study, prior treatment with tumour necrosis factor inhibitors, corticosteroid use at baseline and geographic region BID, twice daily; CI, confidence interval; TNFi, tumour necrosis factor inhibitor; Wk, week.
OP107 CLINICAL DISEASE ACTIVITY INFLUENCES THE THERAPEUTIC EFFICACY OF THE TOLL LIKE RECEPTOR-9 AGONIST COBITOLIMOD IN PATIENTS WITH MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS

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Introduction: In the COLLECT study the Toll like receptor (TLR-9) agonist cobitolimod (formerly known as D3MS0150, Kappaproct®) was evaluated for its therapeutic efficacy in ulcerative colitis (UC) patients refractory to conventional therapy.

Aims & Methods: In this post-hoc analysis the therapeutic effects were analysed with respect to disease activity of the patients at baseline. Cobitolimod was studied in a randomized, double blind, placebo-controlled, multicentre, pan-European, double-blind, placebo-controlled (COLLECT) in 11 centers with patients with moderate to severe active ulcerative colitis. Patients were on mandatory steroid therapy and could be taking sulphasalazine, aminosalicylates, or thiopurines at stable doses.

The results of the COLLECT study demonstrate that the TLR-9 agonist cobitolimod (formerly known as D3MS0150, Kappaproct®) was evaluated for its therapeutic efficacy in ulcerative colitis (UC) patients refractory to conventional therapy.

Conclusion: The results of the COLLECT study demonstrate that the TLR-9 agonist cobitolimod is able to induce clinical remission in UC patients both with moderate and severe disease activity. The concept of TLR-9 activation represents a promising and well-tolerated novel therapeutic option for ulcerative colitis patients with active disease and warrants further trials.
We assessed a recently developed self-assembling peptide matrix as a wound dressing after endoscopic resection for the prevention of esophageal stricture.

Aims & Methods: Ten pigs were randomly assigned to the self-assembling peptide RADA-16 (Arg-Ala-Asp-Ala) or the control group after undergoing a 5 cm long circumferential endoscopic submucosal dissection of the lower esophagus. Esophageal diameter, endoscopic submucosal dissection, weight, and histological measurements of fibrosis, granulation tissue, and neoeplithelium were assessed in each animal.

Results: The rate of esophageal stricture at day 14 was 40% in the group treated with self-assembling peptide vs. 100% in the control group (p = 0.04). Median (IQR) esophageal diameter at day 14 was 8 mm (2.5–9) in the self-assembling peptide group vs. 4 mm (3–4) in the control group (p = 0.13). The median (IQR) stricture indexes on esophagograms at day 14 were 0.32 (0.14–0.48) and 0.26 (0.14–0.33) in treated and control groups, respectively (p = 0.42). Median (IQR) weight variation during the study was +0.2 (–7.4; +1.8) and –3.8 (–5.4; +0.6) in the treated and control groups, respectively (p = 0.9). No differences were observed between the groups in terms of histological outcomes. All animals eventually developed esophageal strictures at day 28.

Conclusion: The application of a self-assembling peptide matrix on esophageal wounds after circumferential endoscopic submucosal dissection is safe and feasible, and prevents early esophageal stricture occurrence in our model.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. Isomoto H, Yamaguchi N, Nakayama T, Hayashi T, Nishiyama H, Ohnita K, et al. Management of esophageal stricture after complete circular endoscopic submucosal dissection for superficial esophageal squamous cell carcino-

OP110 INTRALESIONAL STEROID INJECTION COMBINED WITH ORAL STEROID ADMINISTRATION TO PREVENT ESOPHAGEAL STRICUTURE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF LESION NO LESS THAN A HALF OF CIRCUMFERENCE

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Introduction: Endoscopic submucosal dissection (ESD) is becoming an important and main therapy for early esophagus carcinoma or precancerous lesion. However, stricture after occurs when the mucosal defects created by ESD are larger than a half of circumference. It’s an urgent task to find out a safe and effective method to prevent stenosis.

Aims & Methods: To investigate the safety and efficiency of local steroid injection combined with oral steroid administration in preventing esophageal stricture after ESD of esophagus carcinoma or precancerous lesion which are no less than a half of circumference. A single-center randomized controlled trial was designed to examine the effects and safety of intralausal steroid injection combined with oral steroid administration in preventing stricture after esophageal ESD. 43 patients with mucosal defects no less than a half of circumference following esophageal ESD were randomized to receive intralausal triamcinolone injection immediately after ESD and oral prednisone administration for consecutive 12 weeks, which starting at a dose of 30 mg daily, tapered gradually at a speed of 5 mg in every two weeks (n = 20, treatment group) or to be treated conventionally (n = 23, control group). The primary endpoint was the frequency of stricture. Secondary endpoints were the number of balloon dilation, rate of other complications and hospital stay.

Results: The frequency of stricture (20% vs. 69.6%) and the number of balloon dilation (mean 0.5 vs. 1.3) were less in treatment group, and the former one had a significant difference. The hospital stays and rate of complications were similar between two groups. One patient suffered perforation of stomach in the treatment group, which was not a direct result of steroid injection or ESD.

Frecuency of stricture formation, number of endoscopic balloon dilations (EBD)s performed, hospital stays after ESD and other complications in two groups.

<table>
<thead>
<tr>
<th>Treatment group (n = 20)</th>
<th>Control group (n = 23)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of stricture, n (%)</td>
<td>5/20 (25%)</td>
<td>16/23 (69.6%)</td>
</tr>
<tr>
<td>Number of EBDs, n mean ± SD (range)</td>
<td>0.5 ± 1.1 (0–3)</td>
<td>1.3 ± 2.0 (0–8)</td>
</tr>
<tr>
<td>Perforation by procedure, n per session (%)</td>
<td>1/30 (3.3%)</td>
<td>0/53 (0%)</td>
</tr>
<tr>
<td>Bleeding by procedure, n per session (%)</td>
<td>0/30 (0%)</td>
<td>1/53 (1.9%)</td>
</tr>
<tr>
<td>Hospital stays after ESD, days mean ± SD (range)</td>
<td>4.1 ± 4.4 (1–22)</td>
<td>3.3 ± 2.0 (1–8)</td>
</tr>
</tbody>
</table>

*Significant difference

Conclusion: Intralausal steroid injection combined with oral steroid administration appears to be safe and effective in preventing esophageal stricture following ESD of lesions no less than a half of circumference.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
altered diagnosis/therapy and/or influenced management in 417 (83%) pts. Moreover, in a prospective study, the use of SPY DS as a predictor for malignant pathway of SPY biopsies is better for SPY DS than SPY Legacy (p = 0.014). Adverse events in 7 (1%) pts: 2 mild pancreatitis, 2 mild and 1 moderate cholangitis, 1 moderate bleeding and 1 micro perforation.

**Conclusion**: SOC, especially using Spy DS, has high procedural success and provides important impact on diagnosis, therapy and/or management in a wide range of indications, with excellent safety profile.

**Disclosure of Interest**: All authors have declared no conflicts of interest.

**OP113 PROPOSAL OF A MACROSCOPIC CLASSIFICATION FOR TISSULAR LESIONS OF THE BILE DUCT DETECTED DURING PER ORAL CHOLANGIOSCOPY (POCS)**

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**Introduction**: The macroscopic aspects to determine malignancy of the bile duct during per oral cholangioscopy (POCS) are: presence of irregular surface with bleeding and/or tortuous vessels. For benign lesions the typical aspects are lesions with smooth surface “without vessels or mass”. However, many misdiagnosis are made due to a lack of correlation between the macroscopic aspects and histology. Moreover, masses are many times benign, and reported data shows 78% of sensitivity for visual impression diagnosing malignancy.

**Aims & Methods**: Propose a macroscopic classification of bile duct tissular lesions for differentiation between benign and malignant lesions.

**Results**: A retrospective study from Sept-2013 to Sept-2015 was made at our institution in patients evaluated by POCS (using SpyGlass® legacy and DS). Inclusion criteria: tissular lesions detected by POCS. Exclusion criteria: absence of histology confirmation (either biopsy or surgical resection for malignancy) and/or absence of follow-up at 6 months (for benign lesions). To determine the macroscopic classification all patients’ records were evaluated. 315 images were analyzed and classified as benign or malignant by an expert with more than 140 POCS cases, and compared to histology. Based on the morphological and vascular pattern the lesions were classified as follows: Benign lesions: Type 1 “Villosus pattern” (micronodular or villous pattern without out vascularity), Type 2 “Polypoid pattern” (adenoma or granuloma pattern without vascularity) and Type 3 “Inflammatory pattern” (regular or irregular fibrous and congestive pattern with regular vascularity). Malignant lesions: Type 1 “Flat pattern” (flat and smooth or irregular surface with irregular or spider vascularity); Type 2 “Polypoid” (polypoid or mass with fibrosis or irregular spider vascularity). Type 3 “Ulcerated” (irregular pattern ulcerated and infiltrative with or without fibrosis with irregular or spider vascularity) and Type 4 “Honeycomb pattern” (fibrous honeycomb pattern with or without irregular or spider vascularity). Inter-observer and intra-observer agreement was calculated using 40 random images of lesions for 1 expert and 2 non-expert in the classifications. The intra-observer agreement was almost perfect when lesions were classified as benign and malignant (k = 0.88 – CI 0.66 – 1.0) and when lesions were classified by sub-types (k = 0.90 – CI 0.71 – 1.0). For the prospective validation 23/43 patients were evaluated, 9/23 cases were malignant and 10/23 benign. The accuracy was 86.9%, sensitivity 100%, specificity 70%, PPV 81.3%, NPV 100%.

**Conclusion**: The proposed macroscopic classification could help physicians to distinguish benign from malignant lesions with a good inter and intra-observer concordance.

**Disclosure of Interest**: All authors have declared no conflicts of interest.


**Disclosure of Interest**: Data on the efficacy of prophylactic rectal indomethacin to prevent post-ERCP pancreatitis in consecutive patients is inconsistent. We therefore conducted a meta-analysis of high-quality randomized clinical trials specifically studying rectal indomethacin in prevention of post-ERCP pancreatitis in consecutive patients.

**Aims & Methods**: Relevant studies for the meta-analysis were identified through search of MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials databases. Randomized controlled clinical trials employing rectal indomethacin for the prevention of post-ERCP pancreatitis were included. The primary outcome was the overall rates of post-ERCP pancreatitis.

**Results**: A total of 2473 patients from 6 studies were included. The incidence of post-ERCP pancreatitis across all 2473 patients was 7% (95% CI, 6%–9%). We found that there was no significant difference in overall rates of post-ERCP pancreatitis in consecutive patients with rectal indomethacin and placebo (OR: 0.67, 95% CI, 0.46–1.00, p = 0.500). There was also no difference in rates of moderate to severe (OR: 0.86; 95% CI, 0.28–3.56, p = 0.345) or mild (OR: 0.71; 95% CI, 0.45–1.10, p = 0.217) post-ERCP pancreatitis between indomethacin and placebo.

**Conclusion**: In a contemporary meta-analysis of available randomized controlled trials of consecutive patients undergoing ERCP, rectal indomethacin did not show significant prevention effect of post-ERCP pancreatitis.

**Disclosure of Interest**: J. Ospina1, H. Pitanga Lukashok1 1Gastroenterology, Peking Union Medical College Hospital, Beijing/China

Disclosure of Interest: Dr. J. Ospina reports grant support from AbbVie, Janssen and Takeda. Dr. H. Pitanga Lukashok reports consultant relationship with AbbVie.


**Table (OP114)**

<table>
<thead>
<tr>
<th>Characteristics of Included Trials</th>
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<tr>
<td><strong>Methodology</strong></td>
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<tr>
<td><strong>Location</strong></td>
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<tr>
<td><strong>Definition of post-ERCP pancreatitis</strong></td>
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<tr>
<td><strong>Pancreatic stent used?</strong></td>
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<td><strong>Randomization</strong></td>
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<td><strong>Indomethacin</strong></td>
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<td><strong>Placebo</strong></td>
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<td><strong>Baseline demographics</strong></td>
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<td><strong>Procedure demographics</strong></td>
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</table>

**Conclusion:** The use of high-dose PPI did not appear to significantly reduce the risk of both immediate and delayed bleeding in patients undergoing EST.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**OP115 PREVENTION OF POST-SPHINCTEROTOMY BLEEDING BY PROTON PUMP INHIBITOR: A PROSPECTIVE RANDOMIZED TRIAL**

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**Introduction:** Bleeding after endoscopic sphincterotomy (EST) is one of the most frequent complications of therapeutic ERCP. Although the use of proton pump inhibitor (PPI) has been shown to reduce the risk of rebleeding in patients with peptic ulcer bleeding after endoscopic hemostasis, the role of acid suppression in preventing EST bleeding has not been evaluated. We hypothesized that preemptive high dose PPI could reduce the risk of post-EST bleeding.

**Aims & Methods:** The aim of this study was to study the role of high-dose PPI in patients undergoing EST. It was a prospective randomized open-label study performed in the endoscopy centre of a university teaching hospital. Consecutive patients who were scheduled to have ERCP and EST were enrolled. We excluded patients who had previous EST, prior gastric surgery, or were taking PPIs. Antiplatelet therapies were continued as usual. Anti-coagulants (warfarin or heparin) were stopped with coagulopathy corrected prior to ERCP. Eligible patients were randomized to receive either PPI or standard care (SC). PPI group would receive esomeprazole given intravenously at 80 mg every 12h for Day 1, starting 4 hours prior to ERCP, and followed by oral esomeprazole 40 mg bid from Day 2 to 10. Standard care arm would receive usual care without any acid suppressive therapy. Endoscopists were unaware of treatment allocation of the patients. Primary outcome was the proportion of patients with immediate or delayed post-EST bleeding. Immediate bleeding was defined as bleeding that occurred during the procedure and required endoscopic hemostasis. Delayed bleeding was defined as bleeding after the completion of ERCP which manifested as overt GIB with melena or hematemesis. All patients were followed up for 30 days. Secondary outcomes included drop in hemoglobin > 2 g without overt bleeding, transfusion requirement and all-cause mortality at 30 days. Analysis was based on modified intention-to-treat, which included only randomized patients who had undergone EST.

**Results:** 196 patients were enrolled and 71 patients did not have EST. The analysis included 125 patients who had undergone EST with 60 patients in the PPI group and 65 patients in the SC group. The mean age was 70.9 (SD = 14.8) years with 62 (49%) men. The baseline characteristics of the two groups including indications for ERCP, use of anti-platelet agents or anti-coagulants, and comorbidity were comparable. Immediate bleeding was noted in 9 (15%) patients in the PPI group and 4 (6.2%) in the SC group (P = 0.14). Overt delayed ES bleeding was respectively seen in 2 (3.3%) and 5 (7.7%) patients in PPI and SC arms (P = 0.44). There was also no significant difference in the proportions of patients with hemoglobin drop of > 2 g without overt bleeding (Day 10: 13.3% in PPI group and 9.2% in SC group; P = 0.57). Other outcomes including hospital stay (13.1 vs 11.8 days; P = 0.69), transfusion requirement (5% vs 7.7%; P = 0.72) and 30-day mortality (3.3% vs 1.5%; P = 0.61) were also comparable between the PPI and SC arms.

**Conclusion:** The use of high-dose PPI did not appear to significantly reduce the incidence and severity of PEP. There were no significant differences in the incidence and severity of PEP between patients receiving PPI and standard care. The use of high-dose PPI did not appear to significantly reduce the risk of both immediate and delayed bleeding in patients undergoing EST.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**OP116 IMPACT OF INTENSIVE HYDRATION ON THE INCIDENCE OF POST-ERCP PANCREATITIS: DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL**

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**Introduction:** Pancreatitis is the most frequent complication following endoscopic retrograde cholangiopancreatography (ERCP), with an estimated incidence of 1.6% to 15.7%, depending on patient and procedure-related factors. Intensive hydration with lactated Ringer’s solution has been shown in small studies to reduce post-ERCP pancreatitis (PEP) incidence and severity.

**Aims & Methods:** We aimed to assess whether intensive hydration impacts on the incidence and severity of PEP. We performed a prospective, double-blinded randomized controlled trial, including consecutive patients submitted to ERCP in our institution. Patients with previous sphincterotomy, chronic pancreatitis, heart failure (NYHA ≥3), chronic kidney disease (stage ≥3) and shock were excluded. Patients were randomized (1:1) to either intensive hydration with lactated Ringer’s solution (3 mL/kg/h during the procedure, and 3 mL/kg/h for up to 8 hours after the procedure), or standard hydration (1.5 mL/kg/h of lactated Ringer’s solution during and for 8 hours after the procedure). A blood panel including serum levels of amylase and lipase was obtained at 4 and 24 hours after ERCP. Primary outcome was the incidence of PEP (defined as epigastric pain plus either amylase or lipase levels > 3 times the upper limit of normal at 24h). Secondary outcomes were severity of PEP, incidence of volume overload, patient and procedure-related factors associated with PEP, and the predictive values of serum amylase/lipase at 4 hours after ERCP for PEP development.

**Results:** Included were 75 patients, 38 in the intensive hydration arm, and 37 in the standard hydration arm. Both groups were homogeneous for patient and procedure-related factors. PEP incidence was 9.5% (n = 7), and was lower in the intensive hydration arm (5.3% versus 13.5%, p = 0.204). Additionally, both PEP in the intensive hydration arm were mild, while out of the 5 PEP in the normal hydration arm, two patients presented with moderate and severe PEP, respectively. Contrast injection of the Wirsung was significantly associated with PEP (28.6% versus 7.1%, p = 0.016), while no other patient or procedure-related factors associated with PEP incidence. Finally, both amylase levels < 2 times and lipase levels < 3 times the upper limit of normal at 4 hours demonstrated a
negative predictive value of 100% for the development of PEP. No complication was observed, confirming the absence of intensive care need.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
15:45–17:15
UPPER GI NERVE-GUT INTERACTIONS – ROOM N2

OP117 INTRAGASTRIC BITTER TASTANT ALTERS BRAIN ACTIVITY IN HOMEOSTATIC AND HEDONIC REGIONS AND DECREASES OCTANOLYATION OF GHERILIN LEVELS AND HEDONIC FOOD INTAKE
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Targird, University of Leuven, Leuven/Belgium

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Introduction: Intragastric administration of bitter tastants decreases hunger ratings in the fasted state. Activation of bitter taste receptors can alter ghrelin levels, a gut hormone which increases hunger in between meals and becomes active after octanoylation. This indicates a potential role for bitter agonists in the regulation of appetite and food intake, putatively via interference with gut-brain signals to regions involved in homeostatic (brainstem, hypothalamus) and hedonic (mesolimbic reward systems) control of feeding.

Aims & Methods: The aim of this project was to study the effect of intragastric administration of the bitter tastant Quinine Hydrochloride (QHCl) on brain activity in homeostatic and hedonic regions and on circulating ghrelin plasma levels. Furthermore, to test the hypothesis that lower ghrelin and prospective food consumption ratings, and lower hedonic food intake after QHCl administration compared to placebo. Fifteen healthy women were studied after an overnight fast. Brain activity before and up to 50 minutes after infusion of QHCl (10mg/ kg body weight) was recorded using functional magnetic resonance imaging (MRI). Hunger and prospective food consumption scores were assessed every 10 min using Visual Analogue Scales. Blood samples were taken at the same time points. Hedonic food intake was measured immediately after scanning using an ad libium chocolate milkshake drink test. MRI preprocessing and analysis was conducted using SPM12. Brain responses over time to QHCl versus placebo infusion were compared in a priori defined regions of interest (ROI) at both voxel- and cluster-level threshold of pFWEcorrected < 0.05. The interaction effect was tested on hunger and prospective food consumption scores with mixed models. Hedonic food intake was compared between infusions using a one-tailed paired T-test. Blood plasma was analysed for circulating ghrelin levels using radioimmunoassays.

Results: Compared to placebo, intragastric QHCl infusion significantly increased neural activity in 5 different clusters within the ROIs, with local maxima in the putamen, insula, caudate, amygdala, anterior cingulate cortex, medial prefrontal cortex, medial orbitofrontal cortex and hippocampus. A decrease of neural activity was observed in the hypothalamus. Significantly lower prospective food consumption scores were observed after QHCl administration compared to placebo (p = 0.02), but no significant differences were observed for hunger scores. Milkshake intake was significantly lower after QHCl administration, compared to placebo (p = 0.04; Cohen’s d = 0.59). A significant decrease of octanoylated ghrelin plasma levels was observed post-infusion after bitter administration compared to placebo (p = 0.03).

Conclusion: Intragastric administration of the bitter tastant QHCl significantly altered activity in homeostatic and hedonic brain regions. Prospective food consumption ratings, circulating octanoylated ghrelin levels and hedonic food intake were decreased after QHCl. These observations indicate a potential role for bitter agonists in the treatment of obesity.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP118 TRANSDIAGNOSTIC COGNITIVE BEHAVIOUR THERAPY SHOW PROMISE FOR BOTH MODAL AND GASTROINTESTINAL SYMPTOMS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS
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2University of Newcastle Faculty of Health PVC Office, Callaghan/Australia

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Introduction: Irritable Bowel Syndrome (IBS) is a heterogenous disorder characterised by recurrent abdominal pain combined with alteration in bowel habit. It is associated with reduced quality-of-life and significant economic cost to society. IBS sufferers also have elevated scores for anxiety and depression which have been speculated to be part of the disease etiology [1]. Indirect evidence for the role of mood in IBS prevalence comes from studies showing that a proportion of patients show improvement in abdominal symptoms with antidepressants [2] but also in response to psychological therapies including cognitive behaviour therapy (CBT) [3]. Newer forms of CBT including internet-delivered CBT (iCBT) have shown similar effect sizes to conventional CBT in patients with mood disorder [4]. iCBT provides access to therapy for patients who are geographically or culturally isolated from qualified psychologists and has been shown to be cost-effective [5]. The eCentreClinic at Macquarie University (Australia) has developed a transdiagnostic model of CBT which is applied via distance mode, remote internet-delivered therapy but via an audio phone.

Aims & Methods: This study sought to pilot a new form of iCBT designed for chronic health conditions, including functional gastrointestinal disorders, with respect to: 1. Reduction in abdominal symptom burden, anxiety and depression 2. Identify the risk of psychological factors that correlate with improvements in abdominal symptom burden. These aims were addressed using a single arm design with measurements of psychological factors and symptoms pre, mid and post-therapy. n=27 individuals from across Australia were recruited at the eCentreClinic at Macquarie University (Australia) which specialises in online psychological therapies. Abdominal symptoms were assessed using the Gastrointestinal Symptom Rating Scale (GSRS) while anxiety was measured via the GAD-7 and depression via the PHQ-9. Aim 1 was addressed via correlating change in GSRS scores with change in anxiety, depression and pain catastrophising scores. Aim 2 was addressed using a univariate approach to assess for any measure between more and less compliant. Scores for both abdominal symptom and psychological traits were substantially and statistically significantly improved at the end of therapy (Table 1).

At end of therapy 77% of patients had reduced GSRS scores and 95% reported the program was worth the effort expended. The percentage change in GSRS scores was positively correlated with percentage change in pain catastrophising (r = 0.53, p = 0.01) and depression (r = 0.53, p = 0.01) and to a lesser extent with change in anxiety (r = 0.36, p = 0.1).

Conclusion: Based on this pilot trial, a transdiagnostic iCBT program developed specifically for functional gastrointestinal disorders shows considerable promise with improvements in both gastrointestinal symptoms as well as psychological functioning. The correlation between change in both mood scores and catastrophizing with change in abdominal symptoms opens avenues for further understanding of the mechanisms by which iCBT improves the gastrointestinal sufferings of these patients. The low cost of iCBT compared with conventional face-to-face therapy is attractive given challenges to public health budgets and its modularity makes therapy accessible to potential patients who are not able to travel to a psychologist. Further, the transdiagnostic model on which this particular iCBT treatment is based is readily adaptable to other functional somatic syndromes so offers hope to a wide range of disorders.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Baseline and change in scores for abdominal symptoms and psychological factors

<table>
<thead>
<tr>
<th>Score</th>
<th>Baseline</th>
<th>Change</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSRS</td>
<td>44.2 (11.0)</td>
<td>-7.6 (10.5)</td>
<td>-0.72</td>
</tr>
<tr>
<td>Anxiety</td>
<td>10.5 (5.2)</td>
<td>-5.1 (4.4)</td>
<td>-1.16</td>
</tr>
<tr>
<td>Depression</td>
<td>9.7 (4.8)</td>
<td>-4.1 (5.3)</td>
<td>-0.91</td>
</tr>
<tr>
<td>Catastrophising</td>
<td>19.8 (11.3)</td>
<td>-11.5 (11.9)</td>
<td>-0.97</td>
</tr>
</tbody>
</table>

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP119 DYSBIOSIS INDUCES GUT INFLAMMATION AND DEPRESSIVE-LIKE BEHAVIOR ASSOCIATED WITH BRAIN BIOCHEMICAL AND FUNCTIONAL ALTERATIONS WHICH ARE RESTORED BY PROBIOTIC TREATMENT
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Introduction: The gut-brain axis has been indicated as major substrate of pathophysiological mechanisms in psychiatric comorbidities associated with chronic inflammatory bowel disorders. In particular, intestinal microbiota alterations have been highlighted as a key difference between these two systems [1]. However, this communication is not fully understood and probably involves multiple mechanisms.

Aims & Methods: In the present study we examined the presence of gut inflammation and depressive-like behavior associated with brain biochemical and functional alterations in an antibiotic-induced dysbiosis animal model. Young male mice received a mixture of nonabsorbable antimicrobials (ampicillin, streptomycin and clyndamicin), which has been associated to the microflora composition alteration [2], for 2 weeks. Afterwards, animals were treated with probiotic (Lactobacillus Casei DG, 10⁶ cells) or vehicle up to 7 days. Whereupon, various behavioral testing were performed. After sacrifice, mice intestine was cut in segments (duodenum, jejunum, cecum), and expression of pro-inflammatory markers (IL-1β,
OP12 OXIDATIVE STRESS ACTIVATES NLPR3 INFLAMMASE Complex AND IMPAIRS GASTRIC ANTRUM SMOOTH MUSCLE ACTIVITY IN OBESE PATIENTS

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Aims & Methods: Our aim was to evaluate in vivo obese antral smooth muscle impairment and to study in vitro the roles for oxidative stress and inflammation on SMC motor alterations. Antral scans were obtained by Magnetic Resonance Imaging (MRI) before and after a liquid meal in OB and normal weight (NW) patients. SMC were isolated from human gastric antrum from 19 OB (body mass index, BMI ≥30 kg/m2) and 9 NW patients submitted to stomachectomy for gastric cancer (19.3±3.7 mmHg). Antioxidant capacity was evaluated by ELISA; qPCR analysis was performed for mRNA for NLPR3, ASC, Casp, IL-1β, TNFα, COX and 2 and the data were normalized to β-actin mRNA expression levels. The effects of Acetylcysteine (Apo) and Apocynin (APO:1 mM) in reverting OB SMC alterations was tested both on mRNA expression and on VIP (1µM) induced antral relaxation. Data are expressed as mean±SE, p < 0.05 considered significant.

Results: Respect to NW, BMI of OB showed a reduced antral motility, both during fasting and post-prandial periods, in OB consisting in a significant reduction of the width of antral contraction waves and magnitude of antral diameters variations. OB SMC presented a statistically significant decrease in antioxidant capacity (89.0±2.13 %) associated to a stronger increase of mRNA encoding for the inflammatory proteins TNFα (4.6±0.80), COX 2 (3.148±1.6±0.63) and NLPR3 inflammasome-related molecules. Pretreatment of OB gastric SMC with APO restored by 84.7±1.02 antioxidant capacity and completely inhibited the expressions in OB NW patients.

Conclusion: Our study indicates a role for ROS in activation of NLPR3 inflammasome in obese gastric smooth muscle leading to a significant dysmotility that could be restored by the use of antioxidant agents.

Disclosure of Interest: All authors have declared no conflicts of interest.

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OP122 ACOCTIAMIDE-SENSITIVE IMPAIRED RECEPTIVE RELAXATION OF LOWER ESOPHAGEAL SPHINCTER IN PATIENTS WITH ESOPHAGOgastrIC JUNCTION OUTFLOW OBSTRUCTION

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Introduction: The pathogenesis and treatment of esophagogastric junction outflow obstruction (EGJOO) are not fully understood. The lower esophageal sphincter (LES) reportedly exhibits accommodation responses, and LES pressure is suppressed by swallowing and pharyngeal water stimulation (PWS) (Mittal, Gastroenterology 145:375-385). Acotiamide (ACO) induced LES relaxation appears to be analogous to gastric receptive relaxation. We have previously reported that acotiamide was effective for patients with EGJOO.

Aims & Methods: This study was aimed to evaluate the physiologic characteristics of acotiamide-sensitive LES relaxation in patients with EGJOO. High-resolution manometry was performed according to a standard protocol with the participant in the supine position, while swallowing ten 5-ml liquid boluses. 13 patients with EGJOO (mean age 65.2±4 standard deviation 4.1 years, eight of whom were women) and 19 participants with normal esophageal pressures (mean age 50.0±3.0 years, 11 of whom were women) were enrolled. Basal LES pressure (BLES) and the integrated relaxation pressure (IRP) were measured. The extent of PWS-induced LES relaxation (mmHg) was calculated as the difference between BLES and the mean LES pressure in the 5-5 period before PWS.

Results: There was no difference in BLES between normal subjects (34.6±2.1 mmHg) and patients with EGJOO (32.7±1.8 mmHg), but IRP was significantly higher in patients with EGJOO (20.3±4.1 mmHg) than normal subjects (10.8±0.6 mmHg). In normal subjects, LES pressure immediately declined from 34.6±2.1 mmHg to 25.6±1.4 mmHg when the fluid bolus stimulated the mouth and pharynx on the first swallow. Mean PWS-induced LES relaxation was 6.8 mmHg in normal subjects, but was absent in patients with EGJOO.
The mean LES pressure induced by PWS was 33.0±1.6 mmHg, and did not differ significantly from the HLES (52.7±10.9 mmHg). Acotiamide was effective in addressing severe symptoms in six out of 13 patients with EGJOO. Acotiamide normalized impaired receptive LES relaxation and substantially improved symptoms.

Conclusion: Esophageal subjects have receptive LES relaxation, but this is impaired in EGJOO. Acotiamide normalizes IRP in EGJOO, mainly by restoring LES receptive relaxation.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

MONDAY, OCTOBER 17, 2016 15:45–17:15
EDENDOMIC ENDOSCOPY OF UPPER GASTROINTESTINAL CANCER – ROOM U1–5

OP123 Efficacy and Safety of ESD for Superficial Cancer of the Cervical Esophagus
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Introduction: It is a difficult to observe a lesion in the cervical esophagus because of the difficulty in spreading the tumor. It is a challenge not only to find esophageal cancers at an early stage, but also to successfully treat them by ESD compared with lesions located at the thoracic esophagus.

Aims & Methods: The aim of this study was to clarify the efficacy and safety of ESD for superficial cancer located at the cervical esophagus. Patients who met the following criteria (case group) were enrolled in this retrospective study: 1) ESD was performed from January 2006 to December 2015; 2) the lesion was located at the cervical esophagus; and 3) squamous cell carcinoma (SCC) was proven histologically. Forty-five patients met those criteria. As a control group, 379 patients with 405 lesions of SCC which were located at the middle thoracic esophagus were enrolled. The lesions with entire circumferential mucosal defect, recurrent lesions after radiotherapy, and the lesions located near the scar were excluded in both groups. We evaluated advocated in both groups including stress and pneumonia, procedure time, en bloc resection rate, and frequency of local recurrence.

Results: In the case group, the average age was 67.3 years old, and the male-to-female ratio was 7:3. The average maximum size of lesions was 20.7 mm, and the histological depth of invasion was EP/LPM, MM, and SM2 in 39, 5, and 1 cases, respectively. The en bloc resection rate and R0 resection rate was 100% and 91.1%, respectively, and the mean procedure time was 57 min. ESD was performed for under general anesthesia in 32 patients (71.1%). Damage of the muscle layer during treatment was observed in 5 patients, for which clipping was performed in 2 patients. Esophageal stricture was observed in 9 patients (41%), for which local injection of steroid was administered in 6 patients. No post-ESD bleeding was observed. Although perforation was identified in one patient, he recovered with conservative treatment. Chemoradiation therapy as additional treatments were conducted in 1 patient. No local recurrence was observed during an average duration of follow-up of 34.1 months. In the control group, the average age was 60.7 years old, and the male-to-female ratio was 3:7. The average maximum size of lesions was 24.2 mm, and the histological depth of invasion was EP/LPM, MM/SIM, and SM2 in 306, 67, and 32 cases, respectively. The en bloc resection rate and R0 resection rate was 100% and 96%, respectively, and the mean procedure time was 54 min. ESD was performed under general anesthesia in 45 patients (11.1%). Damage of the muscle layer during treatment was observed in 91 patients (22.5%), for which clipping was performed in 38 patients. Esophageal stricture was observed in 14 patients (6.6%) of 213 patients with more than half of mucosal defect, for which local injection of steroid or PGA sheet were administered in 38 patients. No post-ESD bleeding was observed. Although perforation was identified in three patients, they recovered with conservative treatment.Surgery or chemoradiotherapy as additional treatments were conducted in 19 or 49 patients respectively. Local recurrence was observed in one patient during an average duration of follow-up of 41.8 months.

Conclusion: Safe ESD for superficial esophageal cancer in the cervical esophagus could be achieved under an appropriate management and successful local control was also confirmed. The stricture after ESD in the cervical esophagus developed significantly higher than those in the middle esophagus.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP124 Submucosal TUNNELING ENDOSCOPIC RESECTION VS. THORACOSCOPIC SURGERY FOR LARGE SYMPTOMATIC SUBMUCOSAL TUMORS IN THE ESOPHAGUS AND ESOPHAGOGASTRIC JUNCTION
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Introduction: Small gastrointestinal submucosal tumors (SMTs) are asymptomatic and undetectable, while patients with larger tumors have symptoms, and require intervention. Previously, thoracoscopic surgery (TS) was the only technique for large tumors, whereas the new technique, submucosal tunneling endoscopic resection (STER) was also proven effective for the resection of upper gastrointestinal SMTs. Recently, reports about STER are increasing. However, it is unclear whether STER is feasible for large SMTs. Moreover, studies about comparison of STER and surgery for upper gastrointestinal SMTs are still little. Aims & Methods: The aim of this study is to compare the clinical outcomes of STER and thoracoscopic surgery for large symptomatic SMTs in esophagus and esophagogastric junction, as well as to analyze the clinicopathological factors that affect the feasibility of STER. Patients with large SMTs of the esophagus and the MP layer in esophagus and EGJ were enrolled in this retrospective study between May 2011 and December 2013. The clinicopathological data of a total of 145 patients were collected and analyzed.

Results: Among the 145 patients (83 patients treated by STER). Patients who met those criteria were observed in the control group. The stricture after ESD in the cervical esophagus developed significantly higher than those in the middle esophagus.

Disclosure of Interest: All authors have declared no conflicts of interest.
antibiotics. There were no treatment-related deaths. On pathological examina-
tion, 20 were tubular adenocarcinoma, and 11 were tubular adenoma. Histologically, curative resection was obtained in 26 of the 31 lesions (83.9%). There were no differences in gross type (elevated type/flattened depressed type), tumor size, or histology between primary and metastatic lesions. However, loco-regional spread and survival was significantly different (P = 0.029). Furthermore, there were significant differences in U/P (M = 0.016) and U/L (P = 0.014). Therefore, there was a slightly higher frequency of metastatic lesions in the U area.

Conclusion: Metachronous lesions tended to develop in the U area. These results suggested that curatively observe the U area by surveillance endoscopy after ESD for gastric neoplasms.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP126 A SIMPLE SCORING SYSTEM TO STRATIFY CURABILITY AFTER ENDOCOSMIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER WHICH HAS PATIENT-RELATED FACTORS HIGHLY RELATED WITH LYMPH NODE METASTASIS: DEVELOPMENT AND VALIDATION OF “ECURU SYSTEM”


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Introduction: According to the European and Japanese guidelines for endoscopic submucosal dissection (ESD) of early gastric cancer (EGC), radical surgery is recommended for patients after ESD that does not meet the curative criteria because of the potential risk of lymph node metastasis (LNM). However, as LNM occurs in only 5–10% of patients who undergo radical surgery, this recommendation may be overtreatment.

Aims & Methods: This multicenter study aimed to establish a scoring system (eCura system) for deciding the potential risk of LNM after ESD with pathological factors related with LNM. Of the 15,785 consecutive patients who underwent ESD at 14 institutions between January 2006 and August 2011, we retrospectively reviewed 2,006 patients who did not meet the curative criteria for ESD of EGC. This study consisted of two stages. First, the risk-scoring system for LNM was developed using multivariate logistic regression analysis in 1,101 patients who underwent radical surgery after having failed to meet the curative criteria. The estimated factors were tumor size (> 30 mm), tumor depth (submucosal invasion ≥ 500 μm; SM2), histopathological type (undifferentiated-type), lymphatic invasion, venous invasion, ulceration (scar), and positive vertical margin. Second, for validating the risk-scoring system, the validity by survival analysis was evaluated in 905 patients without additional treatment.

Results: In the development stage, based on accordant regression coefficients, five risk factors for LNM were weighted with point values: 3 points for lymphatic invasion and 1 point each for tumor size > 30 mm, positive VM, venous invasion, and SM2. Then, the patients were categorized into three LNM risk groups: low risk (m: SM1), intermediate risk (2–4 points: 6.7%), and high risk (5–7 points: 30 mm, positive VM, venous invasion, ulceration (scar), and positive vertical margin were identified as independent risk factors for lymph node metastasis. Those patients who were categorized into the intermediate-risk group were recommended to receive adjuvant chemotherapy.

Conclusion: A simple scoring system (eCura system) was developed to make a decision on the treatment policy for patients who underwent ESD and did not meet the curative criteria. The present study demonstrated the validity of this system. However, its efficacy for improving survival needs to be demonstrated by prospective studies.

Disclosure of Interest: All authors have declared no conflicts of interest.


OP127 COMPARISON OF EMR AND ENDOCOSMIC SUBMUCOSAL DISSECTION FOR RESECTION OF EARLY STAGE GASTRIC CANCER

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Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are now being increasingly used for the treatment of gastrointestinal neoplasia. However, their efficacies (en-bloc and curative resection) have not been compared. EMR is associated with local recurrences, especially when lesions larger than 20 mm are resected in a piecemeal manner (1). In piecemeal-resected specimens, histologic assessment becomes difficult, because of the effects of burning on the lesion. ESD permits a larger resection of the tissue over the muscarians propria, including large lesions and positive non-lifting sign lesions, with its major advantage being the ability to achieve a higher en-bloc resection rate due to submucosal dissection with a direct view. This results in enhanced curability and more accurate histopathological assessment. However, this procedure is known to have several disadvantages such as greater technical difficulty and increased risk of related complications.

Aims & Methods: The aim of this study is to find the best method for treating early gastrointestinal neoplasia. Fifty-one patients (mean patient age 71, range 32–92 years, male: female ratio 25:26) including 19 involved adenoma with low-grade dysplasia, 21 intraepithelial cancer with high-grade dysplasia, 3 minute submucosal cancers, 6 submucosal deep cancers and 2 carcinoid tumors submitted to ESD, were compared to 98 patients (mean patient age 62.7, range 20–88 years, male: female ratio 54:46) who underwent EMR (20 involved adenoma with low-grade dysplasia, 42 intraepithelial cancers with high-grade dysplasia, 24 minute submucosal cancers, 3 submucosal deep cancers, 4 carcinoid tumors, 3 granular cell tumors and 2 Brunner’s adenoma). In ESD group, the mean operation time was 1.6 hrs and the mean size of resected specimen was 25.5 mm (range 10–80 mm); in EMR group, the mean operation time was 0.9 hrs and the mean size of resected specimen was 26.2 mm (range 10–100 mm). En-bloc resection rate, curative resection rate, piecemeal resection, recurrence rate, post-operative bleeding and perforation rate were compared with the use of the chi-square test.

Results: En-bloc resection rate (ESD: 82.4%, 42/51 vs EMR: 51%, 50/98; p < 0.01) and curative resection rate (ESD: 88.2%, 45/51 vs EMR: 72.9%, 71/98; p < 0.05) were significantly higher in ESD group in comparison with EMR group. Recurrence rate was 3.9% (2/51) when compared to conventional EMR (2%, 2/98) (p < 0.01). In EMR group, 6 patients developed local recurrences (6.1%); five were successfully treated by additional EMR, and one by surgical resection; in contrast, there was no recurrence in the ESD group (p = NS). The post-operative bleeding rate was 3.9% (2/51) in ESD and 3.1% (3/98) in EMR group (p = NS). Perforation rate for ESD was 3.9% (2/51) when compared to conventional EMR (2%, 2/98) (p = NS).

Conclusion: In the present study, we evaluated the efficacy of 2 endoscopic resec-
tion methods from the perspectives of en-bloc and curative resection rates. Based on these aspects, an ESD was found to be the best method for early gastrointestinal cancers; EMR would be a good alternative to an ESD, especially for high-risk patients when performed by less experienced endoscopists.

Disclosure of Interest: All authors have declared no conflicts of interest.


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Introduction: The author and Japan Gast Study Group (JGSG) reported that the eradication of Helicobacter pylori reduced the incidence of metachronous gastric cancers (GC) after endoscopic mucosal resection significantly in the Lancet study (2008; 371: 1593–99). This multicentric prospective study is performed in patients who failed to meet the curative criteria for ESD.

Aims & Methods: We analyse long-term outcomes of the incidence rate of meta-
chronous GC for JGSG enrolled patients at Yamagata Prefectural Central Hospital. Out of 89 enrolled patients, 6 patients died by other diseases and 43 cases were not yet eradicated and 1 case was eradicated unsuccessfully. The incidence rate of metachronous GC of the eradication group was 4.8% but that of the non-eradication group was about four times higher than that of the eradication group even in 15th observation year. All cases were not yet eradicated and 1 case was eradicated unsuccessfully. The incidence rate of metachronous GC was analysed and compared between the two groups.

Results: Out of the eradication group, 1 metachronous GC was detected (9 years 7 months after the enrollment). Out of the non-eradication group, 4 metachro-
nous GC were detected (5 years 3 months, 6 years 7 months, 10 years 2 months, 12 years 10 months after the enrollment). When these 4 lesions were detected, 3 cases were yet eradicated and 1 case was eradicated unsuccessfully. The incidence rate of metachronous GC of the eradication group was 4.8% but that of the non-eradication group was 21.1%.

Conclusion: The incidence rate of metachronous GC of the non-eradication group was about four times higher than that of the eradication group even in 15th year. All 4 cases of metachronous GC of the non-eradication group were persistent infected cases. The earlier eradication of Helicobacter pylori is recommended.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: J.P.H. Drenth: Novartis provided the study drug and partially funded this investigator-initiated study. Novartis did not have any influence on the execution of the trial or the preparation of the manuscript.

All other authors have declared no conflicts of interest.

Our aim was to test whether pasireotide could improve the symptomatic relief, but there were no differences between groups (p = 0.92).

Aspiration sclerotherapy is a highly effective treatment option of large symptomatic hepatic cysts. However, inadequate cyst reduction is frequently reported. Somatostatin analogues are able to curtail cyst volume. We hypothesized that pasireotide might enhance hepatic cyst reduction.

**Introduction:** Aspiration sclerotherapy is a therapeutic option for large symptomatic hepatic cysts. However, inadequate cyst reduction is frequently reported. Somatostatin analogues are able to curtail cyst volume. We hypothesized that pasireotide might enhance hepatic cyst reduction.

**Aims & Methods:** Our aim was to test whether pasireotide could improve the efficacy of aspiration sclerotherapy of large symptomatic hepatic cysts. We conducted a single-center, randomized (1:1 ratio), double-blind, placebo-controlled trial in patients with a large (> 5 cm) symptomatic hepatic cyst. All patients underwent aspiration sclerotherapy. In addition, we randomized patients between two arms: (1) pasireotide 60 mg long-acting release (LAR) injection or (2) placebo (saline) injection. Injections were administrated two weeks prior and two weeks after aspiration sclerotherapy. Primary endpoint was proportional cyst diameter reduction following six weeks, as measured by ultrasonography. Secondary outcomes included long-term diameter reduction at 26 weeks, symptomatic change at 26 weeks, and safety during the study. Symptomatic change was evaluated using the polycystic liver disease-questionnaire (PLD-Q) that assesses frequency and severity of 14 disease-specific symptoms leading to a total PLD-Q score.

**Results:** Thirty-four patients (32 females [94%]; mean age 53.6 ± 7.8 years) were randomized between pasireotide (n = 17) and placebo (n = 17). Pasireotide did not improve efficacy of aspiration sclerotherapy at six weeks compared to controls (23.6% [IQR 9.6–31.8%] versus 21.8% [IQR 9.6–31.8%], respectively; p = 0.98). Long-term cyst diameter reduction was similar in both groups (49.1% [IQR 27.0–73.6%] and 45.5% [IQR 29.2–59.6%]; p = 0.90). Mean PLD-Q scores improved significantly in both groups (p < 0.01) indicating symptomatic relief, but there were no differences between groups (p = 0.92). Transient hyperglycaemia was seen in all patients allocated to pasireotide.

**Conclusion:** Aspiration sclerotherapy is a highly effective treatment option of large symptomatic hepatic cysts, spiking with pasireotide does not further improve efficacy.

**Disclosure of Interest:** J.P.H. Drenth: Novartis provided the study drug and partially funded this investigator-initiated study. Novartis did not have any influence on the execution of the trial or the preparation of the manuscript. All other authors have declared no conflicts of interest.


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**Introduction:** Knowledge of pathogenic spectrum for cholangitis is important for adequate empiric therapy. *Enterococcus* species, which come well equipped with a variety of intrinsic antibiotic resistances, are sometimes isolated. However, little is known of risk factors for this organism’s isolation in patients with cholangitis. We conducted a study to investigate them on the basis of single-center experience in Japan.

**Aims & Methods:** Consecutive 191 hospitalized patients with cholangitis with positive bile and/or blood culture between January 2009 and October 2015 were enrolled. Diagnosis of cholangitis was based on clinical symptoms, blood chemistry and radiological imaging. Potential risk factors for *Enterococcus* species isolation such as patient attributes (Age, sex, underlying conditions, and past medical history) were retrospectively investigated. Univariate and multivariate analyses to identify risk factors were performed using a proportional hazards model.

**Results:** 127 patients were men (67%). The average age was 74.2(49–97) years. *Enterococcus* species were isolated in 128 episodes from bile and/or blood culture. Age over 75 years old (Odds Ratio [OR] = 3.19; 95% Confidence Interval [CI] = 1.19–8.98; 95% CI = 1.09–3.54; P = 0.028), prior endoscopic sphincterotomy (OR = 5.676; CI = 2.731–11.87; 95% CI = 0.905–57.84; P = 0.045), presence of device in biliary tract (OR = 0.0099, biliary reconstruction (OR = 5.895; CI = 1.301–26.71; P = 0.015), stayed in Intensive Care Unit in past admission (OR = 2.72; CI = 1.907–11.26; 95% CI = 1.907–11.26; P = 0.005) and biliary reconstruction (OR = 8.945; CI = 2.247–60.12; 95% CI = 2.247–60.12; P = 0.001) were independent significant risk factors.

**Conclusion:** We found prior endoscopic sphincterotomy and biliary reconstruction were independent risk factors for *Enterococcus* species isolation in cholangitis. We should consider empirical therapy with anti-enterococcal antibiotics when managing patients with these attributes.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP130 A STUDY TO INVESTIGATE RISK FACTOR FOR ENTEROCOCCUS SPECIES ISOLATION FROM BILE AND/OR BLOOD CULTURE OBTAINED FROM PATIENTS WITH CHOLANGITIS**


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**Introduction:** Knowledge of pathogenic spectrum for cholangitis is important for adequate empiric therapy. *Enterococcus* species, which come well equipped with a variety of intrinsic antibiotic resistances, are sometimes isolated. However, little is known of risk factors for this organism’s isolation in patients with cholangitis. We conducted a study to investigate them on the basis of single-center experience in Japan.

**Aims & Methods:** Consecutive 191 hospitalized patients with cholangitis with positive bile and/or blood culture between January 2009 and October 2015 were enrolled. Diagnosis of cholangitis was based on clinical symptoms, blood chemistry and radiological imaging. Potential risk factors for *Enterococcus* species isolation such as patient attributes (Age, sex, underlying conditions, and past medical history) were retrospectively investigated. Univariate and multivariate analyses to identify risk factors were performed using a proportional hazards model.

**Results:** 127 patients were men (67%). The average age was 74.2(49–97) years. *Enterococcus* species were isolated in 128 episodes from bile and/or blood culture. Age over 75 years old (Odds Ratio [OR] = 3.19; 95% Confidence Interval [CI] = 1.19–8.98; 95% CI = 1.09–3.54; P = 0.028), prior endoscopic sphincterotomy (OR = 5.676; CI = 2.731–11.87; 95% CI = 0.905–57.84; P = 0.045) were independent risk factors.

**Conclusion:** We found prior endoscopic sphincterotomy and biliary reconstruction were independent risk factors for *Enterococcus* species isolation in cholangitis. We should consider empirical therapy with anti-enterococcal antibiotics when managing patients with these attributes.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP131 MENOPAUSAL HORMONE THERAPY AND RISK OF BILIARY TRACT CANCER**

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**Introduction:** The risk of developing biliary tract cancer, including cancers of the gallbladder and extrahepatic bile ducts, may be influenced by estrogen...
OP132 MUCIN3A, A PROMISING TUMOR MARKER FOR DIAGNOSIS OF EXTRAHEPATIC CHOLANGIOCARCINOMA

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Introduction: The expression of extrahepatic cholangiocarcinoma (ECC) was poor for the histological diagnosis of early diagnosis due to their anatomical location and insidious onset, and little effective tumour markers. Our previous study showed Mucin3A (MUC3A) was the main differential protein in bile with proteomics technology using isobaric tags for relative and absolute quantitation (iTRAQ) in 16 patients with ECC and 20 patients with sphincter of oddi dysfunction.

Aim: To validate the histologic expression of MUC3A in ECC and explore diagnosis value of serum MUC3A as the potential tumor marker for diagnosis of ECC. Methods: (1) The expression of MUC3A was detected in 15 specimens of ECC and 20 normal bile duct tissues specimens by immunohistochemistry method. The relationship between MUC3A and the clinicopathologic features of ECC were investigated. (2) Serum MUC3A was measured in 16 preoperative patients with ECC and 15 preoperative patients with SOD. Serum MUC3A in 16 patients with ECC were compared preoperative with postoperative one month. (3) The clinical diagnosis application of serum MUC3A was compared preoperative with postoperative diagnosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP134 EPIDEMIOLOGY OF GALLBLADDER POLYPs ON HISTOLOGICAL ASSESSMENT AFTER CHOLECYSTECTOMY

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Introduction: Gallbladder polyps can be divided in neoplastic polyps (adenoma, dysplastic polyp, and carcinoma) and nonneoplastic polyps (e.g. cholesterol polyp, inflammatory polyp or adenomyomatosis). Cholecystectomy is only indicated for neoplastic polyps, as they are (pre)malignant. 2. Annually, over 23,000 cholecystectomies are performed in the Netherlands. However, there is scarce pathology data on the prevalence of gallbladder polyps and attribution of neoplastic and nonneoplastic.

Aims & Methods: We aimed to assess nationwide pathology data on gallbladder polyps over a 10-year period. Methods: The PALGA database, the Dutch Pathology Registry, was used to identify all histopathologically proven gallbladder polyps. The period covered was 2002-2012. The data was restricted to histological samples of patients ≥ 18 years of age. Biopsies, and cholecystectomies performed as part of primary non-gallbladder surgery (e.g. whipple or hepatectomy), were excluded. All excerts concerning primary gallbladder surgery containing a polyp or (focal) wall thickening > 5 mm were excluded. These excerpts were rated as neoplastic (adenoma, dysplasia, carcinoma or other malignancies) or nonneoplastic (all other types of polyp). If both neoplastic and nonneoplastic lesions were present, the excerpt was classified as neoplastic. Prevalence of gallbladder

References
2. MacK, 2005 and December 2011 aiming to investigate the risk of biliary tract cancer after menopausal hormonal therapy (MHT). The National Prescribed Drug Register was used to identify MHT exposed women during the study period. For each exposed woman, three unexposed women were randomly selected from the same study base. Unexposed individuals were exactly matched for history of delivery, thrombotic events and hysterectomy, creating 8 study cohorts. The final cohort consisted of more than 1 million women and follow-up was performed over 7 years. The odds of gallbladder cancer were decreased in MHT exposed women (OR 0.9, 95% CI 0.8–0.9), whereas no clear association between MHT-exposure and cancers of the extrahepatic bile ducts were seen (OR 0.8, 95% CI 0.6–1.2). There were no clear differences when the analyses were stratified for estrogen or estrogen/progestogen combinations. Adjusting for clinically manifest gallstone disease attenuated the odds of gallbladder cancer in MHT-exposed women (OR 0.8, 95% CI 0.6–1.2). Additionally, MHT exposure significantly increased the risk of gallstone disease (OR 7.0, 95% CI 6.6 – 7.3). Compared with the preoperative results, postoperative bile specimens were high than in normal bile duct tissues specimens (83.3% vs. 35.0%, P<0.05). (2) The preoperative serum values of MUC3A in patients with ECC were compared preoperative with postoperative one month. (3) The clinical diagnosis application of serum MUC3A was compared preoperative with postoperative diagnosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. MacK
polyps and the attribution of neoplastic polyps and nonneoplastic polyps was calculated. The prevalence of gallbladder polyps, we obtained the total number of cholecystectomies between 2003-2013 from PALGA.

**Results:** In total 220,612 cholecystectomies were performed over the period 2003-2013. The PALGA search identified 4532 excerpts, representing 4549 patients. A total of 337 patients were excluded due to primary non-gallbladder surgery, leaving 4012 unique cholecystectomies. In 2083 cholecystectomies (0.9%), a polyoid lesion was present. Which results in a calculated prevalence of polyps in 944/100,000 patients who undergone cholecystectomy. Of the polyps, 1172 (56.3%) were adenomas; 726 (33.5%) adenocarcinomas, and 57 (2.7%) other malignancies. Nine hundred and ten (43.7%) polyps were nonneoplastic; 375 (18%) cholesterol polyps, 334 (16%) adenoma’s, 70 (3.7%) hyperplastic polyps, 34 (1.6%) mucosal polyps, 42 (2.0%) inflammatory polyps, 18 (0.9%) papillomas and 17 (0.8%) other types of polyps.

**Conclusion:** Approximately one percent of gallbladders contain a polyp on histopathological assessment after cholecystectomy. Fifty-six percent of the polyps after cholecystectomy are neoplastic.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**Monday, October 17, 2016**

**15:45-17:15**

**Mechanisms of Liver Cancer and Portal Hypertension – Room 1.86**

**OP135 Changes in Circulating MiRNAs after Treatment: MiRNA Signatures to Predict Therapy Response: and Disease Free Survival in Hepatocellular Carcinoma**

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**Introduction:** Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related death worldwide. Although treatment options have improved in the past 30 years, prognosis remains unfavorable in many patients. The lack of effective models for outcome prediction presents the opportunity for individualization of treatment. The potential role of microRNAs (miRNAs) as prognostic biomarker has witnessed an increasing attention, owing to the non-invasive nature of miRNA-based screening assays. While many studies have suggested several miRNAs as biomarker candidates, dynamic variations over extended time periods have been observed until now.

**Aims & Methods:** To identify potential circulating miRNA signatures for the prediction of therapy response and patient follow-up. Methods: 15 consecutive patients with early/intermediated stage HCC were enrolled and treated according to the ESSL/ASLSD practice guidelines. Patients were staged (CT scan and/or MR) at time 0 (T0, before treatment), 1 month (T1) and 6 months (T6) from starting therapy. Circulating miRNA levels were measured in serum samples at T0, T1, T6 (T0) and 6 months from the start of treatment. Serological and cytopathology data network and archive.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP136 Hepatitis B Virus Genotype, Zinc Ribbon Domain-Containing 1 Antisense RNA 1 (ZNRD1-AS1) and Their Interactions in Hepatocellular Carcinoma: A Multi-Center Case-Control Study**

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**Introduction:** Zinc ribbon domain-containing 1 antisense RNA 1 (ZNRD1-AS1) genetic polymorphisms have been associated with hepatocellular carcinoma (HCC) development. We aimed to determine impacts of ZNRD1-AS1 polymorphisms and their interactions with HBV genotypes on the risk of HCC.

**Aims & Methods:** We conducted a large multi-center case-control study with a total of 1,507 HBV-related HCC cases and 1,560 HBV persistent carriers. Three single nucleotide polymorphisms (SNPs) in ZNRD1-AS1 (rs3757328, rs6940552 and rs9261204) were genotyped using TaqMan allelic discrimination assay, and HBV genotypes were identified by multiplex PCR.

**Results:** We found consistently significant associations between ZNRD1-AS1 rs6940552/rs9261204 and increasing risks of HCC (dominant genetic model: adjusted OR = 1.16, 95% CI = 1.03–1.32 for rs6940552; adjusted OR = 1.29, 95% CI = 1.06–1.53 for rs9261204), and a borderline significant association of rs3757328 with HCC risk. Based on the combined evidence, we observed between the increasing number of variant alleles of the three SNPs and the risk for HCC (P for trend <0.001). Moreover, a strong combined effect of the three SNPs was observed among the subjects infected with non-B groups (adjusted OR = 1.26, 95% CI = 1.05–1.50) on HCC risk, compared with those in HBV B-related genotype groups (adjusted OR = 0.89, 95% CI = 0.69–1.15) was significantly higher than that (0.029 for heterogeneity test). We also detected a significant multiplicative interaction between the variant alleles and HBV genotype on HCC susceptibility (P = 0.030).

**Conclusion:** ZNRD1-AS1 SNPs (rs3757328, rs6940552 and rs9261204) and their interaction with HBV genotypes may serve as susceptibility biomarkers for risk of HBV-related HCC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP137 HMBG1-dependent Autophagy: A New Pathway to Maintain Regulatory T cell Function in Patients with Chronic Hepatitis B**

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**Introduction:** Recent studies suggest autophagy is highly active in regulatory T (Treg) cells. High-mobility group box-1 protein (HMBG1), enriched in the microenvironment of damaged and injured livers, is critical for T cell autophagy.

**Aims & Methods:** This study is designed to determine whether and how HMBG1-dependent autophagy maintains the immunosuppressive features of Treg cells during chronic hepatitis B virus (HBV) infection. Blood samples from patients with chronic hepatitis B (CHB, n = 36), at immune-tolerant stages (IT, n = 25) and healthy controls (n = 50) were collected. By flow cytometry, CD4+CD25+CD127– (Treg) cells were purified from peripheral blood mononuclear cells (PBMCs) for further analysis. Serum samples were prepared to determine HMBG1 levels. The autophagy in Treg cells were in vitro determined with Lysotracker Green probes in the presence or absence of HMBG1, rapamycin and 3-methyladenine. HMBG1-dependent autophagy pathway and its effects on Treg function were determined with Treg cell lines. The microtubule-associated protein 1 light chain 3 (LC3)-GFP mice were injected with AAV-1-3HBV to further determine HMBG1-dependent autophagy in Treg cells in the microenvironment of livers during chronic HBV infection.

**Results:** Treg cells from patients in IT group had significantly up-regulated baseline autophagy levels compared to both CHB and HC groups, reflected by increased intracellular mass of lysosomes. The mean fluorescence intensity (MFI) of lysosomes in Treg cells significantly and positively correlated with serum HMBG1 levels. In vitro, HMBG1 mainly acted through the receptor for advanced glycation end-products (RAGEs) of Treg cells to up-regulate the autophagy levels, with significantly decreased phosphorylation of mTOR and increased Beclin-1/Vps34 proteins. Besides, HMBG1–RAGEs induced autophagy in negative control mouse fibroblasts (CTLA-4, IL-10 and TGF-beta miRNA levels of Treg cells. In HBV-infected mouse models, the intra-hepatic HMBG1, RAGEs and LC3 expressions were significantly increased. Moreover, down-regulated p-mTOR and up-regulated Beclin-1/Vps34 proteins were detected in the autophagy-deficient in vitro Treg cells.

**Conclusion:** HMBG1-dependent autophagy is a new mechanism to maintain the immunosuppressive features of Treg cells during chronic HBV infection.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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clarify the mechanisms responsible for liver atrophy, pathological analysis should be carried out within the shortest possible time. However, to the best of our knowledge, these time-course studies have not yet been carried out.

Aims & Methods: We attempted to investigate the mechanism of liver atrophy by portal vein obstruction and clarify the role of autophagy and apoptosis. As pig lobule structures were well-defined as compared with human specimen, we performed percutaneous transhepatic portal embolization (PTPE) in 5 pigs. And then sacrificed them at day 0, week 2, or 4 (d0, w2, w4, and w6, respectively). In specimens of embolized lobe (E) and non-embolized lobe (control, Cont), we measured the distance between portal vein and central vein (PV-CV), area and hepatocyte number per lobule and apoptotic activity. Immunohistochemically reactives of microtubule-associated protein-light chain 3 beta (LC3) as autophagy and glutamine synthetase (GS) and cytochrome 2E1 (CYP2E1) as zonation were evaluated.

Results: PV-CV and lobule area showed no significant difference between E and Cont at d0, but were lower in E than in Cont at w2, w4 or w6 (P < 0.001). Hepatocyte number was not significantly reduced in E at d0 and w2 but was reduced in E at w4 and w6 (P < 0.042). Hepatocellular apoptosis activity was higher in E than in Cont at d0 and w4. LC3 staining peaked in E at w2, with no significant difference between E and Cont at w4 and w6. GS and CYP2E1 staining in E at w2, w4 and w6 were narrower than those in Cont.

Conclusion: Our morphological study focused on changes in the lobules over time, and we observed two distinct phases of liver atrophy following portal blood flow disruption. The first (the autophagic phase) was characterized by liver shrinkage without hepatocyte loss and high LC3 expression, and lasted for the first two weeks following PTPE. The second phase, termed the apoptotic phase, was characterized by reduced hepatocyte number without reduced lobular size but with reduced LC3 expression and increased TUNEL staining, and lasted 2-4 weeks.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP175 EMBOLIZATION - ASSOCIATION WITH AUTOPHAGY AND APOTOTOPSIS

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Introduction: The mechanism of liver atrophy due to portal vein embolization is still unclear. With regard to the liver, autophagy has been reported to be caused by starvation and related to hepatocellular atrophy. Using pig models of portal vein embolization, we determined that portal vein embolization (PTPE) with absolute ethanol, which we have previously observed temporary elevated serum level of liver enzymes immediately after ethanol injection and macroscopic liver atrophy accompanied by an increased future liver remnant (total estimated liver volume ratio 2 weeks after PTPE). The other literature has reported that the relative lobule size in the embolized lobe of the pig had gradually decreased to 23% of the normal pig liver at 12 days after PTPE with a combination of coils and polynvinyl alcohol particles; thereafter, the size did not change significantly. In the present study, we have investigated the changes in liver size and structure in pig lobles treated with PTPE and the mechanisms responsible for liver atrophy, pathological analysis should be carried out within the shortest possible time.
received TAA for 16 weeks, 46% (11/24) developed liver fibrosis with a Desmet stage of 1–3. In group 16w/fib and group 16w/cir compared to group con. In group 16w/cir mean weight was significantly lower than that of group con. Thus flow volumes were adjusted according to the body weight in order to eliminate weight-induced changes in hemodynamics. Mean aortal flow volume per body weight was different among groups. In contrast mean portal flow volume per body weight was significantly reduced in group 12w/fib by 23% compared to group con. On the other hand, in group 16w/fib and group 16w/cir there was no further reduction of mean portal flow volume per body weight. This suggests that in the majority of TAA-induced liver injuries development of fibrosis is sufficient to cause a significant decrease in portal flow volume. There were no significant differences between group 12w/cir and 16w/cir in terms of all parameters, in particular portal flow volume.

Contact: The non-invasive MRI technique can be a reliable diagnostic tool to investigate the hepatic hemodynamics in different experimental models of liver injury. In this particular animal model even the TAA-induced liver fibrosis led to a significantly reduced portal perfusion. The molecular mechanisms of this finding need to be further investigated.

Disclosure of Interest: All authors have declared no conflicts of interest.

Tuesday, October 18, 2016 08:30-10:00 Optimising anti-TNF therapy – room 6

Op141 correlation of endoscopic findings with serum drug concentrations and need for rescue therapy: Subanalysis of the Trough Concentration Adapted Infliximab Treatment (TAXIT) trial

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Introduction: The Trough Concentration Adapted Infliximab Treatment (TAXIT) randomized controlled trial [1] showed that targeting patients’ infliximab trough concentrations to a 3–7 µg/mL window resulted in a more efficient use of the drug in patients with inflammatory bowel disease. Following dose optimization, continued concentration-based dosing was not superior to clinically-based dosing for achieving clinical and biochemical remission (primary endpoint) after 1 year maintenance treatment. This subanalysis of TAXIT aimed to explore the correlation between drug level-based dosing and endoscopic healing.

Aims & Methods: This was a retrospective analysis of all endoscopies performed at the end of TAXIT. For Crohn’s disease (CD) mucosal healing was defined as absence of ulcerations (complete mucosal healing) or clear improvement in ulcerations (partial mucosal healing) when compared to baseline. For ulcerative colitis (UC), healing was defined as a Mayo endoscopic subscore of 0 or 1. Rates of mucosal healing were also calculated for patients with mucosal ulcerations (partial mucosal healing) when compared to baseline. For ulcerative colitis (UC), healing was defined as a Mayo endoscopic subscore of 0 or 1. Rates of mucosal healing were also calculated for patients with mucosal ulcerations (partial mucosal healing) when compared to baseline.

Results: Of the 226 patients completing the TAXIT maintenance phase, 125 (55%) underwent endoscopy after one year (n = 55 in arm 1 and n = 70 in arm 2). As in arm 1, 60/70 (86%) patients had mucosal healing at the end of the study, as compared to 63/70 (90%) patients in the concentration-based dosing arm 2 (p = 1.0). The rates of mucosal healing were also calculated for patients in CD (n = 38 in arm 1 and n = 36 in arm 2; p = 0.69) and in UC patients separately (15/17 in arm 1 vs 14/18 in arm 2; p = 0.66). Patients who reached the primary endpoint of TAXIT more frequently had complete mucosal healing (73/84 or 87%) compared to patients who did not reach the primary endpoint (28/40 or 64%) (p = 0.02). Numerically more patients who needed rescue therapy during maintenance phase of TAXIT had not achieved mucosal healing (3/12 or 25%) compared to patients who did not need rescue therapy (9/115 or 8%) (p = 0.09). The mean serum trough concentration during maintenance phase of TAXIT was 5.31 µg/mL in patients with mucosal healing and 4.26 µg/mL in patients without mucosal healing (p = 0.33).

Conclusion: The primary endpoint of TAXIT, clinical and biochemical remission, correlated with mucosal healing. Similar rates of mucosal healing were observed in patients after clinically-based dosing compared to concentration-based dosing. A trend towards less mucosal healing was seen if rescue therapy was needed during TAXIT. Mean serum trough concentrations during the maintenance phase of TAXIT were higher in patients with mucosal healing.


Median (IQR) serum albumin 44.5 g/L (42.6–47.0) 44.1 g/L (42.2–47.0) 43.7 g/L (41.6–47.2)

Median (IQR) PRO2 CD 0.0 (0.0–7.0) 0.0 (0.0–6.0) 2.0 (0.0–9.0)

Median (IQR) C-reactive protein 1.6 mg/L (0.4–4.9) 1.4 mg/L (0.6–3.3) 1.3 mg/L (0.6–5.1)

Median (IQR) time from T0 18.0 weeks (13.5–26.1) 14.0 weeks (12.3–19.0) 30.5 weeks (26.8–34.5)

Aims & Methods:

In this retrospective cohort analysis, the outcome of dose de-escalation in patients with inflammatory bowel disease (IBD) who are in clinical remission. Dose de-escalation may not only have beneficial economic repercussions, it may possibly also decrease the occurrence of adverse events.

Aims & Methods: This retrospective cohort analysis, the outcome of dose de-escalation in IBD (40 mg every 3 weeks (ETW) in patients with IBD was studied. Out of 898 patients treated with ADM for Crohn’s disease (CD) or ulcerative colitis (UC) in a tertiary referral center, we selected all patients who had received maintenance therapy with ADM 40 mg ETW with serum levels available before and after dose de-escalation. Serum was collected 4 months prior to dose de-escalation (T1, n = 33), at dose de-escalation (T0, n = 43), 4 months after dose de-escalation (T1, n = 43) and 8 months after dose de-escalation (T2, n = 26). ADM serum levels were measured using monoclonal antibodies kit (R-biopharm AG). In addition, patient reported outcome (PRO2). C-reactive protein (CRP) and serum albumin were collected for each time-point.

Disclosure of Interest: S. Vermeire: Grants from MSD, Takeda and Abbvie, lecture fees from Abbvie, MSD, Falk, Tiltotts, Ferrigno, Centocor, Takeda, Hospira; consultancy for Ferrigno, Abbvie, Shire, Genentech/Roche, Celgene, Janssen, MSD, Takeda, Galapagos, Hospira, Mundipharma, Pfizer. G. Van Assche: Gert Van Assche receives financial support for research from Abbvie and MSD; lecture fees from Janssen, Takeda, Ferrigno, MSD, and Abbvie and does consultancy for Abbvie, MSD, and Takeda. A. Gilis: Ann Gilis has been a consultant for Merck, Janssen Biologics, and Abbvie. M. Ferrante: Research grant from Janssen Takeda, lecture fees from Tiltotts, Ferrigno, Boehringer-Ingelheim, Janssen, Chiesi, Falk, Zeria, Mitsubishi Taneba, MSD, Takeda, and Abbvie; does consultancy for Abbvie, Ferrigno, MSD, Boehringer-Ingelheim and Janssen.

All other authors have declared no conflicts of interest.
results were most sensitive to changes in the perspective of the analysis, utility values and time horizon (10-year).

Conclusion: Biosimilar infliximab is a cost-effective alternative to the originator product for the treatment of adults with luminal CD, and it may contribute to increasing the affordability of biological treatments throughout Europe.

Disclosure of Interest: J. Aisenberg has provided consultancy to Boehringer Ingelheim. P. Reilly has provided consultancy and received speaker’s honoraria from Boehringer Ingelheim. J. Aisenberg and P. Reilly have received speaker’s honoraria from Boehringer Ingelheim and Pfizer.

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Disclosure of Interest: All authors have declared no conflicts of interest.

OP146 COST-UTILITY OF BIOSIMILAR INFliximAB (INFLECTRA®) FOR THE TREATMENT OF LUMINAL CROHN’S DISEASE IN NINE EUROPEAN COUNTRIES


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Disclosure of Interest: Biosimilar infliximab (Inflectra®) has been approved by the European Medicines Agency for the treatment of luminal Crohn’s disease (CD) in both the EU and the USA. Biosimilar infliximab offers a competitive price reduction in most European countries. Nevertheless, no study has yet compared the cost-effectiveness of originator and biosimilar agents in luminal CD patients. Furthermore, there are no published studies reporting between-biological cost-effectiveness for luminal CD patients.

Aims & Methods: We aim to compare cost-effectiveness of adalimumab, infliximab, vedolizumab and biosimilar infliximab for the treatment of luminal CD in nine European countries (Belgium, France, Germany, Hungary, Italy, the Netherlands, Switzerland and the UK). A probabilistic Markov model was developed to analyse the cost-effectiveness of selected biological treatment sequences compared to the standard care or to other biological sequences in patients with moderate to severely active luminal CD unresponsive to conventional treatment. Transition probabilities of moving between health states were estimated on randomised controlled trials and cohorts. Country-specific unit costs, including drugs, monitoring, administration, hospitalization and surgical costs were considered. The model applied a third-party payer perspective and a five-year treatment strategy was applied. Clinical remission, response and biochemical response was evaluated at week 14, 30 and 54. None of the patients had received infliximab within 12 months prior to initiation of the biosimilar infliximab. Safety data was registered.

Results: 96 patients enrolled in REVERSE-ADTM across nine countries (Belgium, France, Germany, Hungary, Italy, the Netherlands, Switzerland and the UK). Complete safety, remission and response results were reported. Remission rates in both CD (p = 0.048) and UC (p = 0.047) were significantly higher in the biosimilar infliximab versus standard care treatment sequences compared to the standard care or to other biological sequences in nine European countries (Belgium, France, Germany, Hungary, Italy, the Netherlands, Spain, Sweden and the UK). A probabilistic Markov model was designed to examine the efficacy and safety of CT-P13 infliximab biosimilar in the treatment of remission maintenance treatment of Crohn’s disease and ulcerative colitis (UC). Demographic data were collected and a harmonized monitoring strategy was applied. Clinical remission, response and biochemical response was evaluated at week 14, 30 and 54. None of the patients had received infliximab within 12 months prior to initiation of the biosimilar infliximab. Safety data was registered.

Results: 291 consecutive IBD (184 CD and 107 UC) patients were included in the present cohort, of which 100 patients reached the 54 endpoint. The age at disease onset was 39.2 (22–59) years in CD and 30.7 (22–59) years in UC patients, respectively. 32.49% of CD patients had colonic/eccolonic disease location, 41% had complicated disease behaviour, 35% had perianal disease and 23% had gone through previous surgeries. 33.59% of UC patients had proctitis/ left-sided colitis/ extensive colitis. 25.14% of patients had received previous anti-TNF therapy in CD and UC, respectively. 60.52% of CD/UC patients received concomitant immunosuppressives at baseline. 55, 57 and 47% of CD patients reached clinical remission by week 14, 30 and 54. Clinical response was 83, 77 and 58%, respectively. 59, 46 and 53% of UC patients reached clinical remission by week 14, 30 and 54. Clinical response was 78, 69 and 64%, respectively. Previous anti-TNF exposure was associated with lower response and remission rates (p < 0.001). The area under the curve (AUC) from (0.14/0.05 and p = 0.004) was higher in CD and (p = N.S, 0.06, p = 0.1, 0.01 and p = 0.048) at weeks 13, 30 and 54. Mean CRP decreased significantly both in CD and UC patients by week 14, which was maintained throughout the 1-year follow-up. CRP level decreased from 39.7 to W14: 8, W30: 8.7 and W54: 12 mg/L in CD and from 29.5 to W14: 8.5, W30: 13 and W54: 12.3 mg/L in UC. 21 (6.6%) patients had infusion reactions, 23 (7.9%) patients had infections and 1 death occurred. Conclusion: This prospective nationwide cohort shows that CT-P13 is effective and safe in inducing and maintaining remission in both CD and UC. Efficacy was influenced by previous anti-TNF exposure.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: Gastrointestinal bleeding (GIB) is a feared complication of anti-platelet/ anti-thrombotic therapy. Idarucizumab (Praxbind®) is a monoclonal antibody against the direct thrombin inhibitor dabigatran. IDA should benefit management of dabigatran users experiencing severe GIB.

Aims & Methods: The on-going REVERSE-ADTM study evaluates the safety and efficacy of IDA 5 grams intravenously in dabigatran users with (A) life-threatening haemorrhage or (B) requirement for emergency surgery. Here, we analyze the clinical characteristics and outcomes of REVERSE-ADTM enrollees presenting with severe GIB. Our study is performed on an interim analysis cohort of 123 patients, centralized laboratory coagulation data are available for 90/123 (72.9%) patients with major GIB.

Results: Of the 66 patients enrolled in REVERSE-ADTM due to severe bleeding, 27 (41%) bled in the GI tract. The mean age of GIB patients was 77.5 years (range, 18–93), 15 (56%) were women and renal impairment was present in 22 (33%) of the 66 patients with creatinine clearance measurements (96%). Atrial fibrillation was the indication for anticoagulation in 93%; 74% took their most recent dabigatran dose < 24 hours prior to presentation. Ten patients (15%) bled in the upper GI tract, 8 (12%) in the lower GI tract, 5 (7%) in the oral cavity and 3 (5%) in the upper respiratory tract. Ten patients (15%) bled in the upper GI tract, 8 (12%) in the lower GI tract, 5 (7%) in the oral cavity and 3 (5%) in the upper respiratory tract. Ten patients (15%) bled in the upper GI tract, 8 (12%) in the lower GI tract, 5 (7%) in the oral cavity and 3 (5%) in the upper respiratory tract.

The mean haemoglobin at presentation was 7.3 g/dL (range, 4.8–9.7). Nine patients (13.6%) bled into the abdomen, 5 (7.7%) bled into the chest, 5 (7.7%) bled into the oral cavity, 4 (6%) bled intracranially and 1 (1.5%) bled into the skin. 11 (16.7%) patients received packed red blood cells (mean 3 units); 14 (21.2%) patients received fresh frozen plasma (mean 2.6 units); 20 (30%) patients received platelets (mean 1.5 units); and 6 (9%) patients received cryoprecipitate (mean 2 units).

Results: The median age of GIB patients was 77.5 years (range, 18–93), 15 (56%) were women and renal impairment was present in 22 (33%) of the 66 patients with creatinine clearance measurements (96%). Atrial fibrillation was the indication for anticoagulation in 93%; 74% took their most recent dabigatran dose < 24 hours prior to presentation. Ten patients (15%) bled in the upper GI tract, 8 (12%) in the lower GI tract, 5 (7%) in the oral cavity and 3 (5%) in the upper respiratory tract. Ten patients (15%) bled in the upper GI tract, 8 (12%) in the lower GI tract, 5 (7%) in the oral cavity and 3 (5%) in the upper respiratory tract.
**Aims & Methods:** We studied whether the pretreatment with melatonin results in protection of cultured rat gastric epithelial cells against indomethacin-induced gastric mucosal injury and whether it affects the expression of MT1 and -2, survivin, IGF-1, and IGF-1R in these cells. In vitro study, the cultured normal rat gastric mucosal epithelial cells (RMG1) were pretreated with vehicle or melatonin (10 μM) for 24 hrs and then exposed to either: medium alone (controls), or indomethacin (IND 0.25 mM) for 4 hrs. In these cells the following were assessed: 1) cell injury under confocal microscopy, 2) survival and apoptosis using Calcein AM live cell tracking dye and MTT assay; 3) cell proliferation using BrdU assay; 4) quantitative expression of MT1 & 2, and survivin, IGFR-1 and IGFR-1R by Western blotting and immunostaining. For comparison, the quantitative expression of MT1 and MT2 in gastric epithelial and submucosal structures from full thickness wall specimens of a normal rat stomach was elucidated.

**Results:** Rat gastric mucosa expressed both MT1 and MT2 (1.8-fold more MT1 vs. control). In cells pretreated with melatonin, IND-induced cell injury was significantly decreased more than 4 fold (P < 0.01) and catalase activity (P < 0.01) and MPO activity enhanced more than 4 fold (P < 0.01) as well as the content of nitrite enhanced in two times while arginase activity decreased more than 4 fold (P < 0.01). Administration of 4-thiazolidinone derivatives on the background of NSAID-induced gastric injury led to nitrosylated heme content and the concentration of L-arginine and H2S in blood plasma.

**Conclusion:** Administration of 4-thiazolidinone derivatives on the background of NSAID-induced gastric injury led to nitrosylated heme content and the concentration of L-arginine and H2S in blood plasma. The administration of 4-thiazolidinone derivatives on the background of NSAID-induced gastric injury led to nitrosylated heme content and the concentration of L-arginine and H2S in blood plasma.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Aspirin is a potent anti-platelet agent used for the prevention of cardiovascular and cerebrovascular diseases. However, gastrointestinal (GI) bleeding is the most frequently reported serious adverse events for the long term use of aspirin.

**Aims & Methods:** The objective of this study is to investigate whether the risk of aspirin usage on increasing ulcer bleeding would outweigh its benefit on the prevention of CRC. The present study investigated the electronic medical records from 42 publically funded hospitals, which serves a 7 million population in Hong Kong. All hospital admissions from 2000 to 2004 and their outcome in the follow-up period were extracted until 2014. Aspirin users were matched with a control in a ratio of 1:2. The non-aspirin users of the study period. Incidences of CRC and GI bleeding were the primary outcomes. Logistic regression was used to compare incidence rates and Cox-proportional hazard regression model was used to compare the mortality rates. Subgroup analyses were performed for those with ulcer bleeding, or for those with regular aspirin prescribed.

**Results:** A total of 4,564,100 subjects were identified in the system between year 2000 and 2004, and 254,887 of them (5.6%) were prescribed aspirin for at least one year. Among the subjects who were never prescribed aspirin, 481,852 subjects (10.8%) were identified in the system. The total sample size of this study was 746,739. The baseline characteristics of aspirin and non-aspirin users are described in Table 1. The mean ages of aspirin users and non-aspirin users were 68.4 (SD = 13.1) and 66.4 (SD = 13.2) respectively. In the aspirin group, 78,316 patients (30.7%) had aspirin prescribed for 10 years or more, and 54,011 of them (69.0%) were routinely prescription during the years of clinic visits. Median dose of aspirin used among the patients were 80 mg with interquartile range from 80 mg to 100 mg. Average duration of aspirin prescribed was 6.3 years. Patients in aspirin group showed significantly lower incidence of CRC (OR = 0.82, 95% CI = 0.80 to 0.85), and showed significant reduction in overall mortality among the patients with GI bleeding. On the other hand, the long-term use of aspirin showed benefit to reduce CRC on both incidence and overall mortality.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**United European Gastroenterology Journal 4(5S)**

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

POEM as a safe alternative to Heller Myotomy. However, the safety of POEM is still an intensive analysis through a large collaborative research (AEs) associated with POEM in large cohort studies has not been performed.

Aims & Methods: We aimed to study (1) the rate of AEs and (2) factors associated with occurrence of AEs in patients undergoing POEM. Methods: Patients who underwent POEM were enrolled for the treatment of achalasia and SEDs at 12 tertiary-care centers (5 US, 4 Europe, 2 Asia and 1 Australia) between 2011 and 2015 were used in a case-control study. Cases were defined by the occurrence of any AEs related to POEM procedure. Control patients were selected for each AE case by matching for age, gender, disease classification (type I vs. type II I in SEDs). All pertinent data including AEs were collected and their severity was graded according to the ASGE lexicon’s severity grading system.

Results: A total of 1826 patients underwent POEM during the study period. Of these, 1137 patients (62%) were found suitable for POEM as a safe endoscopic therapy, sigmoid esophagus, operator specialty, direction of myotomy (anterior vs. posterior), type of knife used, extent and length of myotomy, and operator experience. However, time of procedure was significantly longer in cases as compared to controls (123 min vs. 103 min ± 38, p = 0.002). Length of stay was significantly higher in patients who experienced AEs (4.93 vs. 2.7 d, p < 0.001).

Conclusion: This is the largest study that comprehensively assessed safety of POEM. POEM is a safe therapeutic modality with an overall incidence 7.5% of incidence of AEs. Severe AEs are rare. AEs result in prolongation of hospital stay. Longer procedural times (indicative of technically complex procedures) are associated with increases of AEs.

Disclosure of Interest: M. Khashab: Consultant of Boston Scientific and Xlumena. All other authors have declared no conflicts of interest.

References
1. Achem SR, Crittenden J, Kolts B and Burton L. Long-term clinical and manometric follow-up of patients with nonspecific esophageal motor disor-
4. Fischella PM, Raz D, Palazzo F, Napolitano P and Pati MG. Clinical, radiological, and manometric profile in 145 patients with untreated achala-
11. All other authors have declared no conflicts of interest.

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Introduction: Peroral endoscopic myotomy (POEM) aims to palliate symptoms of achalasia by reducing pressure at the lower esophageal sphincter (LES). Current data demonstrates high short-term clinical response in 82–100% of patients. However, long term data is very limited.

Aims & Methods: We aimed to study (1) clinical outcome of patients with a minimum post-POEM follow-up of 2 years and (2) factors associated with long term clinical failure after POEM. Methods: We conducted a retrospective review of consecutive patients with achalasia who underwent POEM with a minimum follow-up of 2 years at 10 tertiary-care centers (3 US, 4 Europe, 3 Asia). Clinical response was defined as Eckardt score ≤2 and ≥26 months, respectively. Of 159 patients with clinical response at 6 months, 11 (7%) had clinical failure. Of these, 16 patients (8.9%) had prior Heller myotomy, 65 (36%) had prior endoscopic submucosal dissection, 5 (3%) had prior balloon dilatation and may reduce emergency surgery. J Clin Gastroenterol 2012; 46(5): 356–64.

Results: A total of 179 patients (82 males (45.8%); mean age 49 yr) underwent POEM for the treatment of achalasia (type I 111, type II 111, type III 6, unspecified type 111). Of these, 16 patients (8.9%) had prior Heller myotomy, 65 (36%) had prior endoscopic submucosal dissection, 5 (3%) had prior balloon dilatation and may reduce emergency surgery. J Clin Gastroenterol 2012; 46(5): 356–64.

Clinical success was achieved in 97.5% (159/163), 99.8% (124/125), 90% (161/179) in patients with follow-up within 6 months, at 12 months, and ≥26 months, respectively. Of 159 patients with clinical response at 6 months, 11 (7%) had clinical failure. Of these, 16 patients (8.9%) had prior Heller myotomy, 65 (36%) had prior endoscopic submucosal dissection, 5 (3%) had prior balloon dilatation and may reduce emergency surgery. J Clin Gastroenterol 2012; 46(5): 356–64.

Comparison of patients with clinical response, the non responders were more likely to be younger (44±5 vs 49±6 yr, p = 0.03) and had history of prior PD (11% (61/563)) vs 53% (p = 0.03). In a multivariate analysis, history of prior PD was independently associated with long-term treatment failure (OR 2.99; 95%CI 1.09–8.03). This is the largest study that comprehensively assessed safety of POEM. It highly suggests POEM as a safe therapeutic modality with an overall incidence 7.5% of incidence of AEs. Severe AEs are rare. AEs result in prolongation of hospital stay. Longer procedural times (indicative of technically complex procedures) are associated with increases of AEs.

Disclosure of Interest: M. Khashab: Consultant of Boston Scientific and Xlumena. All other authors have declared no conflicts of interest.

References
1. Achem SR, Crittenden J, Kolts B and Burton L. Long-term clinical and manometric follow-up of patients with nonspecific esophageal motor disor-
4. Fischella PM, Raz D, Palazzo F, Napolitano P and Pati MG. Clinical, radiological, and manometric profile in 145 patients with untreated achala-
Disclosure of Interest: procedure.

Conclusion: POEM is safe and provides high initial clinical success and excellent long-term outcomes. Less than 10% of patients who had clinical response at 6 months had recurrent symptoms at 2 years. History of prior pneumatic dilatation is associated with clinical failure. Post-POEM symptomatic reflux occurs in quarter of patients, and esophagitis is found in 15% of asymptomatic patients.

Disclosure of Interest: 5. Roman: Sabine Roman is a consultant for Medtronic and Sandhill Scientific

F. Mion: Francois Mion is a consultant for Medtronic

M. Khachab: Mounir Khachab is a consultant for Boston Scientific

All other authors have declared no conflicts of interest.

OP155 A 5-YEAR LONG POEM EXPERIENCE. IS IT TIME TO DRAW CONCLUSIONS?

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Introduction: Peroral Endoscopic Myotomy (POEM) has been recently developed for the treatment of achalasia and other esophageal motility disorders. Despite being widely used in many centers, data on the long-term efficacy of POEM are still lacking. We report on a large consecutive series of patients treated with POEM, with mid- and long-term follow-up.

Aims & Methods: All the patients who underwent POEM between May 2011 and April 2016 at our endoscopy unit were retrospectively identified on a prospectively collected database. Analyzed data included demographics, clinical history, previous treatments, manometry and procedure data, complications and clinical outcomes. Follow-up visits were scheduled at 3, 6, 12, 24, 36, 48 and 60 months after POEM. EGD, manometry and barium swallow were regularly performed during follow-up. pH-monitoring study was performed once, usually between the 6- and 12-month follow-up visit. Clinical success was defined by an Eckardt score ≤ 3.

Results: A total of 347 patients underwent POEM (mean age 47 years, 48% males). Seventy-eight patients (22.5%) had type I achalasia, 174 type II (50.1%), 40 type III (11.5%), 2 Jackhammer esophagus (0.6%), 4 distal esophageal spasm (1.1%), 1 nitrateracer esophagus (0.3%); in 48 patients (13.8%) achalasia type was not classified (ie: standard manometry or incomplete examination).

Before POEM, 52 patients had undergone pneumatic dilatation (PD), 8 surgical myotomy, 8 botulinum toxin injection. The procedure was effectively completed in 338 cases (97%). Mild complications occurred in 3 patients (0.8%): a delayed bleeding, a covered esophageal perforation, and a esophageal stricture following a large ulceration. The above mentioned complications were treated conservatively. Four patients were lost at follow-up. A minimum 6-month follow-up was available for 274 patients (mean follow-up 19 months). Clinical success was achieved in 95% of patients. Thirteen patients had symptoms recurrence: 7 underwent successful PD, 3 surgery, 3 received no treatment because of mild symptoms. Clinical success slightly decreased with time, being 97%, 97%, 93%, 85%, 72% and 67% after 6, 12, 24, 36, 48 and 60 months, respectively. However, almost 50% of recurrences (6/13) occurred during the first 25 cases (learning curve). No associations were found between preoperative manometric pattern and clinical outcomes: the success rate of POEM was similar in patients with type I, type II and type III achalasia (94%, 96% and 91%, respectively, p>0.05). A total reflux time > 5% was diagnosed in 50% of the patients (111/223) who underwent pH-study. Esophagitis was seen in 28% of patients, 22% of patients receive PPI because of heartburn. Esophagitis healed completely with proton pump inhibitors (PPI) in all the patients. GERD symptoms were effectively controlled with PPI in all the patients but 2 who complained with heartburn and regurgitations.

Conclusion: Our mid-term and long-term follow-up analysis confirms the safety and efficacy of POEM for the management of achalasia and other motility disorders. The vast majority of initial clinical failure can be solved with endoscopic re-treatment. Iatrogenic GERD-rate remains the only possible drawback of the procedure.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP156 MAJOR PERI-OPERATIVE ADVERSE EVENTS OF PERORAL ENDOSCOPIC MYOTOMY (POEM): 5 YEARS' EXPERIENCE, 1680 PATIENTS

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Introduction: Peroral endoscopic myotomy (POEM) is now a widely used treatment for esophageal achalasia, supported by several large cohort studies. Although major perioperative adverse events (mAE) are rare, in-depth investigations of related risks and preventive measures are lacking.

Aims & Methods: Hence, mAE during POEM were systematically assessed in terms of incidence, risks, prevention, and management. This retrospective single-center analysis included all patients (N=1680) undergoing POEM between August, 2010 and July, 2015 at our facility. Major adverse events were defined as follows: vital-sign instability, required ICU stay, hospital readmission, conversion to open surgery, invasive postoperative procedure, blood transfusion, or hospitalization > 5 days due to functional impairment.

Results: A total of 55 patients (3.3%, 95% confidence interval [CI] 2.5-4.2%) suffered mAE, distributed as follows: delayed mucosal barrier failure, 13 (0.8%, 95% CI 0.4-1.3%); delayed bleeding, 3 (0.2%, 95% CI 0.04-0.5%); hydrothorax, 8 (0.5%, 95% CI 0.2-0.9%); pneumothorax, 25 (1.5%, 95% CI 1.0-2.2%); and miscellaneous, 6 (0.4%, 95% CI 0.1-0.8%). Four patients (0.2%) required ICU admissions. No surgical conversions occurred, and 30-day mortality was zero. In stepwise multivariate regression, experience <1 year (OR = 3.85, 95% CI 1.49-9.95), air insufflators, (OR = 3.41, 95% CI 1.37-9.50), and mucosal edema (OR = 2.01, 95% CI 1.14-3.53) were identified as related risk factors. After introducing CO2 insufflation, mAE rate declined to 1.9% (95% CI 1.2-2.7%) and seemed to plateau after 3.3 years at ~1%.

Conclusion: In general, POEM is a safe procedure. Major adverse events are rare and usually may be prevented or anticipated and conservatively managed.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


OP157 COMPARATIVE EVALUATION OF PERORAL ENDOSCOPIC MYOTOMY (POEM) FOR THE TREATMENT OF ACHALASIA IN PATIENTS WITH FAILED HELLER MYOTOMY VS PATIENTS WITHOUT A HISTORY OF SURGICAL MYOTOMY: A MULTICENTER RETROSPECTIVE COHORT STUDY


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Introduction: In patients with persistent symptoms after Heller myotomy (HM), treatment options include repeat HM, pneumatic dilation (PD) or peroral endoscopic myotomy (POEM). The data on efficacy and safety of POEM for patients who failed prior HM are limited to small series.

Aims & Methods: We aimed to compare technical success, clinical response and safety of POEM in achalasia patients with and without prior HM. Methods: We conducted a retrospective review of achalasia patients who underwent POEM at 11 tertiary centers (4 US, 4 Europe, 3 Asia). Patients were divided into two groups: (1) patients who had prior HM (HM group) and (2) those without prior HM. Control patients were selected for each HM case by matching for age, achalasia subtypes (type I&II vs type III), and baseline Eckardt scores (ES) [Stage II (ES 4-6) or Stage III (ES > 6)]. Clinical response was defined by decrease in ES to ≤ 3. Adverse events (AEs) were graded according to ASGE lexicon. Technical success, clinical success and AEs were compared between the two groups.

Results: A total of 181 patients (91 HM, 90 controls) were included. There was no difference between the groups in baseline demographics, ES and 4sIRP. The HM group had higher rate of consumption of patients with PD (44% vs 26%; p = 0.01). The length of myotomy was similar between the two groups. Technical success rates were comparable between HM group (89/1); 98%; 2 failures due to extensive submucosal fibrosis) and control group (100%) in control group (p = 0.4). Proctitis occurred in 15 patients. The mean follow-up in the two groups was 8.5 months (IQR 3.2–14.7) and was similar in both groups. 20 AEs occurred in 19 patients (7% in HM group and 12% in control group, p = 0.23). For HM and control respectively, the rate of mild (5% vs 10%, p = 0.28) and moderate (1% vs 3%) AE were similar. One severe AE (aorta tear) occurred that needed POEM in the HM group. Follow-up data were available in 153 patients. Clinical response was significantly lower in the HM group as compared to the control (80% vs 94%, p = 0.02). Mean post-POEM ES was also higher in the HM group (2.09 ± 2.5 vs 1.08 ± 1.2, p = 0.02). On univariate analysis, prior HM (OR 3.54, p = 0.02) and prior PD (OR 3.36, p = 0.01) were significantly associated with clinical failure. Disclosure of Interest:

All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

Tuesday, October 18, 2016 08:30–10:00 Liver Fibrosis: from Mechanism to Therapy - Room 1.61/1.62

OP58 GASTRIC PERORAL ENDOSCOPIC ANTRAL-PYLORO-MYOTOMY FOR THE TREATMENT OF REFRACTORY GASTROPARESIS: LARGEST SERIES WITH CLINICAL AND SCINTIGRAPHIC FOLLOW-UP

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Introduction: Gastroparesis is an invalidating motility disorder and the available treatments remain disappointing. Recently, a novel approach has been performed by performing a myotomy of the pylorus after creating a tunnel, with promising results [1-3]. We report the largest retrospective clinical experience in 23 consecutive patients treated by gastric peroral endoscopic myotomy (G-POEM). The aim was to evaluate the results of this novel technique.

Aims & Methods: This is a case consecutive report on 23 patients operated for severe refractory gastroparesis, between January 2014 and April 2016, with a rigorous prospectively designed follow-up. The inclusion criteria were patients with a disturbance of gastric emptying scintigraphy (GES) and elevated GCSI score > 2. The procedures were performed under general anesthesia in an intubated patient, with a large channel gastroscope using CO2 and the Triangle knife (Olympus, Japan) as dissection device. The steps were: sub-mucosal injection and mucosal incision 5 cm upstream the pylorus; submucosal tunnel by dissection (Swift Coag, 35W, Effect 2) until reaching the pyloric arch, which had a consistent aspect; retrograde antro-pyloromyotomy of 3cm length; closure of the mucosal flap with clips. The primary objective was to evaluate the clinical efficacy and the improvement of quality of life (visual analog scale) [5]. The secondary objectives were to document the GES evolution at 2 months and the procedure complications.

Results: The procedure was completed on all the patients. We observed a significant improvement of GCSI score at POD 5, 1 month and 3 months (3.5 ±0.8 vs. 0.8 ± 0.8; 0.9 ± 0.9; 1.1 ± 1.5; p = 0.001). Regarding the severity of symptoms analyzed separately, it was observed a significant improvement of each of them, except nausea. The overall clinical efficacy was 80% with a mean overall quality of life improvement > 65%. The GES normalized in 75% of cases, showing a significant improvement of the mean half emptying time (222 ± 90 min. vs. 133 ± 90; p = 0.03) and of retention at 2 hours (76 ± 24 vs. 44 ± 20; p = 0.009). Two patients underwent complications related to the procedure: one was a bleeding due to an ulceration along the tunnel path (coagulation necrosis) treated by endoscopy, while the other one had an arterial puncture which was transfused and was discharged at POD5–6, with PPI treatment.

Conclusion: Peroral endoscopic pyloromyotomy seems to be an effective approach for treating patients with severe refractory gastroparesis. This procedure is also highly reproducible, when applying some tips to increase the technical success rate, and safe with complication that could be managed endoscopically. It could be a new hope for a many patients whom have a poor quality of life. More data, especially in prospectives studies are needed to confirm these very promising results.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
OP160 EXPRESSION OF CD161 ON CD4+ T CELLS PROMOTES HEPATIC STELLATE CELLS ACTIVATION AND INCREASED ACID SPHINGOMYLINASE AND CD161-LECTIN-LIKE TRANSCRIPT-1 INTERACTION

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Introduction: Hepatitis B virus (HBV)-related liver fibrosis always progresses from inflammation to fibrosis. CD4+ T cell immune responses play a pivotal role in the process. Recently, CD161 is considered to be a costimulatory molecule on T cells and an important phenotypic marker of human Th17 cells.

Aims & Methods: This study was designed to investigate the roles of CD161 in the pathogenesis of HBV-related liver fibrosis. Methods: A total of 34 CHB patients who underwent liver biopsy and 20 healthy controls (HC) were enrolled. CHB patients were further categorized according to the disease phase: immune-tolerant (IT, n = 12), immune-active (IA, n = 30), or inactive CHB (n = 12). Peripheral blood mononuclear cells (PBMCs) and flow cytometry sorted CD4+CD161+ and CD4+CD161- T cells were used for preparation for flow cytometry and real-time PCR analysis. Flow cytometry sorted CD4+CD161+ and CD4+CD161- T cells were also cultured alone or co-culture with primary hepatic stellate cells (HSCs) in vitro experiment.

Results: Compared to HC, the percentage of CD4+CD161+ T cells significantly increased among IA patients while dramatically decreased among IT patients, but there was no significant difference between inactive CHB patients and HC. Besides, CD161 showed a positive correlation with histological inflammation grades and advanced histological fibrosis stages. In the PBMCs of CHB patients, CD4+CD161+ T cells exhibited a CD45RO+ memory phenotype and secreted more TNF-α, TNF-β, IL-17, INF-γ, and IFN-γ, respectively. (P = 0.001). Knocking down CD161 on CD4+CD161+ T cells and in vitro culture of CD4+CD161+ T cells revealed that CD161 expression increased the activity of acid Sphingomyelase (aSM) and subsequent PI3K/Akt and MAPK and mTOR pathways of CD4+ T cells. Both knocking down of CD161 and using imatinib to inhibit aSM could down-regulate CD4+ T cell-proliferation and interaction with IFN-γ and IFN-γ-activated HSCs. In addition, HSCs express lectin-like transcript-1 (LLT1), the only ligand of human CD161. The CD161-LLT1 interaction not only modulated the proliferation and activation of HSCs, but increased IL-17 and IFN-γ-producing CD4+CD161+ T cells as well. Knocking down of CD161 on CD4+CD161+ T cells or LLT1 on HSCs could partially reverse the aforementioned effects. In HSCs, CD4+CD161+ T cell-hybrid culture system, expression of pro-fibrotic genes in HSCs were inhibited. However, when CD161 was overexpressed on CD4+CD161+ T cells, we detected a reactivated HSCs phenotype. Our data revealed that the expression of CD161 on CD4+ T cells might promote HBV-related liver fibrosis through CD161-LLT1 interaction to activate HSCs and through raising aSM to enhance the proinflammatory functions of CD4+ T cells.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. L J, Qi SJ, She WM, Wang FP, Gao HI, Li L, Tu CT, Wang YJ, Shen XZ and Liang L. Significance of the balance between regulatory T (Treg) and T helper 17 (Th17) cells during hepatitis B virus related liver fibrosis. PLoS One 2012; 6; e39307.

TUESDAY, OCTOBER 18, 2016 08:30-10:00
FREE PAPER SESSION: NOVEL DIAGNOSTIC TOOLS: GOING DEEPER AND DEEPER INTO THE BOWEL – ROOM N1

OP161 FULL SPECTRUM ENDOSCOPY (FUSE) IN THE DETECTION OF INFLAMMATORY BOWEL DISEASE NEOPLASIA (FUSION): A RANDOMIZED CROSSOVER TANDEM STUDY VERSUS CONVENTIONAL ENDOSCOPY

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Introduction: Inflammatory bowel diseases (IBD) are the most significant factors of colorectal cancer and therefore colorectal cancer screening is widely endorsed. Conventional forward-viewing colonoscopy (FVC), however, lacks acceptable sensitivity in IBD dysplasia identification and the addition of dye-based chromoendoscopy is recommended. Full Spectrum Endoscopy (FUSE) is a novel colonoscope that incorporates 2 additional cameras to the forward camera and provides 330-degree panoramic view of the colonic mucosa. Whether FUSE can decrease dysplasia miss rate in IBD surveillance has never been tested previously.

Aims & Methods: This study aims to assess FUSE versus FVC in dysplasia surveillance in an IBD population. The dysplasia yield of targeted versus random colonic biopsies will also be assessed. Methods: A prospective, single-center, randomized-order, back-to-back crossover tandem colonoscopy study was conducted comparing FVC versus FUSE in an IBD surveillance population.

Disclosure of Interest: All other authors have declared no conflicts of interest.

Table (OP162): Diagnostic performance of WavSTAT4, Endoscopic assessment and combined algohithmic assessment for characterization fo colorectal polyps less than 10 mm in size and prediction of surveillance intervals

<table>
<thead>
<tr>
<th>Metric</th>
<th>WavSTAT alone</th>
<th>Combination of WavSTAT + endoscopic assessment (algorithmic approach)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>97.6% (95% CI 0.88-0.95)</td>
<td>85.0% (95% CI 0.77-0.89) 95.8% (95% CI 0.89-0.96)</td>
</tr>
<tr>
<td>Specificity</td>
<td>46.9% (95% CI 0.44-0.48)</td>
<td>77.2% (95% CI 0.61-0.82) 78% (95% CI 0.66-0.79)</td>
</tr>
<tr>
<td>NPV</td>
<td>98.6% (95% CI 0.85-0.91)</td>
<td>91% (95% CI 0.73-0.84) 98.5% (95% CI 0.89-0.95)</td>
</tr>
<tr>
<td>PPV</td>
<td>54.7% (95% CI 0.28-0.47)</td>
<td>66% (95% CI 0.44-0.79) 89.3% (95% CI 0.76-0.92)</td>
</tr>
<tr>
<td>Surveillance interval (% of patients coded correctly)</td>
<td>81.2%</td>
<td>97%</td>
</tr>
<tr>
<td>Surveillance interval (% of patients called earlier)</td>
<td>18.8%</td>
<td>3% 0%</td>
</tr>
</tbody>
</table>

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Introduction: Optical biopsies of colonic polyps < 10 mm in size could potentially replace standard histological assessment. WavSTAT version 4 is a novel optical biopsy system designed by SpectraScience Inc, San Diego, California, USA, for prediction of histology based on laser induced autofluorescence spectroscopy.

Aims & Methods: The primary aim of this study was to demonstrate the accuracy of WavSTAT version 4 in characterizing colorectal polyps < 10 mm that can be readily resected and discarded (or left in-situ) without adverse clinical impact. The secondary aim was to compare the real time diagnostic performance of WavSTAT version 4 with NBI and a combination of endoscopic and WavSTAT assessments. Patients attending the endoscopy unit for lower gastrointestinal endoscopy as requested by their responsible physician were approached to participate in the study. Adult patients aged above 18 years were included.

Disclosure of Interest: R. W. Leong: Endoscope USA investigator-initiated study. All other authors have declared no conflicts of interest.
Patients known to have inflammatory bowel disease or colorectal cancer were excluded from the study. Polyps sized <10 mm were assessed in real time by high-definition white light, NBI, and WavSTAT version 4 optical biopsy forceps. Standard techniques were used for polypectomy. Histopathological specimens were read separately by two expert GI pathologists blinded to the results of the WavSTAT assessments. The primary outcome measure was the negative predictive value in distinguishing adenomatous from non-adenomatous colorectal polyps. The secondary outcome measure was the accuracy of on-site recommended surveillance intervals.

Results: Nineteen polyps were <10 mm and 10 were >10 mm. Nineteen polyps were <10 mm and 10 were >10 mm. In total, 10 polyps were not included in the analysis due to discrepancies in histological analysis between two pathologists. We failed to retrieve 5 polyps. 28 patients were excluded from the study (No polyps seen in 17 patients, polyps <10 mm were not seen in 3 patients, and device failure in 4 patients). A total of 126 polyps <10 mm were included in final analysis. The diagnostic performance for WavStat version 4 and endoscopic assessment is detailed in the table. WavStat4 had a NPV of 96.9% with high specificity of surveillance intervals correctly predicted. Endoscopic assessment had a NPV of 91.1% and was more specific. Since the specificity of WavSTAT was poor mainly for hyperplastic recto-sigmoid polyps, we evaluated an algorithmic approach where we classified the polyps according to the WavStat4 result when proximal to the recto-sigmoid junction. We classified them according to the endoscopic classification only if Wavstat4 prediction was also as an adenomatous polyp in the recto-sigmoid area. This combined algorithmic approach met the PIVI and had a NPV of 95.8% and predicted 100% of surveillance intervals in the recto-sigmoid area. This combined algorithmic approach met the PIVI threshold and had a NPV of 95.8% and predicted 100% of surveillance intervals correctly.

Conclusion: Wavstat version 4 has a high NPV for characterizing colorectal polyps less than 10 mm in size but only predicts surveillance intervals correctly in 81% of patients. An algorithmic approach combining Wavstat4 and endoscopic assessment had a high NPV with accurate prediction of surveillance intervals.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP164 A ROLE FOR T CELL CLONAL EXPANSIONS IN THE POST-OPERATIVE RECURRENCE OF CROHN’S DISEASE: A STUDY FROM THE REMIND GROUP


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Introduction: Operative resection in Crohn’s disease is not curative. Indeed, a majority of CD patients undergoing ileocolic resection have an endoscopic recurrence in the neo-terminal ileum as soon as six months after surgery. T cells are major players in the intestinal immune response. We previously demonstrated the persistence of T cell clonal expansions over time in the inflamed mucosa of CD patients1. The presence of T cell clonal expansions at time of surgery could play an important role in the post-operative recurrence.

Methods: The aims of this study were to explore the impact of the presence of T cell clonal expansions in the inflamed tissue at time of surgery on the risk of post-operative endoscopic recurrence, and to analyse the correlation between the persistence of these T cell clones in the neoterminal ileum and inflammation. The REMIND Post-Operative study has been performed in 9 centers, collecting data at time of surgery (M0) and of endoscopy (M6), associated with an extensive bio-banking. Clinical, biological and endoscopic parameters were collected at month 6. Endoscopic recurrence was defined by Rutgeerts score1. Biopsies of ileal mucosa were collected on surgical specimen men and by endoscopy six months after surgery. T cell Receptor (TCR) analysis was performed on DNA extracted from biopsies by next generation sequencing (Illumina Inc., Seattle, Washington, USA). The TCR repertoire was analyzed in biopsies obtained on the surgical specimen and during the control endoscopy at six months. Sequences, numbers, frequencies and clonality indexes were assessed; and further analyzed to determine TOP100 clone frequencies and persistent clonal expansions present at both M0 and M6 in each patient. REMIND-77 patients in the REMIND cohort were analyzed. 33 (43%) were male; median age at surgery was 38 years old (±14). We found that the TCR repertoire in biopsies from CD patients display a large number of unique TCR sequences (mean 1000 unique sequences) suggesting a high variety of T cell specificities. However, measures of diversity of the TCR repertoire showed an important range of clonality within the cohort (0.001 to 0.5). Importantly, the frequency of the 100 most represented clones in the tissue at M0 was significantly increased in patients with endoscopic recurrence (Rutgeerts score1) at M6, compared to those without (p<0.05). More than half of the 100 most represented clones at M0 were observed at M6. The frequency of the 100 most represented clones in the tissue at M0 was significantly increased in patients with endoscopic recurrence (Rutgeerts score1) at M6, compared to those without (p<0.05). More than half of the 100 most represented clones at M0 were observed at M6. Furthermore, the presence and frequency of persistent clones (present at M0 and M6) was significantly increased in patients who had an endoscopic recurrence. High or low proportion of persistent clones could define two subgroups of patients with endoscopic recurrence in regard to their TCR repertoire. Interestingly, expanded clones could be found in different T cell subsets.

Conclusion: T cell clonal expansions in the inflamed tissue at time of surgery and persistence of T cell clonal expansions in the neoterminal ileum after surgery are both associated with post-operative endoscopic recurrence in Crohn’s disease.

Disclosure of Interest: M. Allez: I received honoraria from MSD, Abbvie, Janssen, Novo Nordisk, Novartis, Takeda, Genentech, UCB, Pfizer. All other authors have declared no conflicts of interest.

Reference


OP165 TARGETED CHEMICAL ANALYSIS OF THE COLON CANCER MICROBIOME USING DESORPTION ELECTROSPRAY IONISATION MASS SPECTROMETRY IMAGING (DESI-MSI)

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Introduction: The gut microbiome is an important modulator of colorectal (CRC) cancer risk. Here we describe a novel methodology for the targeted analysis of the
OP167 COMPREHENSIVE CIRCULATORY TRANSCRIPTOME AND PROTEOMIC PROFILING IN NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASES: A MULTI-CENTRE COHORT STUDY

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Introduction: There is an unmet need to gain functional insights into pathways that are relevant in Inflammatory Bowel Diseases (IBD). By performing transcriptomic and proteomic profiling in newly diagnosed IBD, we can gain an understanding into the molecular mechanisms that may be relevant in disease.

Aims & Methods: Gene expression patterns from whole blood RNA and proteomic profiles from serum were assessed from patients using targeted RNA-seq (Ion Ampliseq Transcriptome Human Gene Expression platform) and Olink multiplex panels (Olink Proteomics). Treatment-naïve newly diagnosed IBD and healthy symptomatic controls were included in the study. Phenotypic data were captured including demographics and disease classification. Statistical analysis was performed using R. Differentially expressed trancriptomes were correlated with serum protein expression to obtain a circulating profile at diagnosis.

Results: RNA expression profiles were available in 639 patients (351 IBD, 288 controls). A total of 567 genes were differentially expressed between IBD and controls. Using hscrP to adjust for inflammatory status, 1440 remained significant. The most differentially expressed genes were CD-177 (Bonferroni corrected p = 2.3 x 10^{-10}) and 11 out of 567 genes showed enrichment for the inflammation/monocyte module. The most differentially expressed proteins were MMP12 (p = 6.8 x 10^{-4}) while in UC, MMP12 levels were significantly higher in extensive bowel involvement (Montreal Classification L1, L3 and L4 vs L2; 0.004 vs MMP12). 6 proteins differentiated UC from CD including CD-177 (p = 2.9 x 10^{-7}) and S100A12 (p = 2.4 x 10^{-10}). Protein expression profiles were available in 635 patients (152 CD, 159 UC, 26 IBD-U, 298 non-IBD) Multivariable analysis identified 59 protein markers that were significantly associated with IBD. The top significant protein upregulated in IBD included MMP12 (Hohmann 2017 p = 4.1 x 10^{-9} and p = 1.7 x 10^{-9}) and FGF4 (p = 8.3 x 10^{-7}). Protein expression profiles were available and correlated with RNA expression. 39 proteins showed significant correlation with gene expression including OSM (rho = 0.51, Holm-adjusted p = 1.4 x 10^{-4}) and vWF (rho = 0.33, p = 3.4 x 10^{-7}) while other markers such as CXCL9 show poor correlation (rho = 0.16, p = 0.04). As biomarkers, top 2 serum markers were able to discriminate IBD from controls with a similar area under the receiver operator characteristics curve (AUC) of 0.75 and 0.74 respectively. Individually these markers outperformed hscrP (n = 619, AUC = 0.64, p for comparison = 2.7 x 10^{-4} vs. MMP12) and albumin (AUC = 0.66, p = 0.004 vs MMP12). 6 proteins differentially UC from CD including MMP12 (p = 4.6 x 10^{-10}). In CD, MMP12 levels were lower in those with small bowel involvement (Montreal Classification L1, L3 and L4 vs L2; p = 0.009) while in UC, MMP12 levels were significantly higher in extensive disease (Paris classification E1 and E2 vs. E3; p = 5.8 x 10^{-8}).

Conclusion: This is the largest integrative multicentre characterisation of the circulating expression profile studied in IBD at diagnosis. These data identify key pathways that may be relevant in IBD pathogenesis and demonstrate the translational potential of these markers in diagnosing and classifying IBD.

Disclosure of Interest: R. Kalla: Funded by IBD Character Ferring Speaker Fees J. Lindstrom: IBD has served as a speaker, a consultant and a advisory board member for MSD, Tilott, Ferring, Abbvie, Celltrion, Orion Pharma, Takeda, Napp Pharm, Meda, AstroPharma, Hikma and Pfizer.


F. Gomollon: Advisor: Grifols, Abbvie, MSD. Travel Grants: Abbvie, MSD. Research Fund: Abbvie, MSD, Janssen Research (Department) MSD J. Satsangi: JS has served as a speaker, a consultant and an advisory board member for MSD, Ferring Abbvie and Shire, consultant with Takeda, speaking fees from MSD and has received research funding from Abbvie All other authors have declared no conflicts of interest.

Aim & Methods: A prospective, multi-centre observational study was performed on patients undergoing elective resections for colorectal cancer at Imperial Healthcare NHS Trust and the Royal Marsden Hospital. Fresh mucosal tissue was snap-frozen, and patients agreed to ascertainment of cancers and adjacent normal tissue and frozen at −80°C. Using 16S rRNA sequencing analysis of corresponding tissue samples (performed in Mother and Stamp), target bacteria including Fusobacterium spp, E.Coli and Bifidobacteria were identified. A chemical data-base was then created using Rapid Evaporative Ionisation Mass Spectrometry (REIMS) from pure cultures of the target microbes. Desorption Electrospray Ionisation Imaging Mass Spectrometry (DESI-MSI) was then performed to provide a spatially resolved map of the mucosal microbial lipidome. This was compared onto the map formed using chemical spectra identified by REIMS. Candidate microbial lipids were validated using cell culture experiments and analysis with REIMS. Multivariate analysis was performed using Matlab (Mathworks) and R. Both unsupervised Principle Component Analysis and supervised Linear Discriminant Analysis were performed. ANOVA was used to perform statistical analysis of single lipid species.

Results: 26 patients with sporadic colorectal cancer were recruited (17 women, median age 68, range 35–84, median BMI 27 kg/m2). Eight tumours were right sided, eleven were left sided and seven were rectal. Two patients had neo-adjuvant chemoradiotherapy. Histology showed six adenomas, one T1, six T2, ten T3 and three T4 cancers. Using DESI-MSI it was possible to geographically identify different tumour sub-regions based on co-variation of the chemical data independently validated H+E stained tissue. Using leave one patient out cross validation, DESI-MSI was able to diagnose cancer from normal colonic mucosa with ROC AUC = 97.3. Increased long chain fatty acids were seen in malignant tissue while phospholipids were seen in healthy mucosa (both p < 0.001). Target spectra just specific to the mucosa were then extracted for analysis. This revealed 102 lipid species that differentiated colon cancer from normal adjacent mucosa, including 24 attributable to taxon-specific markers for Fasculilabiales, Bifidobacteriales and Enterobacteriales. These were positively validated using cell culture REIMS.

Conclusions: Chemical mapping of the colonic lipidome permits spatially resolved analysis of the cancer microbiome and its metabolic functions, and this has diagnostic value. DESI-MSI provides a completely novel methodology for studying microbial-host interactions critical to the aetiology of inflammation and cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: A cohort of CRC patients.

OP166 UNSUPERVISED, TRANSCRIPTOMICS-BASED CLUSTERING OF ULCERATIVE COLITIS PATIENTS REVEALS MARKED HETEROGENEITY THAT RELATES TO ANTI-TNF TREATMENT RESPONSE

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Disclosure of Interest: None.

Conclusion: We find that there is pronounced molecular heterogeneity in the pathways present in colorectal biopsies from UC patients. We also show that this heterogeneity is the ability of patients to respond to anti-TNF therapy. This suggests that molecular stratification may be a key step towards designing smaller clinical trials and identifying meaningful personalized medicine approaches for IBD patients.
**Table 1 (OP168): Demographics, procedural outcomes, bowel cleanliness and adenoma detection.**

<table>
<thead>
<tr>
<th>P value</th>
<th>WE vs WI</th>
<th>WE vs AI</th>
<th>WI vs AI</th>
<th>ANOVA</th>
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<td>WE N = 408</td>
<td>WI N = 408</td>
<td>AI N = 408</td>
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<td></td>
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<tr>
<td>Females, n (%)</td>
<td>184 (45.1)</td>
<td>185 (45.3)</td>
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<td>Males, n (%)</td>
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<td>223 (54.7)</td>
<td>225 (55.1)</td>
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<tr>
<td>Age, mean (SD)</td>
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<td>61.0 (6.3)</td>
<td>60.9 (6.2)</td>
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</tr>
<tr>
<td>Body Mass Index, mean (SD)</td>
<td>26.4 (4.1)</td>
<td>26.4 (4.4)</td>
<td>26.6 (4.4)</td>
<td></td>
</tr>
</tbody>
</table>

**Indications for colonoscopy, n (%)**

- Screening FIT: 242 (59.3), 242 (59.3), 222 (54.4), p = 0.0005
- Screening FOBT+: 18 (4.4), 19 (4.7), 19 (4.7), p = 0.865
- Family history of colorectal cancer: 47 (11.5), 47 (11.5), 45 (11.0), 1
- Primary colonoscopy: 101 (24.8), 100 (24.5), 122 (29.9), p = 0.920

**Procedure outcomes**

- Cecal intubation rate (final), n (%): 402 (98.5), 400 (98.0), 399 (97.8), p = 0.590
- Cecal intubation time, mean (SD), min: 9.1 (3.2), 9.5 (3.6), 8.9 (3.1), p = 0.870
- Withdrawal endoscopists' correct guesses of insertion method: 119 (29.2), 135 (33.1), 116 (28.4), -
- Cecal intubation rate (final), n (%): 402 (98.5), 400 (98.0), 399 (97.8), p = 0.590
- Cecal intubation time, mean (SD), min: 9.1 (3.2), 9.5 (3.6), 8.9 (3.1), p = 0.870
- Overall Boston Bowel Preparation Scale (BBPS) score, mean (SD): 2.6 (0.6), 2.4 (0.6), 2.4 (0.7), -
- Cecal intubation rate (final), n (%): 402 (98.5), 400 (98.0), 399 (97.8), p = 0.590
- Cecal intubation time, mean (SD), min: 9.1 (3.2), 9.5 (3.6), 8.9 (3.1), p = 0.870
- Overall Boston Bowel Preparation Scale (BBPS) score, mean (SD): 7.9 (1.5), 7.4 (1.6), 7.5 (1.7), 0.0005
- Overall Boston Bowel Preparation Scale (BBPS) score, mean (SD): 2.6 (0.6), 2.4 (0.6), 2.4 (0.7), 0.0005
- Infused water during insertion, median (range), mL: 550 (50-6500), 500 (50-2000), 0 (0-1000), -
- Withdrawal endoscopists' correct guesses of insertion method: 119 (29.2), 135 (33.1), 116 (28.4), -
- Cecal intubation rate (final), n (%): 402 (98.5), 400 (98.0), 399 (97.8), p = 0.590
- Cecal intubation time, mean (SD), min: 9.1 (3.2), 9.5 (3.6), 8.9 (3.1), p = 0.870
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- Infused water during insertion, median (range), mL: 550 (50-6500), 500 (50-2000), 0 (0-1000), -

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**References**


**Disclosure of Interest:** S. Cadoni: Recipient of the 2013 ESGE Research Grant. All other authors have declared no conflicts of interest.
OP170 DEVELOPMENT AND VALIDATION OF A SIMPLE CLASSIFICATION SYSTEM FOR DIFFERENTIATING TUMOR-LIKE NEOPLASMS FROM LARGE NON-PEDUNCULATED COLORECTAL POLyps: EXPERIENCE-BASED DATA AT A UNIVERSITY HOSPITAL

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Introduction: Tumor-like neoplasms (TLPs) are high-risk lesions that may lead to colorectal cancer (CRC). The delay in detection of these lesions has a negative impact on the outcomes of patients. This study aims to define a simple classification system for differentiating tumor-like neoplasms (LNPCPs) from large non-pedunculated colorectal polyps (LST-LNPCPs).

Methods: The study included 9353 patients (mean age: 55 years, 53.5% men) who underwent colonoscopy at Maastricht Medical Centre between 1 January 2008 and 30 April 2015. The diagnosis of LNPCPs was made based on the presence of at least one of the following criteria: intestinal-type dysplasia, sessile shape, or size ≥20 mm. The patients were divided into two groups: LNPCPs and LST-LNPCPs. The classification was made using a logistic regression model.

Results: Of the 9353 patients, 7166 neoplasms were identified. LNPCPs were found in 16.7% of patients, with a prevalence of 8.5% in men and 11.7% in women. The median size of LNPCPs was 20 mm (range: 5-50 mm). The classification model achieved an area under the receiver operating characteristic curve of 0.82. The sensitivity of the model was 96%, specificity was 86%, and the positive predictive value was 96%.

Conclusion: A simple classification system for differentiating tumor-like neoplasms from large non-pedunculated colorectal polyps was developed using logistic regression analysis. The model achieved high sensitivity and specificity, making it a valuable tool for endoscopists to improve the detection of high-risk lesions and reduce the risk of CRC.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP171 FREQUENCY AND PREDICTORS OF ADVANCED HISTOLOGY IN LARGE NON-PEDUNCULATED COLORECTAL POLyps

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Introduction: Colorectal cancers (CRC) detected shortly after a colonoscopy are referred to as a post-colonoscopy colorectal cancer (PCCRC), and has been reported to represent 2-9% of all CRCs, depending on the definition, setting and methods for estimating its incidence. The delay in detection of the CRC might imply higher mortality, effect on the quality of life of the diagnosed individuals, and association with extra costs for health services.

Aims & Methods: The aim of this study was to estimate the loss of health and the cost of CRC-diagnosis due to PCCRC in Sweden.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP169 EFFICACY OF ENDOCUFF-ASSISTED COLONOSCOPY IN THE DETECTION OF COLORECTAL POLyps

A70

United European Gastroenterology Journal 4(5S)

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Disclosure of Interest: Colonoscopy is the gold standard for detecting colorectal adenomas and advanced adenomas. Endocuff-assisted examination is a novel endoscopic technique that has been shown to be effective for preventing colorectal cancer. Although the detection of colorectal polyps at an early stage is important, the endoscopic visualization of early neoplasia can be difficult.

Aims & Methods: The Endocuff is a new device that can be attached to the tip of the colonoscope to hold the colonial folds away from the field of view during withdrawal. The aim of this study was to compare the polyp and adenoma detection rates between Endocuff-assisted colonoscopy and standard colonoscopy. This randomized prospective study was conducted at two academic endoscopy departments in Japan. Subjects were recruited from April 2015 to September 2015. The Endocuff group included 239 patients. Cecal intubation rate, insertion time, withdrawal time, pain score, complications, polyp detection rate, and adenoma detection rate were assessed.

Results: There were no differences between the groups in cecal intubation rate, insertion time, withdrawal time, or pain score. Cecal intubation was achieved in 235 patients (98.8%) in the Endocuff group. In four patients, the Endocuff-assisted examination had to be stopped in the sigmoid colon due to severe stenosis caused by diverticula or cancers. These examinations were completed with a standard colonoscope. Superficial mucosal erosions occurred in 54 patients (23.0%) during withdrawal in the Endocuff group but no major complication occurred. The polyp detection rate in patients increased by 12% (62% vs. 50%, P=0.013) and the adenoma detection rate increased by 15% (55% vs. 40%, P=0.001) with the use of Endocuff. The advanced adenoma detection rate was higher in the Endocuff group but no statistically significant difference was found (6.1% vs. 3.2%, P=0.17).

Conclusion: Endocuff-assisted colonoscopy enabled a significantly higher polyp and adenoma detection rate than standard colonoscopy. This attachment improved important quality measures used for screening colonoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP172 HEALTH EFFECTS AND COSTS DUE TO POST-COLONOSCOPY COLORECTAL CANCER

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Introduction: Colorectal cancers (CRC) detected shortly after a colonoscopy are referred to as a post-colonoscopy colorectal cancer (PCCRC), and has been reported to represent 2-9% of all CRCs, depending on the definition, setting, and methods for estimating its incidence. The delay in detection of the CRC might imply higher mortality, effect on the quality of life of the diagnosed individuals, and association with extra costs for health services.

Aims & Methods: The aim of this study was to estimate the loss of health and the cost of CRC-diagnosis due to PCCRC in Sweden.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
recent register study of colonoscopies in Sweden during 2001–2010 revealed that 18,244 individuals were diagnosed with CRC within 0–36 months after a colonoscopy. A CRC was defined as a PCCRC if it was detected within 6–36 months after a colonoscopy in which no cancer was detected. A total of 1,473 (8.1%) PCCRCs were found in the register study and included in this study. A lifelong mathematical Markov model was employed to calculate the lifelong health effects and resource usage for PCCRC. The effects were calculated by simulating the hypothetical lives of the individuals diagnosed with PCCRC if their condition had instead been diagnosed at the time of colonoscopy. These lives were then compared with simulated lives of individuals diagnosed with PCCRC, in terms of life expectancy, quality of life and costs. The simulation model was constructed by using Swedish registry data, supplemented with data from the published scientific literature and databases.

Results: Our simulation indicated that if the CRC of the individuals diagnosed with PCCRC had been diagnosed at the prior colonoscopy, there would have been a down-staging of the cancer. The proportion of patients at each cancer stage shifted from 53% in stage I-II, 35% in stage III and 9% in stage IV at the time of the index colonoscopy, to: 47% in stage I-II, 31% in stage III and 22% in stage IV, respectively, when diagnosed as a PCCRC. Additionally, based on our simulations 3% of the PCCRCs was expected to be at an adenoma stage at the time of the colonoscopy and were, thus, theoretically able to prevent. The 1,473 PCCRCs were associated with a loss of 1,551 life-years, compared to being ones detected at colonoscopy. The extra cost per case is €1,305.

Conclusion: Our simulation results imply that false negative colonoscopies cause significant loss of life-years and quality of life in the affected individuals. This, together with higher costs, motivates further efforts to improve the quality of colonoscopies.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**Table 1 (OP172): Logistic regression model adjusted for age and gender**

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<tr>
<th>Feature</th>
<th>Total (n = 205)</th>
<th>LGD (n = 108)</th>
<th>HGD or early CRC (n = 97)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>135 (65.9%)</td>
<td>87 (64.4%)</td>
<td>48 (35.6%)</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Distal</td>
<td>70 (34.1%)</td>
<td>21 (30.0%)</td>
<td>49 (70%)</td>
<td>1.0</td>
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<tr>
<td><strong>Size</strong></td>
<td></td>
<td></td>
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<tr>
<td>20–29 mm</td>
<td>109 (53.2%)</td>
<td>67 (61.5%)</td>
<td>42 (38.5%)</td>
<td>p &lt; 0.001</td>
<td>p = 0.191 &amp; 0.001</td>
</tr>
<tr>
<td>30–39 mm</td>
<td>57 (27.8%)</td>
<td>29 (50.9%)</td>
<td>28 (49.1%)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>≥40 mm</td>
<td>39 (19.0%)</td>
<td>12 (30.8%)</td>
<td>27 (69.2%)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Shape</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LST</td>
<td>109 (53.2%)</td>
<td>71 (65.1%)</td>
<td>38 (34.9%)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Sessile</td>
<td>96 (46.8%)</td>
<td>37 (38.5%)</td>
<td>59 (61.5%)</td>
<td>1.0</td>
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</tbody>
</table>

*Logistic regression model adjusted for age and gender.

OP173 COMPARISON OF COLONOSCOPY, SIGMOIDOSCOPY AND MULTIPLE ROUNDS OF FIT-BASED COLORECTAL CANCER SCREENING: LONG-TERM FOLLOW-UP


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Introduction: Several methods for colorectal cancer (CRC) screening are available, the most often used include colonoscopy, sigmoidoscopy and fecal immunochemical testing (FIT). To date, comparison between these screening methods was mainly focused on one-time endoscopic screening to one-time FIT screening. A fair comparison of diagnostic yield (DY) of FIT would comprise cumulative DY after multiple rounds of FIT screening. The aim of our study is to compare the DY of multiple rounds of FIT-screening to one-time screening by sigmoidoscopy and colonoscopy.

Aims & Methods: Demographic data of 30,007 randomly chosen individuals aged 50–74 were obtained from municipal populations of three cities (Rotterdam, Amsterdam and Birmingham). Of these, 15,046 were invited for four rounds of FIT, 8,407 for one-time sigmoidoscopy, and 6,600 for one-time colonoscopy screening. We compared 2 rounds of FIT to one-time sigmoidoscopy and 4 rounds of FIT to one-time colonoscopy. Cumulative (cum.) participation rate, positivity rate, number of colonoscopies, and diagnostic yield were calculated for each method. The DY was calculated relative to eligible invitees and participants. Between-group differences for participation, number of colonoscopies and DY were evaluated using multivariable logistic regression analysis adjusted for age and gender.

Results: In total, 28,515 eligible persons (median age 60 years, IQR 55–66; 50% males) were invited. Cum. participation was significantly higher for FIT (77%) than for sigmoidoscopy (31%; p < 0.001) and colonoscopy (24%; p < 0.001). Number of colonoscopies performed relative to eligible invitees was highest for colonoscopy (24%) compared to FIT (13%; p < 0.001) and sigmoidoscopy (3%; p < 0.001). For invitees the DY for advanced neoplasia (AN) was significantly higher after two rounds of FIT compared to one-time sigmoidoscopy (3.1% vs 2.3%; p < 0.001) and after four rounds of FIT compared to one-time colonoscopy (4.5% vs 2.2%; p < 0.001). For participants, DY for AN was significantly higher for endoscopically screening: 4.7% for 2 rounds of FIT compared to 7.3% for sigmoidoscopy (p < 0.001), and 6.1% for 4 rounds of FIT compared to 9.1% colonoscopy (p < 0.001).

Conclusion: In this population-based CRC screening cohort, we demonstrated that multiple rounds of FIT screening detects significantly more advanced neoplasia per invitee compared to one-time sigmoidoscopy and colonoscopy screening, and with significantly fewer colonoscopies needed. Colonoscopy detected more advanced neoplasia per participant. However, due to low participation in colonoscopy screening, FIT seems most effective in population-based CRC screening.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 08:30-10:00
Surgery in IBD – Room L7

OP174 OUTCOMES OF EMERGENCY ADMISSIONS WITH CROHN’S DISEASE IN ADULTS IN ENGLAND BETWEEN 2004 AND 2014

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Introduction: Between 2006 and 2010, the UK national audit of adult inflammatory bowel disease admissions revealed a small but non-significant fall in mortality. John’s disease (CD) fell from 1.3 to 0.8%, an increase in the rate of prescription of anti-TNF therapy on admission from 3.9 to 8% and a fall in surgery from 23 to 18%.

Aims & Methods: Hospital Episode Statistics (HES) is an administrative database of data on all elective and emergency care episodes in hospitals in England. Using HES, patients aged between 18 and 60 years coded with a first emergency admission with CD were identified. The influence of demographic factors, comorbidity and infused anti-TNF therapy on mortality, surgery and emergency readmissions was examined using multivariate logistic regression.

Results: Between 2004 and 2014, 24,830 patients (55% female, mean age of 35 (IQR 25–44) were identified. Mortality was 0.22% at 30 days, 0.29% in hospital and 0.81% within 1 year. During admission, 19.2% of patients underwent surgery (median time to surgery 2 days (IQR 1–6)) and 1.9% received infused anti-TNF therapy. Surgery during admission rose from 16.1 to 22.9% (OR 1.52 (95% CI 1.32–1.75), p < 0.001) between 2004 and 2014, and infused anti-TNF therapy rose from 1.8 to 2.8% between 2006 and 2014. In-hospital and 1-year mortality fell from 0.51 and 1.03% in 2004 to 0.10 and 0.57% in 2013 (0.18 (95% CI 0.04–0.77), p = 0.021 and 0.46 (0.23–0.91), p = 0.026 respectively). Patients aged 35–60 had a higher 30-day (3.99 (1.97–8.05), p < 0.001) and 1-year mortality (4.57 (1.75–11.72), p < 0.001) and were more likely to have been diagnosed aged 18–34. Increasing comorbidity (15.38...
OP75 IS THE ‘RESET’ THERAPY EFFECTIVE FOR CROHN’S DISEASE PATIENTS REFRACTORY TO ANTI-TNF THERAPY?

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Introduction: Anti-TNF-alfa agents (anti-TNFα) are currently the most effective therapeutics for Crohn’s disease (CD). Some of CD patients under anti-TNFα therapy, however, need surgery because of disease progression. Surgical resection (‘Reset’) usually leads to the elimination of the intestinal regions with active disease. However, little is known about whether retreatment with anti-TNFα is effective for patients who underwent ‘Reset’ surgery. The aim of this study was to evaluate the efficacy of anti-TNFα therapy for CD patients who underwent surgery due to the refractoriness to previous anti-TNFα.

Aims & Methods: From July 2005 to November 2015, 65 CD patients underwent intestinal resection at Okayama University Hospital. Of these, 34 patients retreated after surgery, 9 refractory to preoperative anti-TNFα (TNFα-naïve group), and 15 anti-TNFα naïve (TNFα-naïve group). The efficacy of post-surgical treatment with anti-TNFα was compared according to the status of pre-operative anti-TNFα therapy. In addition, clinical factors predicting relapse in patients with anti-TNFα retreatment after precedent surgery were evaluated. The evaluated factors were clinical backgrounds, duration of TNFα therapy, concomitant medications before and after surgery, laboratory data before surgery, and the residual of the affected intestine after surgery, etc. CD activity was assessed as an intensification of medical therapy, hospitalization, or surgery due to worsening of abdominal symptoms, CRP elevation with the evidence of endoscopic recurrence.

Results: Patients of the TNFα-naïve group showed significantly higher rate of disease relapse than the TNFα-naïve group (12/19 (63%) vs. 3/15 (20%), p < 0.05). In the evaluation of factors predicting relapse in patients with retreatment of anti-TNFα after surgery, only the residual of the affected intestine after surgery could be identified as a predictive factor of relapse with anti-TNFα treatment: (vs. without residual the affected intestine: 11/12 (92%) vs. 3/7 (43%), p < 0.05).

Conclusion: The ‘Reset’ surgery was not so effective for CD patients refractory to anti-TNFα therapy. In particular, patients with the residual of the affected intestine after surgery had higher risk of relapse despite retreatment with anti-TNFα after surgery. Those patients may need additional treatment besides anti-TNFα therapy or increase in the dosage amount of the anti-TNFα agent.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP76 IMPACT OF MINIMALLY INVASIVE SURGERY ON QUALITY OF LIFE AFTER SURGERY FOR CROHN’S DISEASE TERMINAL ILEITIS


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Introduction: Crohn’s disease (CD) is a chronic disease that interferes with the daily life of those affected. Surgical treatment is required in about 70% of CD patients during the course of disease and risk of surgery is among the highest rated concerns among them. Quality of life is often worsened by intestinal surgery.

Aims & Methods: The aim of the study is to assess the impact of minimally invasive surgery on quality of life after surgery for Crohn’s disease terminal ileitis. From June 2010 to December 2015, one surgeon interviewed by telephone and responded to the generic European Global Quality of Life (CGQL) questionnaire and the Body Image Questionnaire (BII). Their disease activity was defined as Harvey-Bradshaw Index (HBI). Comparisons and correlations were carried out with non-parametric tests. Survival analysis was performed with log rank test.

Results: In our study group 46 patients had minimally invasive surgery for terminal ileum CD while 66 had open surgery for the same indication. Twenty seven patients had a recurrent CD. The total CGQL score and its single items (quality of life and physical activity) were significantly higher (and thus, better) in the laparoscopic group patients. Similarly, all the BII items were significantly better in patients who had a minimally invasive surgery compared to those who had open surgery. At univariate analysis, total CGQL score was directly correlated with minimally invasive surgery. Total surgery was inversely correlated with quality of life at the moment of the interview (rho = −0.44, p = 0.001), the use of steroids (rho = −0.20, p = 0.02) and recurrent CD as indication for surgery (rho = 0.19, p = 0.05). At multivariate analysis, only anti-TNF therapy was effective for patients who underwent ‘Reset’ surgery. The aim of this study is to assess the impact of minimally invasive surgery on quality of life and body image perception. This results is probably due in part to the beneficial effect of minimally invasive surgery on body image but also by the less severe disease of these patients (less recurrent Cd as indication for surgery or simpler surgery). Quality of life is essentially predicted by current disease activity and minimally invasive surgery. Finally, minimally invasive surgery tended to be associated to a less frequent CD recurrence (p = 0.08).

Disclosure of Interest: All authors have declared no conflicts of interest.
Evidence has been accumulating indicating that the appendix has an immunomodulatory role in patients with ulcerative colitis (UC) potentially reducing the risk of inflammatory bowel disease (IBD) recurrences. Clinical responses in UC patients who underwent appendectomy and that this effect is maintained for a longer period of time.

In this study was to examine the effect of an appendectomy to modulate the disease endpoints were remission, improvement in IBDQ score and failure. Results: After 3 months, clinical response was seen in 16 (53%) patients of whom 7 (30%) were in remission (7 patients refused endoscopy at this point time). Improvement in IBDQ was seen in 14 (47%) patients with a mean of 120 (SD 29) that increased to 168 (SD 29). After 12 months, 11 patients failed (7 colectomy, 4 trial medication) and 5 did not yet reach the endpoint. In the remaining 14 patients, 9 (36%) had lasting clinical response of whom 5 (23%) were in remission (3 patients refused endoscopy).

Conclusion: Appendectomy was effective in at least 30% of therapy-refractory UC patients. These early results suggest that UC patients may benefit from appendectomy and that this effect is maintained for a longer period of time.

Disclosure of Interest: All authors have declared no conflicts of interest.

Correction: A. Bemelman5, D. Laharie8, M. Allez9, M. Nachury10, A.L. Pelletier11, V. Abitbol12, Paris/France
microbiota-based drug candidate targeted at recurrent CDI, is sourced from human-derived microbes from extensively colonized donors and manufactured using standardised, quality controlled processes.

Aims & Methods: To compare the bacterial abundance in the source material for RBX2660 (DS) with the bacterial abundance in the finished drug product (DP) used in the Phase 2B PUNCH CD 2 study. A total of 70 DS samples sourced from 17 unrelated donors (mean age 27; range 18 to 57 years; 94% male) from August 2014 to February 2016 were compared with 70 matched DP samples using the GA-map Dysbiosis Test (GA-test), Genetic Analysis AS, Oslo, Norway. The GA-test uses 54 probes targeting V3 to V7 of the bacterial 16S rRNA gene to characterise and identify bacteria present. Approximately 300-400 bacteria at different taxonomic levels are covered, providing for an assessment of the microbial community using multiple variable regions. The GA-test enables serial assessment of the faecal bacterial abundance profile as well as potentially clinically relevant alterations in the microbiome over time. These capabilities of the GA-test were used to assess the production processes for RBX2660. The differences in bacterial abundance between the DP and DS were calculated from log10 of the probe values (DP-DS); averaging the differences.

Results: The GA-test found that the bacterial abundance in the RBX2660 DP was lower than in the DS in 38 of the 54 probes; equal in number in 6 of the probes; and higher in 10. More specifically, Firmicutes and Actinobacterium showed reduced signal strength in the DP compared with the DS. Bacteroides showed increased signal strength in the DP compared with the DS, while Proteobacteria demonstrated equal signal strength in both samples. The comparative abundance in the DP vs. the DS is shown in Table 1. Accuracy was as high as 83.4% at cross-validation. Principal component analysis found that the bacterial profiles in the RBX2660 DP, though lower than in the donor source material, were largely kept intact during the production process for all 17 donors.

Table 1: Comparative Signal Strength of Bacteria

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Signal Strength in DP vs. DS</th>
<th>Mean Difference (95% CIM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteroides</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>Increased</td>
<td>0.07 (0.03, 0.11)</td>
</tr>
<tr>
<td>Parabacteroides</td>
<td>Increased</td>
<td>0.12 (0.07, 0.17)</td>
</tr>
<tr>
<td>Alstipes</td>
<td>Increased</td>
<td>0.17 (0.11, 0.23)</td>
</tr>
<tr>
<td>Firmicutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lachnospirae</td>
<td>Decreased</td>
<td>-0.13 (-0.15, -0.11)</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Decreased</td>
<td>-0.16 (-0.20, -0.13)</td>
</tr>
<tr>
<td>Negativicutes</td>
<td>Increased</td>
<td>0.03 (0.01, 0.06)</td>
</tr>
<tr>
<td>Clostridia</td>
<td>Decreased</td>
<td>-0.18 (-0.20, -0.16)</td>
</tr>
<tr>
<td>Actinobacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bifidobacterium</td>
<td>Decreased</td>
<td>-0.33 (-0.38, -0.28)</td>
</tr>
<tr>
<td>DP</td>
<td></td>
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</tr>
<tr>
<td>DS</td>
<td></td>
<td></td>
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<tr>
<td>CIM</td>
<td>confidence interval of mean</td>
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</table>

Conclusion: GA-test analysis confirmed that RBX2660 can be manufactured in a consistent and reliable manner with the preservation of key bacterial diversity believed critical for protection from recurrent CDI.

Disclosure of Interest: C. Jones: Employee of Rebiotix Inc., Roseville, MN USA

References

OP182 A METHYL DONOR MOLECULES-SUPPLEMENTED DIET ERADICATES E. COI POPULATION AND METHYLATES CEACAM6 PROMOTER DURING ITS INFLAMMATION IN COLONIC EPITHELIAL CELLS IN MICE.

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Introduction: Adherent-invasive Escherichia coli (AIEC) pathogenicity, a pathotype associated with Crohn’s disease, still needs to be well resolved. Nowadays the identification of the pathotype is performed with time-consuming techniques based in phenotypic screening of cultured bacteria; obtaining new molecular tools would therefore be of great significance.

Aims & Methods: Our aim was to identify putative genetic elements involved in AIEC phenotype to gain insight into the mechanisms of its pathogenicity and to find molecular targets for its identification. To achieve this objective we performed comparative genomics of three E. coli strain pairs consisting in one AIEC and one non-AIEC of identical pulsed field gel electrophoresis fingerprint. Each pair belonged to a distinct phylogroup. This approach was designed in order to increase the chance of finding sequences AIEC-specific and not strain-specific. The six strains’ genomes were sequenced de novo by combining paired-end libraries of HiSeq Illumina and PacBio. Two different approaches for comparative genomics were used: i) assembly with Velvet and genome comparison analysis with Mauve; ii) assembly with SPAdes and genome comparaison between pairs in relation to a genome of reference (AIEC UM146) with Mauve. Only non-synonymous Single Nucleotide Polymorphisms (SNPs) in coding regions were selected. Sanger sequencing was performed to confirm the presence of SNPs and to evaluate the distribution of the SNPs in a collection of 22 AIEC and 29 non-AIEC isolates. Nucleotides for each SNP were analysed taking into account AIEC phenotype, adhesion and invasion indexes of isolates by χ2 test or ANOVA as required.

Results: Genome sizes of Velvet assemblies for AIEC strains ONT-HNT-D, O6:H1-B2 and O22:H7-B1 were 4.86, 5.16 and 4.79Mb respectively. When SPAdes was used, they presented +95,362bp, +47,933bp and +30,178bps respectively. Comparative genomics of the first approach reported 114, 80 and 31 SNPs whereas the second resulted in 19, 27 and 31 SNPs respectively. Six SNPs were found with both strategies. From all, 23 SNPs were confirmed by Sanger and analysed among the study collection. These SNPs were comprised in 14 genes from which 3 were involved in metabolic processes, 2 in stress tolerance and 2 in adhesion and invasion pathways. Most of the SNPs were strain-specific, except from one found in a gene putatively implicated in adhesion/invasion, that was differentially distributed among AIEC and non-AIEC strains (p = 0.029). Interestingly, this SNP plus 3 other SNPs positions located in the same gene were associated with invasion (p = 0.024) and one of them also with adhesion (p = 0.04).

Conclusion: To conclude, we have detected SNP variations in a single gene that could be associated with AIEC phenotype. However, further studies with specific mutations are needed to confirm the implication of this gene in the AIEC pathogenicity and the SNP effects. Our study indicates that there is not an AIEC-specific genetic marker and widely distributed in all AIEC.

Disclosure of Interest: All authors have declared no conflicts of interest.
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Introduction: Enterohemorrhagic Escherichia coli (EHEC) are food-borne pathogens associated with diarrhea, hemorrhagic colitis and life-threatening complications such as hemolytic-uremic syndrome. EHEC interact with the Fucose-Associated Epithelium (FAE) of Peyer’s patches of the distal ileum in humans and translocate across the intestinal epithelium via M cells. Molecular mechanisms are still unknown but Long Polar Fimbriae (Lpf), which contribute to interactions with FAE and translocate across the intestinal epithelium via M cells, are said to be involved. Current research focuses on specific transcription factors involved in EHEC infections and use of antibiotics remains controversial. Probiotic could be an alternative strategy.

Aims & Methods: The objectives of the study were to investigate the role of Lpf in EHEC tropism to Peyer’s patches, and to explore the influence of probiotic yeasts on EHEC interactions with intestinal mucosa. The expression of Lpf genes (encoded by two Lpf operons) of EHEC O157:H7 strain EDL933 was analyzed using in vitro models of the human ileum or gastrointestinal tract and large intestine. To investigate the involvement of Lpf in the ability of EDL933 to target Peyer’s patches, we generated the DlpA1, DlpA2, DlpA1-DlpA2 isogenic mutants and trans-complemented them with Lpf genes. Lpf interaction with M cells was assessed using an in vitro model of specialized colonocytes. In vivo interactions of EHEC with murine Peyer’s patches were analyzed in ileal loop assays. Mice were infected with a mixture of two bacterial strains, and the numbers of Peyer’s patches-interacting bacteria were determined using a competitive colony hybridization technique. To investigate the effect of robotic yeasts, mice were given the probiotic for 7 days before ileal loop assays were conducted with O157:H7 wild type.

Results: Lpf isogenic mutants (i) were not able to interact with ileal biopsies compared to wild type strain in competitive colonization assays and (ii) translocated across M cells at levels significantly lower than those observed for the wild type strain. Trans-complementation of the mutants with the cloned Lpf genes restored their ability to interact with Peyer’s patches, suggesting that expression of lpfA1 and/or lpfA2 genes is required for interactions with Peyer’s patches. Bloodshot Peyer’s patches were macroscopically observed following EHEC infection of murine ileal loops. We showed that or pre-treatment with yeasts significantly inhibited O157:H7 interaction with Peyer’s patches and reduced the number of hemorrhagic Peyer’s patches in murine ileal loops. Since yeast cell surface is rich in mannose, the role of carbohydrates in EHEC interactions with Peyer’s patches was investigated. Among the carbohydrates tested, only mannose specifically limited the interactions of O157:H7 with Peyer’s Patches.

Conclusion: We conclude that Lpf are involved in the interactions of EHEC with Peyer’s patches in murine ileal loops. Since yeast cell surface is rich in mannose, the role of carbohydrates in EHEC interactions with Peyer’s patches was investigated. Among the carbohydrates tested, only mannose specifically limited the interactions of O157:H7 with Peyer’s Patches.

Disclosure of Interest: All authors have declared no conflicts of interest.

OPIS4 ENTEROHEMORRHAGIC ESCHERICHIA COLI TROPISM TO PEFER'S PATCHES: ROLE OF LONG POLAR FIMBRIA AND INHIBITION BY A PROBIOTIC YEAST

TUESDAY, OCTOBER 18, 2016
08:30-10:00

OPIS6 SELF-EXPANDABLE METALLIC STENT AS BRIDGE TO SURGERY IS MORE SUPERIOR THAN TRANSDURAL DRAINAGE TUBE AT QUALITY OF LIFE FOR THE PATIENTS WITH PRIMARY MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: Self-expandable metallic stent (SEMS) or transanal drainage tube (TDT) is endoscopic decompression for malignant colorectal obstruction. SEMS is said to be superior to TDT at quality of life (QOL) for the patients, but the comparison between SEMS and TDT for malignant colorectal obstruction was few reported include the clinical efficacy, safety and prognosis.

Aims & Methods: The aim of this study is to evaluate QOLs, clinical efficacy and safety between SEMS and TDT for the patients with malignant colorectal obstruction. We retrospectively analyzed 69 patients who underwent SEMS or TDT insertion for malignant colorectal obstruction from April 2009 to March 2016 on the basis of single-center experience in Japan. SEMS was inserted for bridge to surgery (BTS) or palliation, and TDT was inserted for BTS or bridge to SEMS insertion.

Results: There were 27 patients in SEMS group (male 37%, median age 75±7.0years) and 42 patients in TDT group (male 54.8%, median age 65±15.2 years). Technical success rate was 100% of SEMS group and 95.2% of TDT group (p=0.15). The endoscopic decompression as BTS for primary colorectal cancer was performed in 57.1% of SEMS group and 85.7% of TDT group (p=0.02). Among these patients, the duration for surgery after decompression was longer in SEMS group (10.5±7.0 days vs 6.6±6.6 days, p=0.04), because the rate of temporary discharge was significantly higher in SEMS group (41.7% vs 0.0%, p<0.001). No significant difference was shown about the hospitalization in both group (36.1±23.5 days vs 46.4±36.0 days, p=0.36). Oral intake (at least soft solids) was significantly higher in SEMS group (89.2% vs 25.0%, p<0.001). The Colonic Stent Safe Procedure Research Group ColonicReStent Obstructing Scoring System (CROSS) score before decompression was no significant difference in both group (1.1±0.9 vs 1.2±0.7, p=0.49), but CROSS score after decompression was significantly improved in SEMS group (3.7±0.8 vs 2.3±0.5, p<0.001). The complications after procedure, such as perforation, migration, re-obstruction, had no significant difference in both group.

Table: Patients characteristics and results

<table>
<thead>
<tr>
<th>SEMS (n = 27)</th>
<th>TDT (n = 42)</th>
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<td>Sex (male)</td>
<td>10 (37.0%)</td>
<td>23 (54.8%)</td>
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<td>(age, years)</td>
<td>73±17.0</td>
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<td>Primary colorectal cancer</td>
<td>21 (77.8%)</td>
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<td>Obstructed location (left side)</td>
<td>23 (85.2%)</td>
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<td>Primary colorectal cancer</td>
<td>21 (77.8%)</td>
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<td>&gt;85 years</td>
<td>9 (33.3%)</td>
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This large study demonstrated the high technical success rate of SEMS placement. Clinical risk factors independently negatively associated with technical difficulty were a history of chemotherapy before SEMS placement (OR, 0.47; 95% CI, 0.22–0.98; p < 0.01). A BRIDGE TO SURGERY IN OBSTRUCTIVE COLON CANCER: A SINGLE CENTER STUDY

OP188 17 YEARS OF SINGLE CENTER EXPERIENCE WITH SELF-EXPANDABLE METAL STENTS IN COLORECTAL OBSTRUCTION

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Introduction: Since 1991, self-expandable metal stents (SEMS) has been used in the treatment of malignant colonic obstruction (1). In 1997, Bispebjerg Hospital was the first hospital in Denmark to initiate the use of SEMS in the treatment of malignant colonic obstruction. This study represents the largest material from a single centre ever published.

Aims & Methods: This is a prospective registration of all patients who underwent SEMS at our institution, in the period from January 1st 1997 to October 1st 2014.

Results: In the period, 521 SEMS procedures were performed in 455 patients, 402 of these had colorectal cancer. Mean age was 74 ± 13 years, and 50.3% were male. The indications for SEMS placement were malignant colonic obstruction in 414 patients, including 158 as bridge to surgery (BTS), 237 as palliation, three with malignant anastomotic stricture and 20 patients with obstruction due to external tumor compression. The benign indications in 37 patients were respectively diverticulitis stricture in 15, diverticulitis fistula in two and benign anastomotic stricture in 20. Two hundred and seventy-seven patients had manifested total colonic obstruction and 121 had small bowel dilatation at the time of the procedure. The placement of the SEMS was in 111 in rectum, 221 in sigmoid colon, 52 in descending colon, 30 in splenic flexure, 30 in transverse colon, 6 in hepatic flexure and 3 in ascending colon. Mean length of stent was 4.5 ± 1.9 cm and mean days of obstruction was 5.2 ± 3.4 days. There was an overall technical success rate at 90.3% and clinical success rate of 87.7%. Stent procedure related complications were 4.2%, mainly guidewire perforations, and none of these patients died within 30 days of the SEMS placement. Procedure-related complications were 4.2%, mainly guidewire perforations, and none of these patients died within 30 days of the SEMS placement.

Conclusion: Our data shows that the use of SEMS insertion is a safe and effective technique for colonic decompression in the setting of malignant large bowel obstruction, as either a palliative measure or as a bridge to subsequent re-interventions. The overall all 30-day mortality rate was 13.4%, 5.8% for BTS group and 17% for palliative group. Follow up time for BTS group was mean 79 ± 70 months and at last follow up 35.3% (36/102) showed clinical signs of recurrence. 5-year survival in BTS group was 32.2% and 2.5% in the palliative group.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP189 LONG-TERM SURVIVAL AFTER ENDOSCOPIC STENTING AS A BRIDGE TO SURGERY IN OBSTRUCTIVE COLON CANCER: A SINGLE CENTER STUDY

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Introduction: Self-expandable metallic stents are increasingly used in the treatment of obstructive colorectal cancer. Although endoscopic stenting is widely accepted in a palliative setting, disagreement exists about its role in a curative setting. This study aims to describe the long-term survival data in a large consecutive patient group, treated with a stent as a bridge to surgery (BTS) for colon cancer.

Results: Ninety-seven patients, who presented in a Belgian secondary hospital between June 1998 and November 2013 with a large bowel obstruction due to colon cancer, were included. All patients underwent endoscopic stenting as a BTS in a potentially curable disease. Procedure-related complications and long-term follow-up survival data were collected and compared with the colon cancer mortality in Belgium in the same era (3).
Results: Overall survival in this observational cohort did not differ significantly from that of a Belgian colon cancer patients in the same period (p = 0.14). One-, five- and ten-year survival was not statistically different in both groups (95.9% vs 79.0%; 54.7% vs 51.2%; 41.0% vs 35.6% respectively). Additionally, for tumour stage II, III and IV no statistical differences between both cohorts were found (p = 0.21, p = 0.58, p = 0.10 respectively). Technical success rate was 94.8%. Seventy patients did not experience any complication. Stent migration occurred in 9 patients, whereas stent-related micro- and macro perforations were observed in 14 patients, without influencing survival. Incidence rates of peritoneal metastasis did not differ significantly between patients with and without any type of perforation (22.2% vs 15.2% respectively, p = 0.47). On average, surgery took place 16.6 days after colonic stenting, ranging from an operation on the same day as the endoscopic procedure, to an interval of maximal 124 days. In 82.5% of patients a laparoscopic resection of the tumor was performed. Five point two per cent of the patients got primarily open surgery. In 5.2% of the patients a laparoscopic procedure was converted to laparotomy, because of adhesions or peritonitis. Stoma rates were low (5.2%).

Conclusion: Based on reports of Dutch surgeons. This leads to an overall mortality risk of 0.08% for every AAD diagnosis. The primary outcomes were the size of perioperative mortality in relation to AAD removal on the effectiveness of CRC screening.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP190 IMPACT OF MORTALITY FROM SURGICAL ADENOMA REMOVAL ON THE EFFECTIVENESS OF COLORECTAL CANCER SCREENING

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Introduction: Implementation of colorectal cancer (CRC) screening programs results in an increase in the number of adenoma diagnoses. Some of the advanced adenomas (AADs) cannot be endoscopically removed and patients may then be referred for surgery. However these surgical resections have an associated mortality. The overall perioperative mortality for AAD resection still remains unknown. So far, the size of this impact is unknown. Therefore the objective of this study is to estimate the size of this perioperative mortality in relation to AAD removal on the effectiveness of CRC screening.

Aims & Methods: We used the MISCAN-Colon microsimulation model to simulate the Dutch population, aged 50 years and older in 2013 and followed them lifetime. The population was offered biennial FIT (FOB-Gold at a cut-off of 46 mg/g feces) screening ages 55 and over. Gradual roll-out was simulated from 2014 to 2020 according to implementation. To assess the impact of perioperative mortality in relation to AAD removal, we simulated a scenario with and without perioperative mortality within the screening program. In the scenario with perioperative mortality, we assumed that 3.9% of all AADs diagnosed during diagnostic colonoscopy need to be surgically removed, based on findings in Dutch pilot studies. The perioperative mortality rate is estimated at 2.1%, based on reports of Dutch surgeons. This leads to an overall mortality risk of 0.08% for every AAD diagnosis. The primary outcomes were the size of perioperative mortality per year, the number of prevented CRC deaths, life years gained (LYG), quality adjusted life years (QALYs) and costs. Sensitivity analyses were performed with a mortality risk of 0.05% and 0.11%.

Results: During the roll-out of the Dutch screening program between 2014 and 2020, perioperative mortality caused up to 18 deaths every year. After 2020 the number of AAD screen detected decreased and thus perioperative mortality decreased gradually through approximately 11 per year in 2033. Between 2014 and 2020, a total of 251 individuals died from perioperative complications. This corresponded with a decrease in prevented CRC deaths of 1.5% (22135 without operation mortality vs 21928 with), with a decrease in LYG from screening of 2.5% and in QALY’s of 1.0%. The impact on costs of the screening program was negligible. With higher and lower perioperative mortality assumptions, the outcomes altered proportionally.

Conclusion: Mortality due to surgical AAD resection has a negative impact on the effectiveness of CRC screening, although the impact is modest. Benefits of CRC screening as a whole are maintained. However, deaths due to surgical AAD resection are an order of magnitude larger than deaths due to complications of colonoscopy. Future studies into the effectiveness of CRC screening should therefore incorporate the harms of surgical AAD removal.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: The aim of the current study was to investigate the occurrence of anaemia as well as differences between Eastern and Western Europe during the first year of disease. Clinical data on surgery, medical treatment, hospitalization, and blood samples were captured throughout the follow-up period. Anaemia and its subtypes were defined according to the World Health Organisation and ECCO guideline.

Results: A total of 827 patients aged 15 years or older from 29 centres (20 in Western, 9 Eastern European) were eligible for analysis of whom 433 (52%) had ulcerative colitis (UC), 300 (37%) had Crohn's disease (CD), and 94 (11%) had IBD unclassified (IBDU). The proportion of patients with anaemia and its subtypes at diagnosis and follow-up is shown in table 1. Overall, anaemia was more frequent in Eastern than in Western European patients for both CD and UC. After 1 year of follow-up significantly more patients in Eastern Europe than in Western Europe (8% UC 9% CD) were anaemic. A comparison of both regions found that changes in anaemia status from normal to anaemia at follow-up (83%) compared to patients not having received biological therapy (70%), while fewer patients receiving biological therapy remained anaemia during follow-up (17% vs 30%). These differences did, however, not reach statistical significance (p = 0.09).

Table 1: Prevalence of anaemia at diagnosis and 1-year follow up.

<table>
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<tr>
<th>Subtype</th>
<th>Eastern Europe</th>
<th>Western Europe</th>
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<th>Western Europe</th>
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<tbody>
<tr>
<td>Overall prevalence (%)</td>
<td>43%</td>
<td>26%</td>
<td>29%</td>
<td>13%</td>
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<tr>
<td>Iron deficiency (%)</td>
<td>6%</td>
<td>3%</td>
<td>3%</td>
<td>2%</td>
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<tr>
<td>Anaemia of chronic disease (%)</td>
<td>9%</td>
<td>3%</td>
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<td>Mixed anaemia (%)</td>
<td>6%</td>
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<tr>
<td>Other anaemia (%)</td>
<td>6%</td>
<td>4%</td>
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<td>2%</td>
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<tr>
<td>Unclassifed (%)</td>
<td>14%</td>
<td>16%</td>
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Conclusion: In this unselected, population-based inception cohort the frequency of anaemia was high at the time of diagnosis, especially for CD, but decreased after the first year of follow-up. More Eastern than Western European patients remained anaemic after 1 year of follow-up. These geographic differences could be caused by differences in awareness of anaemia or they might reflect differences in global care and inflammation control of IBD patients in Europe. Geographic variations in the use of biological therapy might contribute to the observed differences in anaemia frequency.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: Use of immunosuppressants in IBD is associated with an increased risk of serious infections that varies considerably according to infection and immunosuppressant subtypes. This study aimed to determine the incidence rate and risk factors for serious viral infection (SVI) according to drug exposure and IBD activity in patients with IBD.

Aims & Methods: Using MIGISTA registry, a prospective observational cohort of IBD patients treated at our tertiary care hospital, we identified between Jan 2005 and Dec 2014 patients who developed SVI as defined by need for hospitalization, definite organ damage or disabling sequelae. Cases of CMV colitis without systemic manifestations were excluded. We first estimated incidence rates of SVI, overall and according to maximal yearly treatment. Additionally, we performed a case-control study (4 controls for 1 case matched for age, gender, IBD subtype and duration) assessing risk of SVI according to IBD drug use and IBD clinical activity in the 3 months preceding the SVI (data extracted from individual health records).

Results: We identified 31 patients with SVI among 2645 patients, followed for a median period of 6.2 years and a total observational time of 16922 patient-years. We identified 13 cases of CMV systemic infection (primary infection (n = 6), reactivation (n = 7)), 10 cases of EBV infection (primary infection (n = 6) including 2 haemophagocytic syndromes, reactivation (n = 4)), 5 cases of VZV infection (varicella (n = 3), shingles (n = 2)) and 3 cases of HSV infection (severe esophagitis, facial nerve paralysis, severe refractory cutaneous manifestation). Most patients required hospitalization (94%) and received IV anti-viral therapy (52%), while 3 patients (9%) received CMV plasma exchange. The incidence rate of SVI in patients with IBD was 1.83 per 1000 patient-years. Table 1 shows the incidence rate of SVI according to the maximal treatment received during the year. In the case control study, risk of SVI was associated with exposure to thiopurine (adjusted odds-ratio (aOR) 5.1; 95% CI, 1.9–13.4; p = 0.001) and methotrexate (aOR, 4.1; 95% CI, 1.0–16.6; p = 0.05), and active clinical disease (aOR, 3.2; 95% CI, 1.3–8.1; p = 0.02). Odds-ratios for corticosteroids and anti-TNF did not reach statistical significance (1.1 and 1.2, respectively).

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Patients with long-standing colonic inflammatory bowel disease (IBD) bear an increased colorectal cancer (CRC) risk. Endoscopic surveillance allows early detection and removal of preneoplastic slowing dysplasia (LGD), and may subsequently prevent CRC. However, the long-term effect of the consequent risk to develop CRC remains uncertain.
since most available studies are small and cover a relatively short follow-up period. We published a validated tool (Risk of Surgery Questionnaire, or RSQ) based on a history of LGD to 1) determine the cumulative CRC incidence, and 2) identify risk factors for developing CRC.

Aims & Methods: Using the Dutch National Pathology Registry (PALGA) we identified all consecutive patients diagnosed with LGD between 1991 and 2005 in the Netherlands. Subsequently, follow-up data were extracted until 2016. We determined the cumulative CRC incidence with Kaplan Meier curves censuring patients at the end of colorectal surveillance or colectomy. A case control study was performed with patients with LGD who developed CRC (cases) versus patients who did not develop CRC (controls), was performed to identify risk factors for developing CRC. Demographic data, including gender, IBD type, age and duration, and LGD age and recurrence, were extracted from PALGA. Subsequently, multivariable Cox regression analyses with backward elimination were used to identify independent risk factors.

Results: We identified 1177 IBD patients with colonic LGD with a median follow-up time of 9.8 years per patient after LGD diagnosis (total follow-up time: 11741 patient years). 825 (70.1%) patients had ulcerative colitis, 216 (18.4%) Crohn's disease and 136 (11.6%) indeterminate colitis. Hundred nine out of 1177 (9.3%) patients underwent colectomy. CRC developed in 86 out of 1177 patients resulting in a cumulative incidence of 2.9%, 5.8%, 11.1%, and 18.7% after respectively 5, 10, 15 and 20 years. Patients with an IBD duration of more than 5 years before LGD development had a significantly higher cumulative CRC incidence (14.7% after 15 years) compared to those with a shorter IBD duration (9.4% after 15 years; log rank p = 0.006). Furthermore, patients with recurrent LGD had a higher CRC risk compared to patients with single LGD (10.5% after 15 years versus 4.5% after 15 years; log rank p = 0.026). Multivariable Cox regression identified both a longer IBD duration (hazard ratio 2.5; 95% confidence interval 1.5-4.3) and recurrent LGD (hazard ratio 1.9; 95% confidence interval 1.1-3.4) as independent factors associated with increased CRC risk.

Conclusion: We showed a cumulative CRC risk of 18.7% after 20 years in a large nationwide cohort of IBD patients with a history of LGD. Both a longer IBD duration and recurrent LGD were identified as independent risk factors for CRC development following LGD. These findings may aid in risk stratification following a diagnosis of LGD in IBD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP195 ROLE OF DIFFUSION-WEIGHTED IMAGING (DWI) IN MRI-ENTEROGRAPHY FOR THE EVALUATION OF SURGICAL RISK IN PATIENTS WITH CROHN'S DISEASE

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Introduction: In Crohn's disease (CD) it's useful to discriminate inflammatory features from stricturing and fibrotic characteristics. Diffusion Weighted Imaging (DWI) is able to identify active inflammation in most pathological tissues.

Aims & Methods: We aimed to define the role of DWI in evaluating the risk of surgery in CD. We performed an observational prospective study including all consecutive patients with active CD enrolled in our unit. MRI-MRI study included: measurement of bowel wall thickness (BWT), CD extension, enhancement pattern, pre-stenotic dilation, presence of oedema and/or comb-sign, presence of fistula/tube/T2 sequences. Primary outcome, all patients with indication for surgery on DWI sequences defining: visual analysis of intensity and analysis of Apparent Diffusion Coefficient (ADC) maps. Statistical analysis was performed dividing all patients in 2 groups (operated vs not operated) using T-student and X-square test when indicated. To identify the variables associated to surgical risk, we performed a logistic multiple regression expressing the risk in terms of Odd Ratio.

Results: 110 patients were enrolled and 127 bowel segments resulted pathologic at MRI. 85 patients (23.6%) and 31 segments were resected during the follow-up period. At all pathological segments, the intensity in DWI sequences, the reduction of ADC max, ADC medium and the presence of fistulas/abscesses were significantly associated with a subsequent surgical intervention (p < 0.05).

In particular, the value of ADC of completion was the variable with the highest risk of surgery (p = 0.008; OR 3.9; 95% CI 1.4-10.7). When excluding the patients with complications, we reported a significant correlation of DWI intensity, ADC max and medium with surgical intervention. The reduction of ADC with respect to the highest risk of surgery (p = 0.03; OR 2.0; 95% CI 0.79-0.92). The cut-off value for discriminating patients at risk of surgery was 1.081x10^{-7} mm²/s (sensitivity 56.6%, specificity 70.3%, PPV 33.3%, NPV 85%).

Conclusion: The presence of fistulas/abscesses remains the variable most associated with surgical risk in CD. In not complicated CD, DWI sequences at MRI-Enterography correlates with the need of surgery. High value of ADC medium shows high surgery for CD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP196 PREDICTORS OF FIRST COLOLNIC EPITHELIAL NEOPLASIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: UNDERGOING COLONOSCOPIC SURVEILLANCE

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Introduction: Patients with inflammatory bowel disease (IBD) are at increased risk for developing colorectal neoplasia (CRN). Little is known about risk factors of first CRN in IBD patients after a surveillance colonoscopy negative for neoplasia.

Aims & Methods: The aim of our study was to identify predictive factors of first CRN in IBD patients after a surveillance colonoscopy negative for neoplasia. All consecutive patients who underwent at least two colonoscopies at Saint-Antoine Hospital between 01/01/1996 and 01/03/2015 and whose first procedure was a surveillance colonoscopy were included. A nested case-control study was performed to assess risk factors of CRN in inflamed mucosa. Information on treatments, endoscopic and histological examination was collected. The identified CRN risk factors were used to build a predictive score that was then tested in the whole study population.

Results: Among 404 patients who underwent 1236 colonoscopies, 38 patients who developed CRN in inflamed mucosa and 92 matched controls were included in a nested case-control study. Independent factors significantly associated with CRN were primary sclerosing cholangitis (PSC) (Odds ratio (OR), 6.26; CI 95% 1.07–36.8, p = 0.04), presence of neutrophils, crypt abscess or histological ulcerations (OR, 8.77; CI 95% 1.71–45, p = 0.009) and presence of crypt architectural irregularities without neutrophils or ulcerations (OR, 8.09; CI 95% 1.21–54.3, p = 0.03) on more than half of procedures during follow-up, exposure to thiopurine (OR, 0.047-0.608, p<0.001) and 5-aminosalicylates (OR, 0.27; CI 95% 0.084-0.876, p=0.03) at the time of neoplasia or last colonoscopy. We developed a score based on these five items at the time of the surveillance colonoscopy negative for neoplasia. Among patients with a score of 0, the negative predictive value in predicting any CRN was 100% in patients with colonoscopies performed 1 and 3 years after the first surveillance colonoscopy.

Conclusion: In IBD patients undergoing endoscopic surveillance, the risk of first CRN is increased in case of PSC, persistence of histological acute inflammation and concurrent disease, and decreased by concurrent treatment with thiopurines and 5-aminosalicylates. The use of a predictive score derived from these factors could be considered for making decisions on optimal intervals between two surveillance colonoscopies.

Disclosure of Interest: A. Bourrier: Anne Bourrier has received lecture fees from UCB
H. Sokol: Harry Sokol received consulting fees from Enterome, Astellas, Roche, Merck, Maat and Danone.
P. Seksik: Philippe Seksik had consulting fees from Abbvie, Merck-MSD and Biocodex and grants from Biocodex.
J. Cosnes: Jacques Cosnes has received lecture fees from Abbvie, consulting fees from Vifor Pharma
L. Beaugerie: Laurent Beaugerie has received consulting fees from Abbott, lecture fees from Abbvie, MSD, Ferring Pharmaceuticals, Janssen, and research support from Abbott, Biocodex and Ferring Pharmaceuticals. All other authors have declared no conflicts of interest.
categories (0 µg Hb/g, > 0–5 µg Hb/g and, > 5–10 µg Hb/g) to calculate cumulative incident of AN. To identify factors associated with AN a Cox proportional hazard regression analysis was performed to calculate hazard ratios (HRs). Consecutive FIT results were analyzed using logistic regression analyses to calculate relative risks of AN. Risks were visualized by generating heat plots for consecutive FIT results. A total of 13,566 subjects were invited for screening of whom 9,561 (70%) participated at least once. Of those, 7,663 (92%) had a positive FIT. Median follow-up was 4.7 years (IQR 2.0–6.1 years). Screenees with a baseline Hb of more than 5 µg Hb/g had a 23% higher cumulative incidence of AN than those with a baseline Hb of 0 µg Hb/g (p < 0.001). In multivariate Cox regression analysis HRs increased from 1.7 (95% CI 1.2–2.2) to 6.0 (95% CI 4.0–9.0) for a Hb concentration of more than 0 to 5 µg Hb/g and more than 5 up to 10, respectively (p < 0.001; Table 1). In logistic regression analysis of two consecutive negative FIT results, HRs increased with Hb concentration, up with a 14-fold risk increase for two consecutive FITs with both a Hb concentration of 8 µg Hb/g (p < 0.001).

**Table 1:** Time-dependent cox-regression analysis of baseline FIT of advanced neoplasia.

<table>
<thead>
<tr>
<th>Gender (male)</th>
<th>Univariate HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.7</td>
<td>1.2–2.1</td>
<td>&lt;0.001</td>
<td>Ref.</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1</td>
<td>1.1–1.1</td>
<td>&lt;0.001</td>
<td>Ref.</td>
</tr>
<tr>
<td>Baseline Hb concentration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 µg Hb/g</td>
<td>Ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 0–5 µg Hb/g</td>
<td>1.8</td>
<td>1.3–2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt; 5–10 µg Hb/g</td>
<td>7.0</td>
<td>4.6–10.5</td>
<td>6.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Socioeconomic status</th>
<th>Univariate HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Ref.</td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>Average</td>
<td>0.7–1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0.4–1.0</td>
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</tbody>
</table>

**Conclusion:** Among FIT negative screenees, baseline Hb concentration is an independent predictor for the risk of future AN. Moreover, Hb concentrations of 0–5 µg Hb/g and positive negative FITs are a strong predictor of the risk of AN with up to a 14-fold risk increase. These findings suggest a role for Hb in personalized screening strategies in population-based screening policies. In addition, the use of Hb of negative FITs may permit alteration of screening intervals. Such strategies could decrease unnecessary burden for screenee and optimize the use of program related resources.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP199 MASS SCREENING FOR COLORECTAL CANCER BY USING A FECAL IMMUNOCHEMICAL TEST IN COMBINATION WITH FLEXIBLE COLONOSCOPY**

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**Introduction:** To date, there have only been a few large-scale community-based screening trials that examined the efficacy of using a fecal immunochrometric test (FIT) in combination with flexible sigmoidoscopy (FS) for colorectal cancer (CRC) screening. Since 1983, we have been conducting community-based mass screening for CRC using fecal occult blood testing in combination with FS in Kyushu, Japan. In 1988, we designed special buses with the necessary equipment to perform FS screening in order to test as many people as possible. The two-day FIT method combined with small caliber electronic endoscopes for FS have been in use since 1992. The aim of this study was to investigate the efficacy of combining FIT with FS to detect CRC and then analyze the CRC detection rates.

**Aims & Methods:** A large sample of 1,597,734 subjects who underwent the FIT procedure to detect CRC and who exhibited a cut-off value of 100 ng/ml were enrolled in this study from 1992 to 2014. Colorectal cancers that were detected using FIT were classified as FIT-positive and FS-detected, respectively. Out of the cases with a negative two-day FIT outcome, 130,779 of them underwent colonoscopy. The positive rate for the negative two-day FIT and FS cases was 8.6% and 90.9% of them underwent work-up examinations. The work-up examinations resulted in a CRC detection rate of 0.15% (mucosal cancer, 0.12%; invasive cancer, 0.03%). In first-time negative two-day FIT and FS cases (n=33,800), the cancer detection rates were as high as 0.27% (mucosal cancer, 0.22%; invasive cancer, 0.05%). On the other hand, 7.1% of all the subjects were detected as positive using only the two-day FIT procedure and 78.0% of them underwent work-up examinations. This resulted in a detection rate of 0.16% (mucosal cancer, 0.07%; invasive cancer, 0.09%). Among first-time subjects (417,352), the cancer detection rate using only the two-day FIT procedure was 0.32% (mucosal cancer, 0.14%; invasive cancer, 0.17%). The CRC detection rate was significantly higher in males than in females and the rates increased with age in both genders. Moreover, the detection rates were significantly higher in males that were 50 years of age or older. Adverse events included 15 cases of ischemic colitis that occurred after FS (incidence rate, 0.0082%). There were no cases of perforation associated with FS.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

OR201 CHANGES IN HEALTH BEHAVIOUR ONE-YEAR AFTER TESTING NEGATIVE AT COLORECTAL CANCER SCREENING – A RANDOMIZED CONTROLLED STUDY

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Introduction: Nine out of ten participants in colorectal cancer (CRC) screening have a negative screening test result. It has been hypothesized that getting a negative screening test result may reduce incentives to strive for a healthy lifestyle.

Aims & Methods: The aim of the present study was to investigate potential differences in changes of health behavior at one-year follow-up between screen-negative attendees to two different screening modalities and controls not invited to screening. Participants of both gender, aged 50–74, were invited to complete a self-reported lifestyle questionnaire (LSQ) on smoking, body weight, physical activity, alcohol intake and selected dietary items at baseline and at one-year follow-up. Participants were randomly assigned to five biennial screening rounds. In total, 1809 and 1327 individuals with a negative screening test result in the FIT and FS group, respectively, completed the LSQ (CI) between the arms at follow-up.

Result: Participants with a negative CRC screening test result in the first round of screening adhere to a healthier lifestyle. The differences in changes of health behavior (and 95% confidence intervals (CI)) at the arms are not significant.

Conclusion: The present study does not suggest unfavorable short-term consequences in health behavior after getting a negative CRC screening test result whether this is from once only FS or first round of FIT screening.

Disclosure of Interest: All authors have declared no conflicts of interest.

OR202 SCREEN-DETECTED AND NON-SCREEN-DETECTED COLORECTAL CANCERS AFTER FOUR INTERVALS OF FECAL IMMUNOCHEMICAL TEST-BASED COLORECTAL CANCER SCREENING

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Introduction: Fecal immunochemical test (FIT)-based colorectal cancer (CRC) screening aims to detect CRC in an early stage, thereby reducing morbidity and mortality from this disease. Whereas data on CRC incidence and mortality, number of colonoopies per detected CRC, life-years lived and costs per individual in the lifetime of 20,000,000 individuals.

Programs based on guaiac fecal occult blood testing are available in literature, few data exist on cancers in FIT-screening programs. Aims & Methods: The aim of our study was to compare patient demographics, tumor site, stage and survival between patients with screen-detected CRCs (SD-CRC) and non-screen-detected CRCs (non-SD-CRC). Between 2006 and 2014, asymptomatic persons aged 50 to 74 were invited to take part in four consecutive biennial FIT-screening rounds. CRC cases were identified through linkage with the Netherlands Cancer Registry and were classified into four groups: SD-CRC, FIT interval cancers (diagnosed between screening rounds after negative FIT), colonoscopy interval cancers (diagnosed after negative colorectal screening after a positive FIT and CRC in non-participants (the latter three representing non-SD-CRC). Information on gender, age, socioeconomic status (SES), tumor site, stage and survival were collected and compared between patients in the four CRC groups using Chi-square-test.

Conclusion: A total of 27,340 people were invited for FIT-screening, of whom 18,752 (68.6%) participated at least once. Median follow-up time was 46 months (IQR 18.5–72.4). Among participants, 3,009 (16%) had a positive FIT in one of the 4 screening rounds. In total, 265 patients were diagnosed with CRC: 116 were SD-CRCs, 27 FIT interval CRCs, 13 colonoscopy interval CRCs and 109 CRCs detected in non-participants. There were no differences between the groups regarding age, gender and SES distribution. Screen-detected CRCs, FIT interval cancers and CRCs in non-participants were mostly located in the distal colon (70.7%, 63% and 61.5% of cases, respectively), whereas colonoscopy interval CRCs were mainly located in the proximal colon (69.2%)(p<0.010). Stage distribution was significantly different between the four groups, with more favorable stages in patients with SD-CRCs (p<0.001). Stage distribution in patients with FIT interval CRC and CRCs in non-participants was similar (p=0.361). Survival rates were significantly higher among patients with SD-CRCs and FIT interval cancers compared to non-participants and patients with colonoscopy interval CRCs.

Discussion of Interest: All authors have declared no conflicts of interest.
Result: FIT screening without a surveillance programme reduced CRC incidence and mortality substantially (0-0.0001, payments for lectures from AbbVie, Bristol-Myers Squibb, Gilead, MSD and Roche).

Disclosure of Interest: M. Mandorfer: M.M. received honoraria for consulting from AbbVie, Bristol-Myers Squibb and Gilead, MSI and Roche.

K. Kozbial: K.K. received travel support from AbbVie, Bristol-Myers Squibb and Gilead.

P. Schwabl: P.S. received payments for lectures from Roche and travel support from Janssen and Roche.

C. Freiselmuth: C.F. received travel support from Gilead and Janssen.

M.A. Reiberger: T.R. received payments for lectures from Roche, as well as travel support from Gilead, MSD and Roche.

S. Beinhardt: S.B. received honoraria for consulting from AbbVie, payments for lectures from Bristol-Myers Squibb, as well as travel support from Gilead, MSD and Roche.

H. Hofer: H.H. received payments for lectures from AbbVie, Gilead, Janssen, MSD and Roche.

A. Fertilich: A.F. received grants from Janssen and payments for lectures from Gilead, MSD and Roche.

P. Ferenci: P.F. received grants from Gilead, MSD, and Roche, as well as honoraria for board membership and consulting from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, Idenix, MSD and Roche.

M. Trauner: M.T. received grants from MSD, honoraria for consulting from AbbVie, Gilead, Janssen and MSD, payments for lectures from Gilead, MSD and Roche, as well as travel support from Gilead.

All other authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
10:30–12:00
VIRAL HEPATITIS: NATURAL HISTORY AND TREATMENT – ROOM M

OP204 SUSTAINED VIROLOGIC RESPONSE TO INTERFERON-FREE THERAPIES AMELIORATES HCV-INDUCED PORTAL HYPERTENSION


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Introduction: Portal pressure, assessed by hepatic venous pressure gradient (HVPG) measurement, drives the development of liver-related complications and mortality in patients with advanced chronic liver disease. Since a decrease in HVPG translates into a clinically meaningful benefit, it is an acceptable surrogate endpoint.

Aims & Methods: We aimed to investigate the impact of sustained virologic response (SVR) to interferon (IFN)-free therapies on portal hypertension in patients with paired HVPG measurements. One hundred and four patients with portal hypertension (HVPG ≥ 6 mmHg) who underwent HVPG and transient elastography (TE) before IFN-free therapy (baseline [BL]) were retrospectively studied. The effect of SVR on portal pressure was investigated in patients with SVR who also underwent follow-up (FU)-HVPG and TE after IFN-free therapy (group A; n = 60). To demonstrate the generalizability of our results, we included a second group (group B; n = 40), comprising all patients who achieved SVR and were available for FU-HVPG measurement. In those patients only information on FU-TE was available. Moreover, we also included 4 patients who did not achieve SVR.

Results: SVR to IFN-free therapies significantly decreased HVPG across all BL-HVPG strata (BL-HVPG of 6–9 mmHg: 10.4 – 15 mmHg: 10–15 mmHg: 16–20 mmHg: ≥ 21 mmHg: P < 0.001, 0.001, < 0.001, 0.004). However, portal hypertension did not resolve in any patient and 20% of patients showed a progression of portal hypertension at FU. Finally, in the subgroup of patients with a BL-HVPG of ≥ 16 mmHg, 5% (1/20) and 35% (7/20) of patients had a regression to a FU-HVPG of 6–9 mmHg or a FU-HVPG of 10–15 mmHg, respectively. Patients with a BL-HVPG of ≥ 16 mmHg, 5% (1/20) and 35% (7/20) of patients had a progression of portal hypertension at FU. Finally, in the subgroup of patients with a BL-HVPG of ≥ 16 mmHg, 5% (1/20) and 35% (7/20) of patients had a regression to a FU-HVPG of 6–9 mmHg or a FU-HVPG of 10–15 mmHg, respectively. However, portal hypertension did not resolve in any patient and 20% (20/100) of patients showed an increase in HVPG at FU. Patients with Child–Pugh stage B were less likely to have a HVPG-decrease (HR: 0.103; 95% CI:0.02– 0.514; P = 0.06), when compared to Child-Pugh A patients. In the subgroup of patients with a BL-HVPG of ≥ 16 mmHg, the relative change in liver stiffness per log/mL (Δlog(mmHg)); P = 0.044) was a predictor of a HVPG-decrease ≥ 10%. The area under the receiver operating characteristic curve for the diagnosis of FU-HVPG ≥ 10 mmHg by FU liver stiffness was 0.931 (95% CI:0.865–0.997). The liver stiffness values at FU for ruling-in and ruling-out FU-HVPG ≥ 10 mmHg were 12.4 (negative predictive value:90%) and 25.3 kPa (positive predictive value:94%), respectively. Changes in liver stiffness, platelet count, and liver function tests were comparable between patients with and without SVR.

Conclusion: SVR to IFN-free therapies ameliorates portal hypertension across all BL-HVPG strata. However, amelioration of portal hypertension was less likely in patients with more advanced liver dysfunction. TE might be useful for the non-invasive evaluation of portal hypertension after SVR. In contrast, patients who did not achieve SVR showed either no significant improvement or even worsening of liver disease.
WITH HEPATITIS C VIRUS GENOTYPE 1B IN JAPAN

OP207 COMBINATION THERAPY WITH DACLATASVIR AND ASV IN CIRRHOTIC PATIENTS WITH HEPATITIS C VIRUS GENOTYPE 1B IN JAPAN


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Introduction: Combination therapy with daclatasvir (DCV; NS5A inhibitor) and asunaprevir (ASV; second-generation HCV NS3/4A protease inhibitor) was approved for patients with HCV genotype 1 in Japan since September 2014. Now, elderly patients and those with advanced hepatic fibrosis including chronic liver disease are approved IFN-free therapy. The objective was to assess the efficacy and tolerability of DCV/ASV combination therapy in patients with hepatic cirrhosis.

Aims & Methods: In total, 153 consecutive patients with HCV 1b initiating DCV/ASV therapy were enrolled. The cohort comprised 52 patients with compensated cirrhosis and 101 patients without cirrhosis. 60 mg of DCV once daily and 100 mg of ASV twice per day for 24 weeks. Clinical, biological, and virological data, including adverse effects, were recorded at baseline and during follow-up.

Result: Only 10 (6.5%) patients had L31M or Y93H RAVs. There was no statistically significant difference in age, sex, IL28B genotypes, HCV viral load at baseline and during follow-up.

Conclusion: DCV/ASV achieved a high anti-HCV effect in patients both with and without cirrhosis. However, careful management is necessary in patients with cirrhosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:


OP208 EXPERIENCE IN THE MANAGEMENT OF DECOMPENSATED HCV CIRRHOTIC PATIENTS WITH LOW DOSE SOFOSBUVIR AND RIBAVIRIN COMBINED WITH DACLATASVIR

A. S. Hanafy

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Introduction: Direct-acting antiviral (DAA) therapy in the management of chronic active HCV, sustained response rates occurred in more than 95% of patients with compensated liver disease with improvement in their survival and the risk of decomposition that necessitates liver transplantation. The postulated explanation of reduced rates of sustained virological response in decompensated cirrhosis was explained by extensive portosystemic collaterals, advanced fibrotic parenchyma which are difficult to be penetrated, and provide dormant foci for viral reactivation. It was claimed that achieving SVR with low MELD and CTP scores with improvement in clinically significant portal hypertension and hepatic venous pressure gradient.

Aims & Methods: Evaluation of the efficacy and safety of managing chronic active HCV in patients with decompensated cirrhosis and if SVR will improve CTP score, and three months after end of treatment (SVR12) were included. LS and HVPG were measured in a fasted, non-seated state.

Conclusion: Beta-blocker treatment was stopped for all measurements. Post-treatment liver biopsies were assessed by METAVIR score.

Result: Of 19 patients (56% male, age: 53.4 ± 6.7 years, 95% concomitant antiretroviral therapy), 16 received SOF/DCV, 2 SOF/RBV, and 1 SOF/LDV. Seven (37%) patients presented a treatment response and HCV genotype (GT) distribution was: GT-1a: 12, GT-1b: 2 and GT-3a: 5. All patients had portal hypertension (HVPG >5 mmHg) and 14 patients (74%) presented with liver cirrhosis (LS >12 kPa). DAA treatment resulted in 100% SVR12. LS decreased significantly from 23.0 ± 16.5 to 16.9 ± 16.1 kPa (mean change (Δ): −6.1 ± 5.2 kPa; p < 0.001). Also, HVPG decreased from 10.4 ± 7.0 to 7.6 ± 4.3 mmHg (Δ: −2.8 ± 2.4 mmHg; p < 0.001). In patients with clinically significant portal hypertension (HVPG ≥10 mmHg, n=9), HVPG decreased from 13.8 ± 3.0 to 10.9 ± 3.8 mmHg (Δ: −2.9 ± 2.8 mmHg; p = 0.015) – resulting in a hemodynamic improvement (13.7 ± 10% in 6/9 (66%) patients. In the subgroup of patients with baseline line HVPG <10 mmHg (n=10), a reduction from 7.3 ± 1.3 to 4.6 ± 1.8 mmHg (Δ: −2.7 ± 2.2 mmHg; p = 0.003) was noted – resulting in cure of PHT (<5 mmHg) in 6/10 (60%). Posttreatment liver biopsies were available in 15 patients (79%) and showed a reduction in necroinflammatory activity (METAVIR A0). 8 of 14 (57%) patients with cirrhosis at baseline, presented a post-treatment histological METAVIR <F3. Serum transaminases were normalized after therapy (AST: 66 ± 34 vs. 33 ± 20, p < 0.001; ALT: 34 ± 15 vs. 8 ± 4, p < 0.001), while hemoglobin, WBC and CD4 cell counts remained stable.

Conclusion: Virological response to IFN-free DAA therapy decreases LS and ameliorates portal hypertension. SVR12 seems to abolish histological necroinflammatory activity in most HCV cirrhotic patients. It remains to be explored if these improvements result in decreased liver-related mortality in the setting of HIV/HCV coinfection.

Disclosure of Interest: P. Schwabl: received payments for lectures from Roche and Becherer Ingelheim, and travel support from AbbVie, Gilead, Jansen, and Roche
M. Mandalor: received honoraria for consulting from Janssen, payments for lectures from Boehringer Ingelheim, Bristol-Myers Squibb, Janssen, and Roche, as well as travel support from AbbVie, Gilead, MSD, and Roche.
B. Schemer: received travel support from Gilead.
T. Buscies: received payments for lectures from Roche and travel support from Bristol-Myers Squibb.
K. Grabmeier-Pilstiashammer: received honoraria for consulting from Gilead, payments for lectures from Bristol-Myers Squibb and ViVi, as well as travel support from Bristol-Myers Squibb, Gilead, and GlaxoSmithKline.
A. Feltlisch: received travel support from AbbVie and Gilead.
M. Trauner: received grants from MSD, honoraria for consulting from AbbVie, Gilead, Janssen, and MSD, payments for lectures from Gilead, MSD, and Roche, as well as travel support from Gilead.
M. Peck: received travel grants from Gilead, MSD, and Roche, honoraria from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, and MSD, and payments for lectures from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, MSD, and Roche.
T. Reihner: received payments for lectures from Roche, as well as travel support from Gilead, MSD, and Roche.
All other authors have declared no conflicts of interest.

**Conclusion:**
New generation of NBI (HQ290) may reduce polyp miss rates and be more effective in reducing polyp miss rates of flat type.

**REFERENCES**

**Disclosure of Interest:**
All other authors have declared no conflicts of interest.

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**OP210 RANDOMIZED, BACK-TO-BACK TRIAL OF NEW GENERATION OF NBI (HQ 290) FOR THE DETECTION OF COLORECTAL POLyps**

**J.H. Goong**

**Aims & Methods:** The benefits of narrow band imaging (NBI) for improving the detection of colorectal polyps remain questionable. The newly available second generation of NBI using 290 system (290-NBI) provides an at least two folds brighter image compared with the previous version.

**Disclosure of Interest:**
All other authors have declared no conflicts of interest.

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**OP211 DIAGNOSTIC CHARACTERISTICS OF DEPRESSED TYPE COLORECTAL NEOPLASMS IN MAGNIFYING ENDOSCOPY AND ENDOCYTOSCOPY**

**S. Kudo**

**Aims & Methods:** The newly available second generation of NBI (HQ190) vs. high-resolution white light endoscopy (HR-WLE) were divided into three types: depressed, flat and protruded. We investigated the frequency of depressed-type neoplasms concerning pit pattern and EC classification.

**Disclosure of Interest:**
All authors have declared no conflicts of interest.

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**OP212 ASSOCIATION OF CHROMOSOMAL INSTABILITY AND MICROSATELLITE INSTABILITY PATHWAYS WITH POSTCOLONOCOLIC COLONCANCER IN A RETROSPECTIVE COHORT STUDY**

**R.M. M. Bogie**

**Aims & Methods:** Over 50% of the postcolonoscopic colorectal cancers (PCCRCs) (i.e. CRC diagnosed after a colonoscopy that excluded cancer) originate from missed precursor lesions, in particular the subtle appearing non-polypoid (flat and depressed) adenomas and sessile serrated lesions. The biologic pathway of PCCRCs is unclear. We hypothesized that PCCRCs and subtle appearing precursors may share molecular features. In a retrospective, cohort study, we examined the occurrence of chromosomal instability (CIN), microsatellite instability (MSI), and CpG island methylator phenotype (CIMP) in PCCRCs and prevalent CRCs.

**Disclosure of Interest:**
All authors have declared no conflicts of interest.

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**OP213 ASSOCIATION OF CHROMOSOMAL INSTABILITY AND MICROSATELLITE INSTABILITY PATHWAYS WITH POSTCOLONOCOLIC COLONCANCER IN A RETROSPECTIVE COHORT STUDY**

**R.M. M. Bogie**

**Aims & Methods:** Over 50% of the postcolonoscopic colorectal cancers (PCCRCs) (i.e. CRC diagnosed after a colonoscopy that excluded cancer) originate from missed precursor lesions, in particular the subtle appearing non-polypoid (flat and depressed) adenomas and sessile serrated lesions. The biologic pathway of PCCRCs is unclear. We hypothesized that PCCRCs and subtle appearing precursors may share molecular features. In a retrospective, cohort study, we examined the occurrence of chromosomal instability (CIN), microsatellite instability (MSI), and CpG island methylator phenotype (CIMP) in PCCRCs and prevalent CRCs.

**Disclosure of Interest:**
All authors have declared no conflicts of interest.

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**OP214 ASSOCIATION OF CHROMOSOMAL INSTABILITY AND MICROSATELLITE INSTABILITY PATHWAYS WITH POSTCOLONOCOLIC COLONCANCER IN A RETROSPECTIVE COHORT STUDY**

**R.M. M. Bogie**

**Aims & Methods:** Over 50% of the postcolonoscopic colorectal cancers (PCCRCs) (i.e. CRC diagnosed after a colonoscopy that excluded cancer) originate from missed precursor lesions, in particular the subtle appearing non-polypoid (flat and depressed) adenomas and sessile serrated lesions. The biologic pathway of PCCRCs is unclear. We hypothesized that PCCRCs and subtle appearing precursors may share molecular features. In a retrospective, cohort study, we examined the occurrence of chromosomal instability (CIN), microsatellite instability (MSI), and CpG island methylator phenotype (CIMP) in PCCRCs and prevalent CRCs.

**Disclosure of Interest:**
All authors have declared no conflicts of interest.

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**OP215 ASSOCIATION OF CHROMOSOMAL INSTABILITY AND MICROSATELLITE INSTABILITY PATHWAYS WITH POSTCOLONOCOLIC COLONCANCER IN A RETROSPECTIVE COHORT STUDY**

**R.M. M. Bogie**

**Aims & Methods:** Over 50% of the postcolonoscopic colorectal cancers (PCCRCs) (i.e. CRC diagnosed after a colonoscopy that excluded cancer) originate from missed precursor lesions, in particular the subtle appearing non-polypoid (flat and depressed) adenomas and sessile serrated lesions. The biologic pathway of PCCRCs is unclear. We hypothesized that PCCRCs and subtle appearing precursors may share molecular features. In a retrospective, cohort study, we examined the occurrence of chromosomal instability (CIN), microsatellite instability (MSI), and CpG island methylator phenotype (CIMP) in PCCRCs and prevalent CRCs.

**Disclosure of Interest:**
All authors have declared no conflicts of interest.

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**OP216 ASSOCIATION OF CHROMOSOMAL INSTABILITY AND MICROSATELLITE INSTABILITY PATHWAYS WITH POSTCOLONOCOLIC COLONCANCER IN A RETROSPECTIVE COHORT STUDY**

**R.M. M. Bogie**

**Aims & Methods:** Over 50% of the postcolonoscopic colorectal cancers (PCCRCs) (i.e. CRC diagnosed after a colonoscopy that excluded cancer) originate from missed precursor lesions, in particular the subtle appearing non-polypoid (flat and depressed) adenomas and sessile serrated lesions. The biologic pathway of PCCRCs is unclear. We hypothesized that PCCRCs and subtle appearing precursors may share molecular features. In a retrospective, cohort study, we examined the occurrence of chromosomal instability (CIN), microsatellite instability (MSI), and CpG island methylator phenotype (CIMP) in PCCRCs and prevalent CRCs.

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colonscopy or incomplete resection) were excluded. We reviewed clinical and pathological records. Whole-genome DNA copy number changes and mutation status of genes commonly affected in CRC (APC, KRAS, BRAF, FBXW7, PIK3CA, NRAS, SMAD4 and TP53) were examined by shallow whole-genome sequencing and targeted sequencing, respectively, using Illumina next generation sequencing platforms. MSI and CIMP status were examined using the pentaplex marker panel from Promega and the Weisenberger CIMP panel using methylation-specific PCR, respectively.

Result: In total, 120 PCCRCs and 100 prevalent CRCs were examined. Using methylation-specific PCR, respectively.

Conclusion: Both CIN and MSI pathways are associated with the occurrence of PCCRC. PCCRCs contain less often deletions of chromosomes 17p and 18q, APC, NRAS and TP53 mutations and more often MSI. CIMP and BRAF mutations than prevalent cancers. Such molecular profiles are similar to those prevalent CRCs. Regarding DNA copy number alterations, PCCRCs contain less often 17p (p = 0.002) and 18q (p = 0.003) deletions than prevalent CRCs. Furthermore, PCCRCs contain less frequently APC (p = 0.04), NRAS (p = 0.03), and TP53 mutations (p = 0.03) than prevalent CRCs. In contrast, MSI (p = 0.004), CIMP (p = 0.02) and BRAF mutations (p = 0.04) are more frequent in PCCRCs than prevalent CRCs.

Disclosure of Interest: S. Sanduleanu: Consultancy: Pentax Medical Systems

S. Bezobchuk: Consulting for Olympus

D. Cave: Consulting and receipt of research funds from Olympus. Consulting for Medtronics.

D. Demarco: Consulting for Spirus

All other authors have declared no conflicts of interest.
statistical precision of 5%. This study protocol was reviewed and approved by an animal ethics committee.

Result: There were 5 (5.2%) pseudo-polyps dislodged, thus 235 simulated endoscopic tools were able to be attempted. The success rate of the Aer-O-Scope colonoscope simulated endoscopic therapy was: 234/235 = 99.6% (95% CI: 97.6–100%). The overall success rate was 234/240 = 97.6% (p < 0.001). The below Table shows the number of successful simulated endoscopic tools per endoscopic tool. All endoscopic tools had a success rate >95%. There were only 2 failures, both during use of a polypectomy snare. Endoscopist-rated subjective usability of the simulated endoscopist was high (easy to perform or only slightly complicated to perform) was very high (98%–100%) for all endoscopic tools.

Disclosure of Interest: S. Bezbuchak: I am a consultant for GI View Ltd. I.M. Gralnek: I am a consultant for GI View Ltd.

References

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Conclusion: The component criteria identified by the expert AAC endoscopists were as follows: - Early focal loss of acetowhitening - Present: Indicates presence of neoplasia - Surface pattern - Normal (Large uniformly distributed pits). - Indicates non-neoplastic Barrett’s - Abnormal (Compact, irregular or absent pits): Indicates neoplasia A total of 560 observations were undertaken to validate these criteria. The sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) is shown in Table 1:

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When the AAC validated criteria are applied by the 13 endoscopists, the sensitivity, specificity, NPV and PPV of detecting neoplastic Barrett’s are 95.7%, 97.5%, 98.8% and 99.0% respectively.

Conclusion: We have developed and established the validity of a simple classification system to identify Barrett’s neoplasia using AAC. When non-AAC trained endoscopists apply these criteria, the sensitivity and NPV meet the recommended PIVI threshold.

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Aims & Methods: limitation can be overcome by using near infrared (NIR) imaging.

lower binding to dysplastic versus non-dysplastic oesophageal endoscopy is challenging due to the inconspicuous nature of dysplasia. Molecular Detection of early neoplasia in Barrett’s oesophagus by white-light

Introduction: Contact E-mail Address: joke.vlebergh@gmail.com

Disclosure of Interest: All authors have declared no conflicts of interest.

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OP220 LONG-TERM FOLLOW-UP RESULTS OF STEPWISE RADICAL ENDOSCOPIC RESECTION FOR BARRETT’S ESOPHAGUS WITH EARLY NEOPLASIA

K. Belgazhi1, F. G. i. Van Vliersten1, B. L. a.m. Weusten2, S. L. Meijer3, J.J. Bergman4, R.E. Pouw5

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2Department Of Gastroenterology And Hepatology, St Antonius Hospital, Nieuwegein/Netherlands
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5Gastroenterology & Hepatology, Academic Medical Centre, Amsterdam, Netherlands, Amsterdam/Netherlands

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Introduction: Stepwise radical endoscopic resection (SRER) allows for complete eradication of Barrett’s esophagus (BE) with early neoplasia. This approach has been shown very effective in reaching complete eradication of high-grade dysplasia (HGD) or early cancer (EC) (CE-neo) in 98% and all intestinal metaplasia (CE-IM) in 85% of patients.

Aims & Methods: The aim of this study was to report the long-term follow-up (FU) results after successful SRER for BE with early neoplasia. We screened all patients treated with SRER in two centers between 2001–2014, for BE ≤5 cm with HGD/EC, without signs of invasion >T1sm1, G3/G4 differentiation, lymph-vascular invasion or irradical deep resection margins in ER specimens. All patients who had reached endoscopic and histologically confirmed CE-neo and CE-IM after SRER were included for evaluation of long-term FU. All information from fluoroscopies and histological outcomes were collected and entered in a dedicated database. Duration of FU was calculated from last treatment till last FU endoscopy. Primary outcomes: recurrence of HGD/EC and recurrence of IM combined with visible BE islands or tongues. Secondary outcomes: Barrett’s esophagus (BB) in neouposiobuses, and IM in biopsies obtained distal to the neo-z-line.

Result: Seventy-three patients were included (64 men, mean age 66 yrs, median BE 2Cm3). Worst baseline pathology: HGD, n = 50; EC, n = 23. Median FU was 55 months (IQR 25–102) with a range 23–242 months. Recurrence of HGD/EC was observed in 1 patient (1.4%) after 129 months FU (T1N0M0 treated with curative surgery). Recurrence of IM combined with visible BE was observed in 22% of patients (of which 2 had LGD) after a median FU of 31 months. In all cases the extent of recurrence was limited to small (<1 cm) islands or tongues. Histological recurrence without visible BE was found in 25 patients: 3 patients had BB in neouposiobuses (4% overall, 0.7% per patient year); 24 patients (33%) showed IM in biopsies just distal to a neouposiobuse or tongues. A finding of IM in the neo-z-line was detected in 50% of patients and BB in none of the patients. Additional treatment was performed in 8 patients: esophagectomy for T1b-cancer, ER of small island with LGD (n = 1), APC for small islands (n = 5), RFA for LGD in the neo-z-line (n = 1). CE-neo and CE-IM (excluding IM in the neo-z-line) at the last FU endoscopy (after additional treatment) was seen in 100% and 96% respectively.

Conclusion: This study presents the longest published follow-up data on SRER to date. The 6-year outcomes show that after successful SRER of BE ≤5 cm recurrence of HGD/EC is rare (1% overall, 0.2% per patient year). Recurrence of endoscopically visible BE was observed with IM or LGD was found in 22% of patients and was generally confined to small islands or tongues. Buried glands were rare (0.7% per patient year) and just as IM of the neo-z-line (33% of cases) of insignificant importance.

Disclosure of Interest: B.L.A.M. Weusten: Financial support for research: Coviden/Medtronic; Erbe Medical; C2Therapeutic, Consultancy: Boston Scientific; C2Therapeutic.
J.J. Bergman: Financial support for research: Coviden/Medtronic; Olympus Endoscopy; Cook Medical; Boston scientific; Erbe Medical; C2Therapeutic; Fuji-film; Ninepoint Medical; Consultancy: Boston Scientific; Cook Medical; Coviden.

All other authors have declared no conflicts of interest.

OP221 SPECIFIC BMP4 INHIBITION AS A POTENTIAL THERAPEUTIC STRATEGY FOR SMAD4 DEFECTIVE ESOPHAGEAL ADENOCARCINOMAS

S. Calpe1, M. Read2, S. Hoefnagel3, M.D.C. Sancho Serra4, D. Straub5, A. Correia6, N. Clemons7, D. Liu6, W. Phillips8, K.K. Krishnadath9

1Academic Medical Center, Amsterdam/Netherlands
2Surgical Oncology Research Laboratory, Peter MacCallum Cancer Centre, Melbourne/Australia
3Gastroenterology, And Hepatology, AMC, Amsterdam/Netherlands
4Amsterdam Medical Center, Amsterdam/Netherlands
5Sir Peter MacCallum Department Of Oncology, Peter MacCallum Cancer Centre, Melbourne/Australia
6Sir Peter MacCallum Department Of Oncology, Peter MacCallum Cancer Centre, Melbourne/Australia

Contact E-mail Address: k.k.krishnadath@amc.uva.nl

Introduction: BMP4 is a growth factor with a key role in carcinogenesis and metastasis. We previously found that BMP4 is aberrantly expressed in Barrett’s esophagus and that together with CDX2 drives the intestinalization of epithelial metaplasia. Its role in the progression and development towards esophageal adenocarcinoma remains uncertain. Celestial cancers that present mutations in the canonical transcription factor SMAD4, BMP4 induces tumorigenic characteristics in epithelial cells through activation of the BMP4 signaling pathways. SMAD4 mutations or deletions are also found in 10% of esophageal adenocarcinoma (EAC) patients and are associated to poor prognosis (1).

Aims & Methods: The aim of this project is to elucidate whether BMP4 is involved in malignancy in EAC. We have recently developed unique low molecule weight llama derived antibodies that specifically and effectively target BMP4 and therefore present less off-target effects, which renders them more apt for clinical purposes (2-3). These antibodies were used to study the effect of specific inhibition of BMP4 on both in vitro as well as in vivo models of EAC: Barrett's Adenocarcinoma

Result: We have found that 70% of EAC tumors express BMP4 at the protein levels. When the analysis was restricted to SMAD4 negative EAC tumors about 90% of those were BMP4+. Using an antibody that recognizes the pro-domain of BMP4, and therefore identifies the cells producing BMP4, we found that patients with high levels of BMP4 expression tend to have a poorer recurrence-free survival than patients with low BMP4 expression, which suggests a more aggressive tumor behavior in BMP4 expressing EAC tumors. Inhibition of BMP4 function in SMAD4 negative EAC cells by the anti-BMP4 antibody leads to an increase in chemosensitivity and a decrease in invasive and migratory capabilities in vitro. Analyses of the signaling pathways showed that inhibition of the BMP4-mediated non-canonical pathways was responsible for these effects. Next, we made use of a patient-derived tumor xenograft (PTDX) mouse model of a SMAD4 negative EAC tumor (4). Preclinical in vivo studies with these mice confirmed that anti-BMP4 antibodies can effectively reduce tumor growth and metastasis.

Conclusion: Our studies support a role of BMP4 as a positive regulator of chemoresistance and invasiveness in EAC, and suggest that inhibition of BMP4 with highly specific antibodies has the potential to ameliorate the malignant behavior of aggressive SMAD4 negative esophageal cancers.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

TUESDAY, OCTOBER 18, 2016 10:30-12:00

ACCURACY IN UPPER GI ENDOSCOPY – ROOM L8

OP222 PREMEDICATION WITH SIMITHECONE AND N-AcETYLCYSTEINE IN IMPROVING MUCOSAL VISIBILITY DURING UPPER ENDOSCOPY – A PROSPECTIVE, DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL

L. Elvas, M. Areia, S. Alves, D. Brito, S. Saraiva, A.T. Cadime Gastroenterology, Portuguese Oncology Institute - Coimbra, Coimbra/Portugal

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Introduction: Upper endoscopy is the most common method for the diagnosis of upper gastrointestinal tract diseases. Our aim is to determine if pre-medication with simethicone or N-Acetylcysteine improves mucosal visualization during upper endoscopy.

Aims & Methods: Randomized double-blind, placebo controlled trial of 297 patients scheduled for upper endoscopy pre-medicated 15–30 minutes before: A) 100-mL water (placebo); B) Water plus 100 mg simethicone; C) Water plus simethicone plus 600 mg N-Acetylcysteine. Primary outcome was the quality of mucosal visualization (score: 1-excellent; 2-decent; 3-inadequate). Trial registered in http://clinicaltrials.gov (NCT02357303). Statistical analysis with X2 and one-way ANOVA with Tukey’s correction.

Result: Visualization scores between groups B and C (versus A) were significantly better in the oesophagus 1.09 and 1.15 vs. 1.31 (p < 0.05) and stomach 1.26 and 1.30 vs. 1.67 (p < 0.01) and better without significance in the duodenum 1.67 and 1.09 vs. 1.20 (p = NS). “Excellent” scores versus others provided similar results (B and C vs. A): oesophagus 91% and 87% vs. 71% (p < 0.001), stomach 76% and 75% vs. 39% (p < 0.001) and duodenum 85% and 82% vs. 73% (p = NS). There was no significant differences in scores between groups B and C for either gastric scores if previous subtotal gastrectomy (B and C vs. A): 1.45 and 1.68 vs. 1.86 (p = NS). The rate of reported lesions was higher in group B (without statistical significance).

Conclusion: Pre-medication with simethicone leads to better mucosal visualization, might improve diagnostic yield and should be considered standard practice. Addition of N-Acetylcysteine had no benefit over simethicone alone.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP223 DIAGNOSIS OF TUMOR EXTENT OF EARLY GASTRIC CANCER USING MAGNIFYING NARROW-BAND IMAGING ENDOSCOPY: A MULTICENTER PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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2Dept Of Endoscopy, Fukuoka University Chikushi Hospital, Fukuoka/Japan
3Dept Of Gastroenterology, Ishikawa Prefectural Central Hosp., Kanazawa/Japan
4Dept. Of Gastroenterology, Academic Medical Center, Amsterdam/Netherlands
5Dept. Of Gastroenterology, Tohoku Red Cross Hospital, Natori/North-East Japan
6Department Of Molecular-targeting Cancer Prevention, Kyoto Prefectural University of Medicine, Kyoto/Japan

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Introduction: Accurate diagnosis of lateral extent of early gastric cancer (EGC) is important in terms of deciding treatment indication and achieving complete resection by endoscopy or surgery. Magnifying narrow band imaging (M-NBI) has been expected to increase yield of endoscopic diagnosis for determining extent of EGC.

Aims & Methods: To compare diagnostic ability of M-NBI for determining lateral extent of EGC with that of chromoendoscopy (CE). This study was conducted as a multicenter prospective randomized controlled trial including one university hospital, one cancer referral center and three general hospitals. Inclusion criteria were patients with EGC sized 1 cm or over who underwent endoscopic or surgical treatment. Exclusion criteria were history of gastric resection and high risk of bleeding for biopsy. After stratification by institution, tumor location, and histological type, patients were randomly assigned to M-NBI or CE groups. In each group, tumor extent was firstly evaluated by white light endoscopy according to difference of mucosal height and color, then outer margin of the tumor was determined by the assigned method. Diagnostic criteria of M-NBI were 1) demarcation line and 2) irregular microvessel/microsurface patterns and that of CE were 1) abrupt change of mucosal structure of the surrounding mucosa and 2) irregular structure patterns. Biopsy specimens were taken from 5-mm-outside and -inside of the oral boundary of the tumor and sent for histological evaluation. When the outside specimen was non-cancer and the inside specimen was cancer, the diagnosis was made. The study was approved by institutional review board in each institution and written informed consent for study participation was obtained from all patients.

Result: A total of 382 patients were enrolled and were assigned to the M-NBI group (n = 191) and the CE group (n = 191). Eight patients in the M-NBI group and 12 in the CE group were excluded remaining 183 in the M-NBI and 179 in the CE group for analysis. Successful delineation rates (95% CI) in the M-NBI and CE groups were 86% (81-91%) and 84% (78-89%), respectively (p = 0.498).

Conclusion: This prospective randomized controlled trial revealed M-NBI and CE were equally accurate for determining extent of EGC, thus both methods are adequate to perform in clinical practice (UMIN000014628).

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP224 FEASIBILITY OF A COMPUTER ALGORITHM FOR DETECTION OF EARLY BARRETT’S NEOPLASIA USING VOLUMETRIC LASER ENDOMICROSCOPY

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Introduction: Volumetric laser endomicroscopy (VLE) incorporates 2nd generation optical coherence tomography technology in a balloon-based system, which is capable of scanning the esophagus circumferentially over 6 cm, up to a depth of 3 mm with near-microscopic resolution. VLE has the potential to improve detection of early neoplasia in Barrett’s esophagus (BE). However, interpretation of VLE images is complex due to subtle differences in architecture and gray-scale color and the large amount of images that needs to be scrutinized by the endoscopist (a 6-cm VLE scan contains 1200 frames). A recently developed clinic prediction model of VLE features for BE neoplasia showed a reasonable accuracy (AUC of 0.81).

Aims & Methods: The aim of this study was to investigate the feasibility of a computer algorithm to identify earlyBE neoplasia on ex vivo VLE images. Sixty VLE images from a database of high-quality one-to-one VLE-histology correlations were used (30 non-dysplastic (ND)BE and 30 neoplastic images; high-grade dysplasia and early adenocarcinoma), consisting of VLE scans from endoscopic resection specimens of Barrett’s patients’ + neoplasia. VLE images were normalized to a height of 400 pixels in order to obtain a standardized zoom factor. Previously identified VLE features predictive for BE neoplasia served as clinical input for the algorithm: 1) higher VLE surface signal than subsurface signal in tissue, 2) lack of layering. From these VLE features an algorithm feature was developed analyzing both tissue surface signal. A signal intensity histogram using 8 intensity categories was calculated over the first 4 layers of 50 pixels, starting at the top of the image. Linear support vector machine was used to classify the images according to the used VLE texture features. Leave-one-out cross-validation was performed for validation of the algorithm.

Result: Using the correlated histology as the reference standard, specificity, sensitivity, c) ability to predict mucosa atrophy.

Opportunity: The aim of this study was to evaluate the utility of System plus Magniview™ in the diagnosis of normal gastric mucosa, Helicobacter pylori associated gastritis, and gastric atrophy.

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Introduction: It has been proposed that high-resolution zoom endoscopes (optical zoom up to 115 times) could predict gastric pit pattern for gastric pathology. Recently an image-enhanced endoscopic technology called Optical Enhancement system (OE System™) was introduced, improving visualization of microvesels. In addition to this, new high-definition zoom scopes called Magniview™ are available allowing an optical zoom up to 136 times with a better evaluation of the mucosa and superficial vascular aspects. In this study, the aim was to evaluate the utility of OE System™ plus Magniview™ in the diagnosis of normal gastric mucosa, Helicobacter pylori associated gastritis, and gastric atrophy. Methods: Prospective, non-randomized and double blind study. All of the participants enrolled, had functional dyspepsia according to the Rome III criteria and were tested for Heliocobacter Pylori (HP) using stool antigen test. After this phase two groups were selected, dyspeptic HP + (1) and dyspeptic HP - (control group). Finally an upper endoscopy using OE system™ plus Magniview™ scopes was performed and the gastric body evaluated using a previously described classification of four patterns based on the combination of the parameters subepithelial capillary network (SECN), collecting venules and round pits. Type 1 pattern predicts normal...

Table 1. (OP225): Overall accuracy of the four patterns predictions

<table>
<thead>
<tr>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
<th>Accuracy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>90.00 (55.50-99.75)</td>
<td>79.03 (66.82-88.34)</td>
<td>40.91 (20.70-63.65)</td>
<td>80.55</td>
</tr>
<tr>
<td>Type II–III</td>
<td>91.43 (76.94-98.20)</td>
<td>78.38 (61.79-90.17)</td>
<td>80.00 (64.35-90.95)</td>
<td>87.70</td>
</tr>
<tr>
<td>Type IV</td>
<td>66.67 (9.43-99.16)</td>
<td>88.41 (78.43-94.86)</td>
<td>20.00 (2.52-55.61)</td>
<td>87.50</td>
</tr>
</tbody>
</table>

a) Ability to predict normal mucosa. b) Ability to predict Helicobacter pylori infection. c) Ability to predict mucosa atrophy.
gastric mucosa, types 2 and 3 HP related gastritis and the type 4 gastric atrophy. 

(1) Intraduodenally recorded and biopsies taken in order to correlate the images with the histology

Result: A total of 72 patients were included, 35 in the dyspeptic HP (+) group and 37 in the control dyspeptic HP (-) group. The average age was 46.3 (37-58.5) years old and 69% were women. The images were analyzed and classified into the four patterns after the agreement of three endoscopists. There were 23 (30.6%) patients with type I, 13 (18.1%) with type II, 27 (37.5%) with type III and 10 (13.9%) with type IV pattern. Almost all patients (90%) with normal mucosa were type I. Most type II and III HP patterns had active chronic gastritis which correlates with HP infection. In fact, 32/34 (91.1%) of patients with HP (+) were type II-III. The 66% of patients with atrophy had type IV pattern. The Table 1 shows the overall accuracy of the four patterns predictions. Type I presented 100% normal mucosa, type II-III HP infection, and type IV atrophy with a sensitivity of 90%, 91% and 66.7% respectively and an accuracy of 80.5%, 84.7% and 85.7% respectively. Finally the intra and inter-observer agreement was calculated with a kappa value of 0.91 and 0.89 respectively.

Conclusion: The illumination and magnification has proved to be useful in the diagnosis of normal gastric mucosa and HP associated gastritis with high accuracy, unlike gastric atrophy evaluation.

Disclosure of Interest: C. Robles-Medranda: Key Opinion Leader for Pentax Medical

All other authors have declared no conflicts of interest.

Reference


OP227 FIRST-IN-MAN PILOT STUDY: FEASIBILITY OF LASER MARKING IN BARRETT’S ESOPHAGUS WITH VOLUMETRIC LASER ENDOMICROSCOPY

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Introduction: Laser endomicroscopy (LME) is an advanced imaging system that provides a 6-8 cm long, circumferential scan of the esophageal wall subsurface layers with near-microscopic resolution. LME has the potential to improve the detection of neoplasia during Barrett’s esophagus (BE) surveillance. A new feature of the VLE system is a laser marking tool that enables direct marking of suspicious areas during VLE scanning, which subsequently can be targeted for histological sampling. We herein describe the first in human use of the VLE marking tool in BE patients.

Aims & Methods: The aim is to evaluate visibility and positional accuracy of LME laser marks in different esophageal tissue types on white light endoscopy (WLE) and VLE. BE patients with and without neoplasia were imaged with VLE. In a learning phase protocol refinements were practiced. In the second phase, visibility of laser marks was assessed by randomly marking 4 quadrants in squamous, BE and gastric tissue. LMs were automatically placed in offset mode; 2 LMs 6 mm apart horizontally. In the third phase, positional accuracy of LMs was tested, whereby previously placed electrocoagulation markers (ECMs) were targeted on VLE and laser marked (2 ECMs per tissue type). In the final phase, in each patient the most suspicious areas for neoplasia were identified on VLE, targeted by laser marks and subsequently biopsied.

Result: In total 17 BE patients were included (15 males, median age 67); 11 patients with non-dysplastic (ND)B, 6 patients with high-grade dysplasia (HGD) or early esophageal adenocarcinoma (EAC). Median BE length: C2 (IQR 1–9) M4 (IQR 4–11). In total 222 LMs were placed, of which 207 (93%) were visible upon WLE and 192 (86%) on VLE, see table for visibility per tissue type. In total 222 LMs were placed, of which 207 (93%) were visible upon WLE and 192 (86%) on VLE, see table for visibility per tissue type. In total 222 LMs were placed, of which 207 (93%) were visible upon WLE and 192 (86%) on VLE, see table for visibility per tissue type. In total 222 LMs were placed, of which 207 (93%) were visible upon WLE and 192 (86%) on VLE, see table for visibility per tissue type.

Conclusion: The first in human use of VLE laser marking in 17 BE patients was found to be feasible and safe. The majority of the LMs was visible upon WLE and VLE, although appearance on VLE can be subtle. Targeting VLE areas of interest proved to be highly successful and VLE laser marking may thus improve the clinical value of VLE in BE surveillance in the future.

Disclosure of Interest: B.L.A.M. Weusten: - Research support for IRB approved studies: Clinical GI Solutions, Earch Medical C2Therapeutic - Consultancy: Boston Scientific C2Therapeutic. All other authors have declared no conflicts of interest.

OP228 ROAD MAP FLUOROSCOPY FOR SUCCESSFUL GUIDANCE OF ENDOSCOPIC INTERVENTIONS IN THE ESOPHAGUS

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Introduction: Digital subtraction angiography is a method to enhance the contrast of vessel structures and differentiate them from structures that are not of interest are deleted from the image by subtraction of image information. A variation of this technique is called Road Map Fluoroscopy (RMF) where an image at peak opacification is used as the mask for subsequent subtracted images. With the help of the advanced RMF system or catheters can be viewed without additional marking or contrast injection. In summary, the opacification is only performed once but the information remains on the image throughout the investigation. In this way anatomic structures such as length or diameter of stenosis can be measured with high accuracy (1–4). Although esophageal stent placement has been reported to be safe also without fluoroscopic guidance most endoscopists prefer to use fluoroscopy during stent deployment (5–7). Mucosal marking using the injection of lipiodol for stent implantation is widely used among endoscopists but may no longer be necessary if RMF is used as guidance of the procedure. The use of RMF has so far not been evaluated for endoscopic procedures.

Aims & Methods: We aimed to evaluate the usefulness of Road Map Fluoroscopy to guide endoscopic interventions in the esophagus. Patients with esophageal strictures were consecutively enrolled in a monocentric observational trial. After identification of the stenosis, a Road Map (Philips Multidigastin Elevated, Philips Healthcare, Netherland) was performed using 20 ml of water-soluble contrast media that was applied through the working channel of a gastroscope (Fujifilm EG5350NW or Olympus GIF-Q 180). RMF recording requires stable fluoroscopy of the region of interest to generate a mask for consecutive subtraction. Thereafter contrast medium is injected. After RMF application all further fluoroscopic images contain the information of the subtraction as steady overlay. Directly after the RMF was finished, the complete fluid was removed from the esophagus to avoid aspiration. Patients were all investigated in recumbent position under sedation with induction of propofol for stent implantation.

Result: 21 investigations were performed in 18 patients (age: 71 ± 13 years male:12 female:6). Indications for interventions were: balloon dilatation of benign stenosis: n = 9 including 1 pneumatic balloon dilatation for the treatment of achaesia, bougienage of benign stenosis: n = 3 and diagnostic radiography without intervention: n = 1. In addition 8 stents, 5 partially covered and 3 fully covered, were placed using RMF as a guide for exact determination of stent length and position. All patients and stents were also evaluated under RMF guidance. The stent control revealed desired stent position in all cases. The choice of stent was made by measurement of the length of the stenosis as well as diameter of healthy esophagus adjacent to the structure. Available stents that fitted best to the measured dimensions were implanted. In all procedures RMF successfully guided the intervention. The feeling of resistance during bougienage was exactly matching the location for RMF projection of the stenosis. With the help of RMF imaging complications like perforation or clogging of the balloon. Complications did not occur.

Conclusion: RMF provides the possibility of permanent radiographic illustration of stenosis or anatomic changes throughout the intervention by using contrast medium only at the beginning of the intervention. RMF is feasible and safe to guide radiology based interventions in the esophagus. RMF directs the selection of stents better than endoscopy because all relevant dimensions can be measured exactly.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 10:30–12:00

SMALL BOWEL DISEASE AND NUTRITIONAL THERAPY – ROOM 1.86

OP229 GASTROINTESTINAL DISEASES IN COMMON VARIABLE IMMUNODEFICIENCY

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Introduction: Common variable immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency in adults. CVID is a combination of humoral and cell-mediated deficiency, and the cornerstone of its treatment is intravenous or subcutaneous immunoglobulin therapy. However, while this treatment prevents infections, many CVID patients may still develop a broad spectrum of gastrointestinal disorders including autoimmune and inflammatory diseases such as atrophic gastritis, small bowel villous atrophy and inflammatory diseases such as Crohn’s disease.
Aims & Methods: Aim of the study: To investigate in detail the gastrointestinal problems living in south India. Patients with IBD were included in this study. We collected data from 1,036 patients, and all were diagnosed to have chronic diarrhea. The patients were followed up at the outpatient clinic and the results were recorded in the electronic database designed for the study. Of this patient cohort, 12 patients died and 11 were lost to follow up.

Result: Upper endoscopy and ileocolonoscopy were done at least once to 1,036 patients, respectively. In 1,036 patients, 38 centres and 1,036 patients were followed up. Of this patient cohort, 12 patients died and 11 were lost to follow up. The results of the study showed that the prevalence of BAD is increased following cholecystectomy, but the clinical profile and idiopathic (type 2), or be linked to other underlying conditions (Type 3). Its activity, was found in 11 patients (11%). In addition, atrophic gastritis was found in 10 patients (10%). 2. Small bowel: All tested patients were seronegative for coeliac disease. Of patients with increased intra-epithelial lymphocytes and villous atrophy of duodenum, 2 had complete histological and clinical response to gluten-free diet and all 4 others were unresponsive but had no enterocyte antibodies. 3. The patients with refractory duodenal villous atrophy and inflammation had also inflammatory changes in colon as well. 3. Hepatobiliary: Primary sclerosing cholangitis or CBD-associated cholangitis was diagnosed in 5 patients. 3. Large Bowel: Inflammatory changes of mucosa ranged from specific colitis and microscopic colitis (involving lymphocytic colitis and collagen colitis) to crypt-destructive and/or graft-versus-host like severe inflammation. Crypt-destructive IBD-like IBD ulcerative colitis ulcerative colitis was found in 5 patients (2 colectomies) and one patient had strictureing ikoeclonic Crohn disease. Altogether, inflammation of colon was more common than small bowel enteropathy and it was found in 20 patients (19%). Prior to ileocolonoscopy, patients were treated with sparse antibiotics and methods including fecal sampling screen. Nodular lymphatic hyperplasia was detected from gastric mucosa to rectum, and ranged from asymptomatic enhanced ileal nodularity to major changes of the gastric and bowel mucosal appearances and function. It was relatively common finding and noted in 36 patients (34%). 4. Mortality and gastrointestinal malignancies: 12 patients died during the follow up and in 3 patients it was directly metastatic malignancies of gastrointestinal tract; 2 patients with gastric adenocarcinoma and one patient with a diagnosis of colorectal cancer had bowel enteropathy that had been found also in other 2 patients that died due to cardiovascular disease. Meanwhile, one patient with unexplained inflammatory nodularity of colon eventually developed caecal large B-cell lymphoma which was timely diagnosed, and treated successfully.

Conclusion: Gastrointestinal and hepatobiliary manifestations are common among patients with CVID and the risk malignancies are increased. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


OP229 BILE ACID DIARRHOEA: EVIDENCE FOR LOWER SEHCAT RETENTION IN TYPE 3 PATIENTS FOLLOWING CHOLECYSTECTOMY

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Introduction: Bile Acid Diarrhoea (BAD) is an under-recognised cause of chronic diarrhoea. BAD can be assessed by measuring SeHCAT retention. BAD can relate to terminal ileal disease or resection (designated as Type 1), be considered as idiopathic (Type 2), or be linked to other underlying conditions (Type 3). Its prevalence is increased following cholecystectomy, but the clinical profile and idiopathic (type 2), or be linked to other underlying conditions (Type 3). Its activity, was found in 11 patients (11%). In addition, atrophic gastritis was found in 10 patients (10%). 2. Small bowel: All tested patients were seronegative for coeliac disease. Of patients with increased intra-epithelial lymphocytes and villous atrophy of duodenum, 2 had complete histological and clinical response to gluten-free diet and all 4 others were unresponsive but had no enterocyte antibodies. 3. The patients with refractory duodenal villous atrophy and inflammation had also inflammatory changes in colon as well. 3. Hepatobiliary: Primary sclerosing cholangitis or CBD-associated cholangitis was diagnosed in 5 patients. 3. Large Bowel: Inflammatory changes of mucosa ranged from specific colitis and microscopic colitis (involving lymphocytic colitis and collagen colitis) to crypt-destructive and/or graft-versus-host like severe inflammation. Crypt-destructive IBD-like IBD ulcerative colitis ulcerative colitis was found in 5 patients (2 colectomies) and one patient had strictureing ikoeclonic Crohn disease. Altogether, inflammation of colon was more common than small bowel enteropathy and it was found in 20 patients (19%). Prior to ileocolonoscopy, patients were treated with sparse antibiotics and methods including fecal sampling screen. Nodular lymphatic hyperplasia was detected from gastric mucosa to rectum, and ranged from asymptomatic enhanced ileal nodularity to major changes of the gastric and bowel mucosal appearances and function. It was relatively common finding and noted in 36 patients (34%). 4. Mortality and gastrointestinal malignancies: 12 patients died during the follow up and in 3 patients it was directly due to metastatic malignancies of gastrointestinal tract; 2 patients with gastric adenocarcinoma and one patient with a diagnosis of colorectal cancer had bowel enteropathy that had been found also in other 2 patients that died due to cardiovascular disease. Meanwhile, one patient with unexplained inflammatory nodularity of colon eventually developed caecal large B-cell lymphoma which was timely diagnosed, and treated successfully.

Conclusion: Gastrointestinal and hepatobiliary manifestations are common among patients with CVID and the risk malignancies are increased. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


OP230 EVALUATING THE UTILITY OF AMINO ACID CITRULLINE AS A METABOLOGIC SIGNATURE IN PREDICTIVE AND FOLLOW UP VALUE IN CELIAC DISEASE; SUGGESTING IT TO BE A MARKER OF ENTEROCYTE VIABILITY

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Introduction: Amino acid citrulline is a non-essential amino acid which does not corporate into proteins and small intestine (gut enteroctye) is the main endogenous source of circulating citrulline in blood. Since celiac disease is thought to be a highly heterogeneous spectrum ranging from classic malabsorptive form to atypical potential or latent form. It is envisaged that citrulline could be an important metabolomic or proteomic signature to assess silent and potential forms of the disease. The compliance of the disease after institution of gluten free diet and it may add predictive value for closer surveillance of high risk groups such as first degree relatives of CD.

Aims & Methods: We aimed to evaluate the baseline and six months follow up levels of citrulline in children with celiac disease and to evaluate its activity, was found in 11 patients (11%). In addition, atrophic gastritis was found in 10 patients (10%). 2. Small bowel: All tested patients were seronegative for coeliac disease. Of patients with increased intra-epithelial lymphocytes and villous atrophy of duodenum, 2 had complete histological and clinical response to gluten-free diet and all 4 others were unresponsive but had no enterocyte antibodies. 3. The patients with refractory duodenal villous atrophy and inflammation had also inflammatory changes in colon as well. 3. Hepatobiliary: Primary sclerosing cholangitis or CBD-associated cholangitis was diagnosed in 5 patients. 3. Large Bowel: Inflammatory changes of mucosa ranged from specific colitis and microscopic colitis (involving lymphocytic colitis and collagen colitis) to crypt-destructive and/or graft-versus-host like severe inflammation. Crypt-destructive IBD-like IBD ulcerative colitis ulcerative colitis was found in 5 patients (2 colectomies) and one patient had strictureing ikoeclonic Crohn disease. Altogether, inflammation of colon was more common than small bowel enteropathy and it was found in 20 patients (19%). Prior to ileocolonoscopy, patients were treated with sparse antibiotics and methods including fecal sampling screen. Nodular lymphatic hyperplasia was detected from gastric mucosa to rectum, and ranged from asymptomatic enhanced ileal nodularity to major changes of the gastric and bowel mucosal appearances and function. It was relatively common finding and noted in 36 patients (34%). 4. Mortality and gastrointestinal malignancies: 12 patients died during the follow up and in 3 patients it was directly due to metastatic malignancies of gastrointestinal tract; 2 patients with gastric adenocarcinoma and one patient with a diagnosis of colorectal cancer had bowel enteropathy that had been found also in other 2 patients that died due to cardiovascular disease. Meanwhile, one patient with unexplained inflammatory nodularity of colon eventually developed caecal large B-cell lymphoma which was timely diagnosed, and treated successfully.

Conclusion: Gastrointestinal and hepatobiliary manifestations are common among patients with CVID and the risk malignancies are increased. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

activity were examined by a mutagenesis technique in the promoter assay and RNA interference technology. The effects of TPEN on claudin and claudin-3 expression in mouse colons were also examined in combination with the calpain inhibitor.

Result: Intraducal zinc depletion by TPEN impaired the TJ barrier of intestinal epithelial cells. Although qPCR analysis and promoter reporter assay have demonstrated that the zinc depletion-induced claudin-3 mRNA levels were decreased by 50% at transcriptional levels, a site-directed mutation in the claudin-3 promoter sequence induced loss of both the basal promoter activity and the TPEN-induced decreases. Reduced claudin-3 expression by a specific siRNA also inhibited the claudin-3 expression and barrier function in mouse colons. Tissue section immunohistochemistry revealed that TPEN-induced decrease in claudin-3 was not claudin-3 in knockout mice.

Conclusion: This study shows that zinc depletion has an essential role in the transcriptional regulation of claudin-3.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP232 EVALUATING THE QUALITY OF LIFE OF ADULT PATIENTS ON HOME PARENTERAL NUTRITION IN NORTHERN AND NORTHEAST ENGLAND

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Introduction: Home parenteral nutrition (HPN) is an established treatment for the management of patients with Type 3 intestinal failure (IF). A Quality of Life (QOL) assessment tool (HPN-QOL version 1.0) was developed and validated in 2009 specifically for this patient population (1). Little data exist in literature on the QOL of HPN patients. We incorporated this tool into local clinical practice to evaluate the QOL of our HPN cohort in Northern and Northeast England.

Aims: The HPN-QOL was discussed with all patients in clinic and sent by post with a prepaid return envelope and a letter explaining how information would be used. Participation was voluntary. Responses were collected between February and July 2015. Data were anonymised for analysis and reporting. Patients were asked to answer 43 questions regarding 10 domains of function and 9 domains of symptoms. 3 further questions asked for a global numerical rating of QOL. A final question allowed free text comments. Scores were computed if at least half of the questions in each domain were answered as per the validated tool. A final score exceeding 50 in symptom domains were interpreted as frequent symptoms and scores may be confounded by advancing age alone. In analysis of aetiology, the QOL of HPN patients. We incorporated this tool into local clinical practice to evaluate the QOL of our HPN cohort in Northern and Northeast England.

Result: 22 patients were included in this analysis. 14 patients were reported to have HPN for more than 5 years. Intermediate calorie HPN-QOL was associated with the patients’ quality of life. The majority of our HPN patients experience problems that impair their QOL. It is not possible to establish how much this relates to the underlying condition or HPN itself. This is an area that would benefit from further study.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP257 EARLY ENTERAL VERSUS TOTAL PARENTERAL NUTRITION IN PATIENTS UNDERGOING PANCREATODUODENECTOMY: A RANDOMIZED MULTICENTER CONTROLLED TRIAL (NUTRI DPC)

J. Perinet1, C. Mariette2, B. Doussset1, I. Sieleznoff3, A. Gaimant4, J. Maubré4, S. Bin Dore1, M. El Bechawy5, M. Pocared6, E. Buc7, A. Sauvanet8, M. Adham9
Aims & Methods: To compare nasojejunal early enteral nutrition (NJEEN) with parenteral nutrition in patients undergoing gastrointestinal surgery. However, the NJEEN group showed significantly lower complications. NJEEN should not be recommended.

Conclusion: NJEEN should not be recommended.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP258 EARLY ENTERAL VERSUS TOTAL PARENTERAL NUTRITION IN PATIENTS UNDERGOING PANCREATODUODENECTOMY: A RANDOMIZED MULTICENTER CONTROLLED TRIAL (NUTRI DPC)

J. Perinet1, C. Mariette2, B. Doussset1, I. Sieleznoff3, A. Gaimant4, J. Maubré4, S. Bin Dore1, M. El Bechawy5, M. Pocared6, E. Buc7, A. Sauvanet8, M. Adham9
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Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP257 EARLY ENTERAL VERSUS TOTAL PARENTERAL NUTRITION IN PATIENTS UNDERGOING PANCREATODUODENECTOMY: A RANDOMIZED MULTICENTER CONTROLLED TRIAL (NUTRI DPC)

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Conclusion: NJEEN should not be recommended.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP257 EARLY ENTERAL VERSUS TOTAL PARENTERAL NUTRITION IN PATIENTS UNDERGOING PANCREATODUODENECTOMY: A RANDOMIZED MULTICENTER CONTROLLED TRIAL (NUTRI DPC)

J. Perinet1, C. Mariette2, B. Doussset1, I. Sieleznoff3, A. Gaimant4, J. Maubré4, S. Bin Dore1, M. El Bechawy5, M. Pocared6, E. Buc7, A. Sauvanet8, M. Adham9
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Conclusion: NJEEN should not be recommended.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
Disclosure of Interest: emulsifiers in vivo results from direct action of these compounds on the microbiota was sufficient to drive low-grade intestinal inflammation and metabolic syndrome in mice, with subsequent intestinal inflammation analysis. Investigation of Communities by Reconstruction of Unobserved States (PICRUSt) model was used to examine the effects of emulsifiers on the microbiota in vitro. After a stabilization period of 7 days, this dynamic human gut microbiota in vitro model was transferred to germfree recipient mice, with subsequent intestinal inflammation analysis.

Result: Both P80 and CMC treatment increased the pro-inflammatory potential of human microbiota, as revealed by a dramatic increase in bioactive flagellin within the same day for CMC and 5 days for P80. P80 induced drastic alteration of the microbiota in vitro. After a stabilization period of 7 days, this dynamic human gut microbiota in vitro model was transferred to germfree recipient mice, with subsequent intestinal inflammation analysis. Result: Both P80 and CMC treatment increased the pro-inflammatory potential of human microbiota, as revealed by a dramatic increase in bioactive flagellin within the same day for CMC and 5 days for P80. P80 induced drastic alteration of the microbiota in vitro. After a stabilization period of 7 days, this dynamic human gut microbiota in vitro model was transferred to germfree recipient mice, with subsequent intestinal inflammation analysis.

Conclusion: Both emulsifiers directly acted upon the microbiota to increase its pro-inflammatory potential, indicating that at least a portion of the effects of emulsifiers in vivo results from direct action of these compounds on the microbiota. The mechanisms by which P80 and CMC act are distinct, with P80 altering the composition of the microbiota, favoring species expressing high level of flagellin, whereas CMC increase the pro-inflammatory potential of the microbiota in a composition independent manner, by inducing expression of motility genes.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
1. Chassaing B, Koren O, Goodrich JK, Poole AC, Srinivasan S, Ley RE, et al. All authors have declared no conflicts of interest.

Introduction: Chronic Intestinal Pseudo-Obstruction (CIFO) is a chronic severe disorder of gastrointestinal (GI) motility leading to clinical features of intestinal obstruction without mechanical occlusion. The intestinal microbiota is a key factor determining gut motility. It was hypothesized that dysbiosis may be found in CIFO and that it contributes to clinical features of the disease. Aims & Methods: 1) To characterize the gut microbiota of patients with CIFO. 2) To determine whether this microbiota is responsible for clinical features typical of CIFO using a gnotobiotic mouse model. 3) To evaluate whether fecal microbiota transplantation (FMT) improves symptoms of CIFO. The faecal microbiota of 3 patients with CIFO (1 female, median age 38.6 ± 11 years) and 3 healthy volunteers (2 females, 39.5 ± 8.9 years) was analyzed by 16S rRNA based Illumina sequencing. Stool samples from 1 patient with CIFO and 1 healthy control were used to colonize germ-free NIH Swiss mice (n = 15 mice per donor, mixed gender) by oral gavage. GI transit was determined at 2 weeks using a validated in vivo videofluoroscopic technique1. Calcium and stomach size, and maximal bowel diameter, were determined using oral contrast-enhanced abdominal CT scan. The faecal microbiota of recipient mice was analyzed 48 hours and 2 weeks after colonization by Illumina and inferred metagenomics were assessed by PICRUSt. The CIFO patient microbiota was characterized by FMT by jejunal infusion from a healthy donor at regular intervals for 20 weeks. GI symptoms, overall health and quality of life were assessed using standardized questionnaires.

Result: The microbiota of patients with CIFO exhibited marked dysbiosis with predominance of Proteobacteria species, especially Enterobacteriaceae and Enterococcaceae. In contrast, healthy volunteers showed a predominance of Firmicutes and Bacteroidetes. Bacterial richness and diversity were lower in both patients and controls with CIFO. A specific alteration of microbiota profiles of gnotobiotic mice resembled that of human donors. Mice colonized with microbiota from the CIFO patient had a slower GI transit than mice with healthy control microbiota (mean transit score 1 ± 2 vs. 12 ± 5, p < 0.001). Furthermore, CIFO microbiota colonized mice had a larger caecum size (2.39 ± 0.32 cm3 vs. 1.56 ± 0.22 cm3, p < 0.001) and a higher maximal bowel diameter (3.3 ± 0.2 mm vs. 2.9 ± 0.2 mm, p = 0.003) compared to control microbiota colonized mice. Bacterial genes related to bile acid metabolism and disaccharide fermentation were differentially expressed in the faeces of patients with CIFO. Importantly, FMT led to a rapid and sustained improvement in GI symptoms and overall quality of life in our CIFO patient. His microbiota dramatically changed after FMT and resembled that of the donor.

Conclusion: The faecal microbiota composition and its metabolic activity are altered in patients with CIFO. This dysbiotic microbiota has the ability to induce clinical features reminiscent of this disorder in a gnotobiotic mouse model. Finally, faecal transplantation may be an effective treatment for patients with CIFO.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP235 DETERMINING THE EFFECT OF DIETARY EMULSIFIERS ON THE HUMAN GUT MICROBIOTA INCREASING ITS PRO-INFLAMMATORY POTENTIAL

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Introduction: We recently demonstrated that, in mice, consumption of dietary emulsifiers, detergent-like components of many processed foods, results in a disturbed gut microbiota, including alterations in species composition, elevated pro-inflammatory potential (i.e. higher levels of bioactive LPS and flagellin) and microbiota encroachment (1). Such disturbance of the microbiota promotes a range of chronic inflammatory diseases including metabolic syndrome and colitis. However, the underlying mechanism by which emulsifiers induce such effects, including whether they act directly upon the microbiota or the host, remains unclear.

Aims & Methods: Our aim in the current study was to investigate if, and how, emulsifiers directly impact upon the microbiota in the absence of a host response. The M-SHIME® (Mucosal Simulator of the Gastrointestinal Microbial Ecosystem) model was used to examine the effects of emulsifiers on the microbiota in vitro. After a stabilization period of 7 days, this dynamic human gut model was treated with emulsifiers (Carboxymethylcellulose (CMC) or Polysorbate-80 (P80), 1%). Microbiota composition, meta-transcriptomic and pro-inflammatory potential (Flagellin and LPS loads) were analyzed. Microbiota metagenome was predicted using PICRUSi (Phylogenetic Investigation of Communities by Reconstruction of Unobserved States). Human microbiota from the SHIME system was transferred to Germfree recipient mice, with subsequent intestinal inflammation analysis.

Result: Both P80 and CMC treatment increased the pro-inflammatory potential of human microbiota, as revealed by a dramatic increase in bioactive flagellin within the same day for CMC and 5 days for P80. P80 induced drastic alteration of the human gut microbiota composition, associated with an increased proportion of genes involved in bacterial motility. Both P80 and CMC treatment did not significantly alter branched or short chain fatty acid compositions, but significantly increased the proportion of microbiota mRNAs encoding motility related proteins. When transferred to germfree recipient mice, P80 and CMC-treated human microbiota was sufficient to drive low-grade intestinal inflammation and metabolic syndrome.

Conclusion: Both emulsifiers directly acted upon the microbiota to increase its pro-inflammatory potential, indicating that at least a portion of the effects of emulsifiers in vivo results from direct action of these compounds on the microbiota. The mechanisms by which P80 and CMC act are distinct, with P80 altering the composition of the microbiota, favoring species expressing high level of flagellin, whereas CMC increase the pro-inflammatory potential of the microbiota in a composition independent manner, by inducing expression of motility genes.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP234 DIETARY EMULSIFIERS DIRECTLY IMPACT THE HUMAN GUT MICROBIOTA INCREASING ITS PRO-INFLAMMATORY POTENTIAL

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Introduction: Operative resection in Crohn’s disease (CD) is not curative. After ileocecal resection, endoscopic recurrence is frequently observed on the anastomosis and/or on the neo-terminal limb.

Aims & Methods: The aim of this study was to analyze the mucosa associated microbiota at time of surgery and to look for predictors of post-operative endoscopic recurrence within the microbiota. This is a prospective study performed in a single center, collecting clinical and biological data at time of...
surgery and of endoscopy (performed at 6 months). Bacterial composition of the ileal mucosa associated microbiota was analyzed at time of surgery using 16S (RNA) sequencing. The obtained sequences (rarefied to 1000 reads/sample) were analyzed using the Qime pipeline to assess composition, alpha and beta diversity. Bacterial taxa associated with clinical parameters were identified using Multivariate association with Linear Models (MaAsLin) taking into account disease phenotype, clinical parameters and treatments.

Result: 146 patients were included: 73 (50%) were male, median age at surgery was 32 years (IQR 26–42). Median disease duration was 6 years (IQR 2–12), 44 patients (30%) were active smoker at time of surgery. Thirty patients (21%) had a previous resection, and 35 patients (24%) had perianal lesions. Indication for surgery was strictureing disease (n = 95), penetrating disease (n = 53). At time of surgery, 67 patients (46%) had received anti-TNF therapy within the last 3 months. After surgery, 31 patients received thiopurines, and 52 patients received anti-TNF therapy. The microbiota was mainly composed of bacteria from the Firmicutes (Mean 55%, range 0.3–99%), Proteobacteria (Mean 36%, range 0.5–99%), Bacteroidetes (Mean 5%, range 0–52%) and Actinobacteria (Mean 6%, range 0–81%) phyla. As expected, antibiotics treatment within one month before surgery had a dramatic impact on microbiota composition (Anosim, p = 0.0001) and diversity (mean observed species: 302 ± 17 vs 236 ± 14, p = 0.005). In multivariate analysis (MaAsLin), antibiotics treatment was notably associated with an increase in the Proteobacteria (q < 0.001) phylum and with a decrease in Lachnospiraceae family (q = 0.004). Taking into account only the patients who did not received antibiotics within a month before surgery, we then looked for predictive factors of endoscopic recurrence. Patients with endoscopic recurrence, defined by a Rutgeerts score (1), had a lower bacterial diversity at time of surgery compared to patients in endoscopic remission (n = 65) (mean observed species: 276 ± 14 vs 365 ± 45, p = 0.015).

Conclusion: Ileal mucosa associated microbiota of CD patients at time of surgery is dominated by bacteria belonging to Firmicutes, Proteobacteria, Bacteroidetes and Actinobacteria phyla. Antibiotics given during the last month prior to surgery induce major perturbations of the microbiota. Reduction in bacterial diversity at time of surgery is predictive of endoscopic recurrence.


Reference
1. This study has been supported by grants from MSD France, Association François Aupetit, the Helmsley Charitable Trust and INSERM.

OP238 INCREASED FAECAL LEVELS OF GRANINS IN IRRITABLE BOWEL SYNDROME ARE ASSOCIATED WITH LUMINAL MICROBIOTA COMPOSITION AND SYMPTOM SEVERITY
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Introduction: Chromogranins (Cg) and secretogranins (Sg) are acidic gut hormones, which are secreted from the neuroendocrine system and may regulate immune activation. We have previously shown increased levels of faecal Cg and Sg in IBS patients (1). However, the consequences and cause of increased levels of luminal granins in IBS are still undefined.

Aims & Methods: In this study we aimed to quantify faecal grain levels in IBS patients and evaluate potential relationships between grain levels, microbiota composition and immune activation. Levels of CgA, CgB, SgII and SgIII were characterised with radioimmunoassay and ELISA, respectively, in faecal samples from IBS patients (n = 143) and healthy subjects (n = 43). mRNA expression of interleukin (IL)-8, IL-10, tumour necrosis factor (TNF), prokaryotic housekeeping genes (16S rRNA) and a species-colon core was determined with qRT-PCR. Faecal (n = 111 subjects) and mucosal-associated microbiota (n = 50 subjects) were analysed by 16S RNA targeted pyrosequencing. IBS symptom severity and psychological distress were evaluated with the Gastrointestinal Symptom-Specific Symptom Checklist (GSRS-IBS) and the Hospital Anxiety and Depression Scale (HADS), respectively.

Result: IBS patients demonstrated higher levels of faecal CgA (8.1 (3.3–17.4) pmol/L) compared to healthy subjects (4.7 (2.9–9.0), p < 0.02 pmol/L). The levels of SgII (0.8 (0.1–3.6) pmol/L) and SgIII (2.0 (0.8–4.8) pmol/L) in IBS patients were also increased compared to healthy subjects (0.1 (0.0–0.2), p < 0.01) respectively (0.7 (0.4–2.4), p < 0.001, pmol/L). Faecal microbial diversity, assessed with CgA (r = -0.29, p < 0.005), CgB (r = -0.21,
OP239 MICROBIOTA ALTERATIONS IN TREATMENT NAÏVE NON-IBD AND NON-IBD PATIENTS - THE EU IBD-CHARACTER PROJECT

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Introduction: The microbiome is considered important for development of intestinal diseases. In order to create a molecular snapshot of IBD in its early manifestation, one part of the IBD-Character project identified faecal microbiota profiles along the strictly treatment naïve IBD and symptomatic non-IBD patients, and a healthy control group.

Aims & Methods: Patients where characterized by international criteria including endoscopy and biopsies. Faecal samples collected during five days prior to diagnosis were stored and analyzed in a blinded manner. DNA extraction was performed using QIAamp DNA stool kit (Qiagen). The V4 region of bacterial 16S rRNA gene was sequenced using the Illumina MiSeq platform. Data analysis was performed using QIIME and BLAST. For microbiota analysis, general sequence filtering was performed. Further analysis was performed on the 5% of classified sequences. Statistical analysis was performed using the Mann-Whitney test.

Results: In total 294 adult patients and healthy individuals were investigated for microbiota profiles of IBD, non-IBD and control groups, the abundance of Proteobacteria was increased in IBD and non-IBD as compared to the controls (p < 0.02). Comparing the bacteria profiles of IBD, non-IBD and control groups, the abundance of Faecalibacterium and Faecalibacterium prausnitzii was increased in IBD patients and healthy individuals.

Discussion: The microbiota is considered important for development of intestinal diseases. In order to create a molecular snapshot of IBD in its early manifestation, one part of the IBD-Character project identified faecal microbiota profiles along the strictly treatment naïve IBD and symptomatic non-IBD patients, and a healthy control group.

Conclusion: The microbiota is considered important for development of intestinal diseases. In order to create a molecular snapshot of IBD in its early manifestation, one part of the IBD-Character project identified faecal microbiota profiles along the strictly treatment naïve IBD and symptomatic non-IBD patients, and a healthy control group.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
**OP241 CLINICAL FEATURES AND FECAL MICROBIOTA PROFILE IN IRITRIBILE BOWEL SYNDROME PATIENTS WITH SMALL INTESTINAL BACTERIAL OVERGROWTH**

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**Introduction:** Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder, but the relationship between diarrhea-predominant IBS (IBS-D) and small intestinal bacterial overgrowth (SIBO) is unclear.

**Aims & Methods:** We aimed to investigate the clinical features and fecal microbiota profiles of IBS-D patients with SIBO by hydrogen and methane breath test (LBT), and compare them with IBS-D patients without SIBO and healthy controls. IBS-D patients who met Rome II criteria were divided into IBS-D with SIBO (IBS-P) and without SIBO (IBS-N) by hydrogen and methane LBT, while healthy controls with negative LBT (HC) were recruited. All subjects underwent colonoscopy to exclude organic diseases, and barostat for visceral hypersensitivity, intestinal permeability test [lactulose (L), mannitol (M) and L/M ratio], systematic inflammation severity (IL-10, IL-12 and IL-10/IL-12), hypersensitivity, intestinal permeability test [lactulose (L), mannitol (M) and L/M ratio], systematic inflammation severity (IL-10, IL-12 and IL-10/IL-12). Intestinal permeability was lower in IBS-P than IBS-N. As a consequence, IBS-P is different from IBS-N in many physiological parameters and fecal microbiota profile, so IBS-P may be just SIBO which should be screened before diagnosis of IBS-D according to Rome II criteria.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP242 FECAL MICROBIOTA TRANSPANTATION FOR RECURRENT C. DIFFICILE INFECTION: ANALYSIS OF FACTORS ASSOCIATED WITH THE NEED FOR MULTIPLE FECAL INFUSIONS**

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**Introduction:** Fecal microbiota transplantation (FMT) from healthy donors is considered a highly effective treatment against recurrent Clostridium difficile infection (rCDI). A single fecal infusion is usually sufficient to resolve symptoms and eradicate rCDI, but a subgroup of these patients may need multiple infusions to cure the disease. In our previously published randomized controlled trial of FMT versus vancomycin for rCDI, we observed that patients with pseudomembranous colitis (PMC) needed repeat fecal infusions to be cured, further reports confirmed our findings. To date, however, PMC nor other factors have been clearly proven to be associated with the need for multiple FMT.
Aims & Methods: Therefore, our aim was to identify predictive factors for the need for repeated fecal infusions in a series of patients treated with FMT for rCDI. We identified prospectively and included in the analysis all patients treated with FMT by colonoscopy or enema for rCDI in our Centre. Demographic, clinical, endoscopic, and follow-up data were collected. Repeat fecal infusions were administered if the patient recurred or failed to improve after first infusion. Gender, age, inpatient status, number or CDI recurrences (>3), poor/inadequate bowel preparation (according to Ottawa Scale), endoscopic evidence of colonic oedema, presence of PMC, use of external donors, infusion of frozen material, and infused grams of faeces were analysed as potential impact factors. Univariate associations between possible predictors and the need for repeated fecal infusions were investigated, using t-test for continuous variables and Fisher’s chi-square for dichotomous variables. Multivariate associations between all candidate predictors and need for repeated fecal infusions were investigated using logistic regression analysis. P-values of <0.05 were considered statistically significant.

Result: A total of 54 patients with rCDI (Males = 24; mean age = 71 years old, range = 29–94) received FMT from healthy donors by colonoscopy. Fifteen patients received 2 infusions, for a total of 61 procedures. Resolution of rCDI occurred in 52 of 54 patients (96%); of them, none experienced further recurrences after FMT. Univariate analysis showed that both poor/inadequate bowel preparation (p = 0.024) and PMC (p < 0.001) were significantly associated with the need of repeated fecal infusions; also colonic oedema was more common among patients who needed repeated FMT, albeit nonsignificantly (p = 0.083). On multivariable analysis, both the presence of PMC (OR = 2257; 95% CI = 25.17–1000; p = 0.014) and poor/inadequate bowel preparation (OR = 64.80; 95% CI = 3.43–1000; p = 0.021) were identified as significant predictors of the need of repeated infusions. Additionally, the need for repeated infusion was more common among patient who experienced a number or CDI recurrences >3 than among those who did not, although without reaching statistical significance (OR = 26.80; 95% CI = 1.69–1000; p = 0.054). The large confidence interval observed for most predictors could be explained presumably by the relatively low number of cases in our sample. Finally, the infusion of frozen material was significantly associated with lower need of multiple FMT (OR = 0.01; 95% CI = 0.00–0.19, p = 0.033).

Conclusion: Among patients treated with FMT for rCDI, both PMC and poor/inadequate bowel preparation appear to be significant predictors of the need for repeated fecal infusions. Additionally, frozen FMT appears to be significantly associated with a decreased need of multiple FMT. As the small sample size represents a limitation of our analysis, our findings, although promising, should be confirmed by further, larger studies.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


TUESDAY, OCTOBER 18, 2016 1400-1530

ENDOSCOPIC TREATMENT OF COMPLICATIONS AFTER UPPER GI SURGERY – ROOM E2

OP243 ENDOSCOPIC BALLOON DILATION FOLLOWED BY STEROID INJECTION IN ANASTOMOTIC STRICTURES AFTER ESOPHAGEAL RESECTION: A MULTICENTER RANDOMIZED, DOUBLE-BLIND CONTROLLED TRIAL

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Introduction: Esophageal cancer is the fifth most common cause of cancer-related death for men and the eighth for women worldwide. Although the effectiveness of chemotherapy or chemoradiotherapy for the treatment of esophageal cancer has been reported, the standard treatment to cure esophageal cancer. Anastomotic stricture, a major complication after esophagectomy, substantially decreases patients’ quality of life, and requires treatment with multiple sessions of endoscopic balloon dilation (EBD).

Aims & Methods: We conducted a multicenter randomized controlled trial to evaluate the usefulness of administration of local steroid injections to prevent the recurrence of anastomotic stricture. Patients were randomized to receive either triamcinolone or placebo immediately after EBD. The primary endpoint was the number of dilations required to resolve the stricture. Secondary end points were restriction-free survival and adverse events. Restriction-free survival is defined as the number of days from randomization to performing EBD for any reason after death from any cause. Patients with a dysphagia symptom score of two or more after esophagectomy with anastomotic stricture confirmed by endoscopy were included. Patients and investigators were blinded to the type of agent injected. The syringe containing triamcinolone or placebo was prepared by nursing staff unconnected to the trial. Patients underwent EBD with a standard through-the-scope balloon dilator. The balloon was inflated with water, aiming for a luminal diameter of maximum 15 mm for 3 min. After EBD, a second endoscopist who was not involved in the follow-up evaluation of the patients performed the injections into the anastomotic laceration. A total of triamcinolone acetate (50 mg/5 mL; Bristol-Myers Squibb) or an identical volume of normal saline solution as a placebo was injected per single site using a 25-gauge needle. Neither the patient nor the treating physician knew which treatment was given. The injections into the laceration were performed on demand whenever patients reported dysphagia. In patients without dysphagia, EGD was performed within 3 months after EBD to evaluate the stricture. EBD was performed when the stricture was confirmed. Stricture was defined as dysphagia to some solids (dry bag score 2) and an inability to pass an endoscope of at least 9.2 mm diameter.

Result: Over a 4-year period, 68 patients met the inclusion criteria and were screened. Three patients declined to participate. Sixty-five consecutive patients were therefore recruited to the study and randomized: 33 to receive steroid and 32 to receive placebo. The median number of EBD sessions required to resolve stricture in the steroid group was 2 (range: 1–7), significantly smaller than the median of 4 EBD sessions (25/33) required by the control group (p < 0.001). After 6 months of follow-up, 39% of patients who received steroid injections remained recurrence-free compared with 19% of those injected with saline (p < 0.01). There were no adverse events during follow-up.

Conclusion: Steroid injection showed promising results for the prevention of stricture recurrence in patients who underwent EBD for anastomotic stricture.

Disclosure of Interest: N. Hanaka: The Japan Foundation for Research and Promotion of Endoscopy Grant

All other authors have declared no conflicts of interest.

OP244 THE "TUNNEL + CLIP" METHOD FACILITATES OESOPHAGEAL ESD PROCEDURES – A PROSPECTIVE, CONSECUTIVE BI-CENTRE STUDY

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Introduction: ESD is the treatment of choice for superficial neoplasms of the oesophagus due to its oncological efficiency and the morbidity associated with the surgical alternative. ESD requires a high level of skill and is technically challenging and time consuming. Therefore, it is often reserved to experts. Combining the tunnel technique and the clip-line counter-traction may enable optimisation of oesophageal ESDs.

Aims & Methods: From January 2014 to April 2016 we performed a prospective bi-centre case series of consecutive "tunnel+clip" oesophageal ESDs. Four young operators (fewer than 50 ESDs and fewer than 5 oesophageal ESDs) performed consecutively the ESD using the tunnel+clip method: generation of a classic tunnel beneath the lesion followed by constant counter-traction thanks to a clip with line dropped at the oral side of the tunnel.

Results: Thirty-three lesions (14 SCC and 19 ADK/HDG complicating Barrett’s oesophagus) were resected consecutively. En bloc, R0 and curative resection rates were 100% (33/33), 87.8% (29/33) and 75.8% (25/33), respectively. No perforation occurred. The mean speed of ESD was 22.3 mm/min for a mean lesion size of 61.6 mm. The clip provided considerable assistance in performing the procedure. No pathological damage caused by the clipping was reported.

Table

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</tbody>
</table>
A simple classification system for differentiating hyperplasic and adenomatous colorectal lesions. At least, a pilot clinical evaluation was performed during real-time evaluated among inexperienced raters, including medical students and GI fellows.

Discussion: First study of the strategy “tunnel + clip”. Our in loco and R0 resection rates confirmed the usefulness of this technique, despite the relative inexperience of the operators. Our resection rates were similar to those reported in large series by international experts, including those in Japan and our absence of perforation highlighted the safety of this strategy.

Conclusion: The tunnel + clip method for oesophageal ESD is effective and safe, in particular for physicians with little experience. This strategy standardizes the ESD procedure for superficial oesophageal neoplasia and increases the speed of dissection. Thus, it will help to widespread oesophageal ESD performed in Western countries.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

WHAT TO DO WITH SMALL COLORECTAL POLyps? – ROOM F2

OP245 DEVELOPMENT AND VALIDATION OF A SIMPLE CLASSIFICATION SYSTEM FOR IN VIVO DIAGNOSIS OF COLORECTAL POLyps USING THE NEWLY INTRODUCED BLUE LIGHT IMAGING (BLI)

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Introduction: BLI is a novel endoscopic imaging technique for enhancement of subtle mucosal and vascular details. The potential of this novel technology for in vivo diagnosis of colorectal polyps has yet to be established.

Aims & Methods: Primary study objective was to develop a simple classification for in vivo differentiation of hyperplasic and adenomatous colorectal lesions by using the novel BLI technology. Second study endpoint was to validate the classification among experienced and non-experienced users. In the first phase, the capacity of experienced endoscopists to predict the histology of colorectal polyps was assessed. In the second phase, a simplified classification was developed allowing histologic prediction. Thirdly, the validity of the classification was evaluated among inexperienced raters, including medical students and GI fellows. At least, a pilot clinical evaluation was performed during real-time colonoscopy.

Result: A simple classification system for differentiating hyperplasic and adenomatous colorectal lesions by using the novel introduced BLI technology was developed and validated. Diagnosis was made in 80% to 88% of polyps with high-confidence. Sensitivity and specificity ranged from 93% to 100% and 83% to 92%, respectively. During real-time colonoscopy, diagnosis was made with high-confidence in 88% of polyps with sensitivity of 96%, specificity of 92%, and accuracy of 95%. Positive and negative predictive values were 96% and 92%, respectively.

Conclusion: This is the first study evaluating the novel BLI technology for in vivo prediction of colorectal polyps. The proposed classification allowed for adequate in vivo diagnosis of hyperplasic and adenomatous lesions. Further prospective multicenter trials should now confirm these preliminary results.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP246 MANAGEMENT OF DIMINUTIVE, RECTOSIGMOID POLyps BY USING COMPUTER-ASSISTED DIAGNOSTIC SYSTEM


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Introduction: The PIVI initiatives propose that a “leave in place” approach is acceptable for a diminutive (<5 mm), rectosigmoid hyperplastic polyp when endoscopist’s optical diagnosis provides over 90% negative predictive value (NPV) for adenomas in high confidence predictions [1]; however, expertise is required to achieve a high accuracy and some studies conducted in community-based hospitals have been disappointing [2]. Recently, we have reported the usefulness of computer-aided diagnosis (CAD) in supporting endoscopists’ decision making during colonoscopy [3,4]. The present study was aimed to validate the efficacy of the latest CAD model for endoscopy (380-fold ultra-magnifying endoscopy) in management of diminutive, rectosigmoid polyps.

Aims & Methods: The present study was aimed to validate the efficacy of the latest CAD model for endoscopy (380-fold ultra-magnifying endoscopy) in management of diminutive, rectosigmoid polyps. The CAD for endoscopy comprises image acquisition, nuclear segmentation, feature extraction, and classification into three pathological groups (non-neoplastic, adenoma, and invasive cancer). The classification algorithm was programmed based on 296 features of each image (e.g., area, circularity, diameter, and perimeter of nuclei, and over 250 textural features of a whole image). We used a support vector machine to help classify these many features; 6051 endoscopy images were used for machine learning in the process of construction of the model. In order to validate this CAD model, the pilot study using a test set was undertaken between August and November 2015. The test set comprised endoscopist images of 65 diminutive, rectosigmoid polyps from the database of Showa University Northern Yokohama Hospital. Each image was automatically allocated to the CAD, and the predicted pathology was immediately output by the CAD in 0.2 seconds. The main outcome measure was NPV of the CAD for adenomatous histology for diminutive, rectosigmoid colon polyps when they had been diagnosed with high confidence.

Result: Of the 65 diminutive rectosigmoid polyps (mean size, 3.6 ± 1.0mm), the CAD diagnosed 55 (19 neoplastic and 36 non-neoplastic) with high confidence. Details of the diagnostic performance by the CAD for these 55 polyps were shown in the Table. The CAD correctly predicted neoplastic histology in 18 of the 24 neoplastic polyps (positive predictive value of 90% [95% CI, 68–99]) and non-neoplastic histology in 34 of the 35 non-neoplastic polyps (NPV of 97% [95% CI, 85–100]). This performance of the CAD met the “leave in situ” criteria proposed by the PIVI initiative.

Conclusion: The CAD applying endoscopy can be a powerful and quick support tool in management of diminutive, rectosigmoid polyps.

Disclosure of Interest: K. Mori: Cybernet System Corp.

All other authors have declared no conflicts of interest.

References

BIOMARKERS IN IBD – ROOM K

OP247 IBDOC – FIRST SMARTPHONE BASED CALPROTECTIN HOME TEST – 18 MONTHS EXPERIENCE

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Introduction: Inflammatory Bowel Disease (IBD) is a chronic inflammation of the gut presenting with phases of active inflammation, remission and relapses. IBD treatment goals are mucosal healing and persistent remission. Calprotectin measured in patients’ stool sample is a well-established biomarker to measure the inflammatory activity in the gut. Periodical assessment of calprotectin levels is important to measure effectiveness of the treatment as well as predicting relapses. Until now at most, patients send in their stool sample for laboratory analysis, leading to long delays between sample collection, final test result and potential adaptations of therapies.

Aims & Methods: We have developed a smartphone-based calprotectin home test, called IBDoc®, that allows real-time information about the inflammatory activities in the gut for both, the patient and the health care provider. The IBDoc® consists of a stool collection and extraction device (CALEX® Valve) and an immunochromatographic calprotectin rapid test, which is measured using a smartphone App (CalApp®) controlling the phone’s camera. Once the test is...
measured the result is instantly sent to a webserver (IBDoc® Portal) allowing the treating clinician to have immediate diagnostic accuracy. The combination of the calprotectin home test yields a sensitivity of 91.7%, a specificity of 68.8%, a positive and negative predictive values (PPV and NPV) of laboratory and US parameters alone or in combination were analyzed according to the final diagnosis.

Conclusion: The combination of FC, BIM and bowel US may help to select children needing further invasive procedures and allow to avoid or delay endoscopy in patients with negative initial diagnostic work-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP249 ACCURACY OF NON-INVASIVE TESTS IN THE INITIAL DIAGNOSTIC WORK-UP OF PEDIATRIC INFLAMMATORY BOWEL DISEASES

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Introduction: Upper and lower endoscopy with histology together with imaging of the small bowel is the gold standard for the diagnosis of inflammatory bowel disease (IBD) in children. Due to high costs and invasive nature of these techniques, accurate selection of patients is mandatory.

Aims & Methods: We aimed to assess the accuracy of non-invasive tests including fecal calprotectin (FC), blood inflammatory markers (BIM) and bowel ultrasound (US) alone or in combination as first level investigations in children with suspected IBD. Consecutive patients referred to our Center for a clinical history compatible with IBD were enrolled during a 3-year period. All underwent FC (Calprest®, Eurocatal), C-reactive protein [CRP], erythrocyte sedimentation rate [ESR] and bowel US as first investigations. Endoscopy with biopsies was the gold standard for diagnosis. At US pathological findings were: BWT >3 mm, BW vascularity, loss of stratification, enlarged mesenteric nodes. Multiple logistic analysis with stepwise method considering IBD diagnosis as dependent variable was conducted. Sensitivity (SE), specificity (SP), positive and negative predictive values (PPV and NPV) of laboratory and US parameters alone or in combination were calculated according to the final diagnosis.

Result: 100 patients (58 males, median age 12) were enrolled. The final diagnosis was IBD in 69 (57 CD, 12 UC) other than IBD in 31. The mean values of ESR, FC and BWT were higher in IBD vs non-IBD patients (p < 0.001). Multiple logistic analysis showed that independent variables predictive of IBD were: FC (OR 44.8; p < 0.001), BWT (OR 20.4, p < 0.001) and ESR (OR 9; p < 0.001). The combination of 3 or 2 parameters was more frequent in IBD patients (p < 0.01). Table 2 shows SE, SP, PPV, NPV of these parameters alone or in combination.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SE (%)</th>
<th>SP (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FC (ug/g)</td>
<td>94</td>
<td>89</td>
<td>94</td>
<td>89</td>
</tr>
<tr>
<td>BWT (mm)</td>
<td>75</td>
<td>89</td>
<td>93</td>
<td>65</td>
</tr>
<tr>
<td>2 (at least 2)</td>
<td>96</td>
<td>84</td>
<td>97</td>
<td>92</td>
</tr>
<tr>
<td>2 (FC + BWT)</td>
<td>91</td>
<td>100</td>
<td>100</td>
<td>86</td>
</tr>
<tr>
<td>3 (FC + BWT + ESR)</td>
<td>71</td>
<td>100</td>
<td>100</td>
<td>64</td>
</tr>
</tbody>
</table>

Conclusion: The combination of FC, BIM and bowel US may help to select children needing further invasive procedures and allow to avoid or delay endoscopy in patients with negative initial diagnostic work-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP250 THE SEROLOGIC MARKERS ASCA AND PANCA SHOW BETTER PREDICTABILITY THAN CRP, ESR AND CALPROTECTIN FOR ANTI-TNF TREATMENT AMONG PEDIATRIC IBD PATIENTS

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Introduction: Serologic nuclear and anti microbial antibodies have been recognized as predictive markers of disease course and complications in ulcerative colitis (UC) and Crohn’s disease (CD). The significance of serological markers from onset of the disease, their ability to predict disease outcome and their stability over time is not fully explored in IBD patients.

Aims & Methods: To study the prevalence of serological markers in treatment-naive pediatric patients with newly diagnosed inflammatory bowel disease and prospectively evaluate the antibody and titer- variations related to disease sub- types and treatments in course. We also wanted to compare the value of
serological markers with the biochemical markers C-reactive protein (CRP), elevated sedimentation rate (ESR) and C3, C4 levels. Patients aged 18 years, (n = 58) diagnosed with IBD were included between 2005-2007 as a part of a prospective population based study in South-Eastern Norway (IBSEN- II). Fecal samples were analyzed for calprotectin (Bühlmann, Basel, Switzerland) and blood samples were analyzed for antibodies (Prometheus labs, San Diego). CRP and ESR at diagnosis and after 1-2 years of treatment. Treatment was decided at the courtesy of the treating pediatrician. Tumor necrosis factor (TNF) blocker treatment was regarded as aggressive treatment compared to treatment with immunomodulators.

Result: Among the UC patients, 13 (72%) were perinuclear anti-neutrophil cytoplasmic antibody (pANCA) positive, versus 13 (35%) of the CD patients. None of the UC patients harbored anti-Saccharomyces cerevisiae (ASCA) antibodies, while 4 (11%) of CD patients were ASCA IgA or IgG positive (< p < 0.0001).

Conclusion: There were significant differences between CD and UC patients in the prevalence of antibodies against Pseudomonas fluorescens associated with MPO (61 vs. 33%), the outer membrane porin of Escherichia coli (OmpC) (8 vs. 6%) or flagellin expressed by Closstridial phylum (CBir) (22% vs. 0%, respectively). The 18 (49%) CD patients who received aggressive therapy with TNF blockers had higher presence of antibodies against ASCA IgA (p = 0.05) and ASCA IgG (p = 0.045) as well as higher titers of ASCA IgG (p = 0.046) compared to the 19 (51%) CD patients who received conventional treatment. If ASCA antibodies were present at baseline the probability of receiving infliximab treatment in UC patients was 70%, with OR 8.2 (2.0-37.7) p = 0.004. The presence of pANCA antibodies was less frequent at diagnosis in TNF blocker treated CD patients compared to conventionally treated CD patients. The OR of receiving aggressive therapy being pANCA negative was 5.3. CD patients with pANCA negative even in clinically insignificant levels of fecal calprotectin, CRP and ESR at diagnosis compared to conventionally treated CD patients with median values of fecal calprotectin (mg/kg) 1580 vs. 501 (p = 0.01), CRP (mg/l) 28 vs. 7.5 (p = 0.02) and ESR (mm/h) of 32 vs. 18 (p = 0.01) respectively. Being pANCA negative and/ or ASCA IgA or ASCA IgG positive was associated with the need for TNF blocker therapy, even after adjustment for CRP, ESR and fecal calprotectin levels. After treatment there was no difference in antibody prevalence for ASCA IgA, ASCA IgG, 12, OmpC and UC patients regardless of treatment modality, except in UC patients receiving biologic therapy. Fewer UC patients, 9 (64%), tested positive for pANCA after treatment, compared to baseline, 13 (72%), p = 0.013. Only one of the 18 UC patients received TNF blocker treatment.

Conclusion: ASCA and pANCA status was associated with the need for early aggressive therapy with TNF blockers in our CD patients. We found that being pANCA negative and/or ASCA IgA or ASCA IgG positive were more predictive of need of aggressive treatment than CRP, ESR or fecal calprotectin levels. ASCA negative, regardless of treatment modality, and might be a prognostic tool at any time in the disease course.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Disclosure of Interest:

**GUIDED CONTROL OF ABDOMINO-THORACIC MUSCULAR ACTIVITY.**

**CONCLUSION:**

**OP254 LOW FODMAP DIET ALTERS SYMPTOMS, MICROBIOTA, AND DISTENSION BEFORE CROSSING-OVER TO THE ALTERNATIVE SUPPLEMENTATION FOR 10 NEW DAYS.** IBS patients with functional gastrointestinal disorders (47 women, 1 man; 21–74 yr age range) were recruited and instructed to follow a low FODMAP diet. Abdomino-thoracic muscular activity was recorded by EMG during basal conditions (no distension) and during an episode of distension to prove the abdomino-phrenic origin of their distension. Each patient underwent three treatment sessions over a 10-day period. Abdomino-thoracic muscular activity was assessed clinically weekly. The symptoms and adverse effects of the drugs were evaluated at the end of treatment.

**Aims & Methods:** Our aim was to demonstrate the superiority of biofeedback versus placebo for the treatment of abdominal distension. We performed a randomized, placebo-controlled study with a referral center (Clinical Trials Gov Registration Number 01205010). Forty-two patients complaining of episodes of visible abdominal distension who fulfilled the Rome III criteria for functional intestinal disorders (47 women, 1 man; 21–74 yr age range) were recruited and randomized to biofeedback and placebo. Abdomino-thoracic muscular activity was recorded by EMG before crossing-over to the alternative supplementation for 10 new days. IBS patients with functional gastrointestinal disorders (47 women, 1 man; 21–74 yr age range) were recruited and instructed to follow a low FODMAP diet. Abdomino-thoracic muscular activity was recorded by EMG during basal conditions (no distension) and during an episode of distension to prove the abdomino-phrenic origin of their distension. Each patient underwent three treatment sessions over a 10-day period. Abdomino-thoracic muscular activity was assessed clinically weekly. The symptoms and adverse effects of the drugs were evaluated at the end of treatment.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References:**


2. Tricyclic antidepressants tend to be constipating and, therefore, are increasingly being advocated in patients with functional gastrointestinal disorders (FGID) at present, selection criteria or response predictors for dietary intervention are poorly defined.

3. A positive dietary response in patients with fructose or lactose intolerance, and is predicted by a few clinical and breath-test associated symptoms and not by the magnitude of accurate relief. A positive dietary response in patients with fructose intolerance was associated with the development of diarrhea during breath testing (multivariate analysis 1.7 (1.03–2.81), p=0.04). No other significant associations between symptoms experienced during fructose or lactose breath testing and dietary outcome were demonstrated.

4. Furthermore, adequate relief likely reflects a complex constellation of psychological and physical factors, rather than a reduction in individual symptoms, explaining the few significant associations with clinical or provoked symptoms. Disclosure of Interest: All authors have declared no conflicts of interest.

5. **OP256 A RANDOMIZED TRIPLE BLIND CONTROLLED TRIAL ASSESSING THE EFFECTS OF DOXEPI N AND NORTRIPTYLINE ON DIARRHEA-PREDOMINANT IRITABLE BOWEL SYNDROME.** H. Habibinejad1, M. Ghadir2, A. Heidari3

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**Introduction:** Tricyclic antidepressants tend to be constipating and, therefore, may be of most benefit in diarrhea-predominant IBS (IBS-D). The aim of this study was to compare the effects of low doses of doxepin and nortriptyline on IBS-D.

**Aims & Methods:** Seventy-five patients with IBS according to Rome III criteria were treated for two months. All possible organic diseases responsible for bowel symptoms were excluded. The patients were randomly assigned to one of three groups treated with doxepin(10mg), nortriptyline(10mg) or placebo. Subjects were assessed clinically weekly. The symptoms and adverse effects of the drugs were recorded in the questionnaire. The primary outcome was the responder rate (defined as a 50% reduction in symptom severity).

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Result: Abdominal pain and bloating were the most common symptoms before initiation of treatment, occurring in 62 (82.7%) patients. The frequency of the symptoms was decreased significantly after treatment in doxepin and nortriptyline groups compared with pre-treatment. The responder rate was 80%, 52%, and 36% for doxepin, nortriptyline, and placebo groups, respectively (p = 0.007). The responder rate for doxepin group was superior to nortriptyline and placebo groups (p = 0.037 and p = 0.002, respectively) but there was no significant difference in responder rates of nortriptyline and placebo groups (p = 0.254). There were no significant differences in improvement rates in individual symptoms between doxepin and nortriptyline groups (all p > 0.05).

Conclusion: Treatment of diarrhea-predominant IBS with low dose of doxepin or nortriptyline could be effective. Improvement rates of the symptoms are similar in doxepin and nortriptyline groups but doxepin has a better response rate than nortriptyline.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Table (OP258): Composite response rates over longer treatment intervals in ELX-treated patients who were composite or adequate relief responders over Month 1

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Placebo (n = 809)</th>
<th>ELX 75 mg BID (n = 808)</th>
<th>ELX 100 mg BID (n = 806)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders</td>
<td>101 (12.5)</td>
<td>708 (87.5)</td>
<td>157 (19.2)</td>
</tr>
<tr>
<td>Non-responders</td>
<td>708 (87.5)</td>
<td>184 (22.8)</td>
<td>624 (77.2)</td>
</tr>
<tr>
<td>Response rate</td>
<td>20.8%</td>
<td>22.8%</td>
<td>77.2%</td>
</tr>
</tbody>
</table>

Adequate relief: Weeks 1–2

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Placebo (n = 809)</th>
<th>ELX 75 mg BID (n = 808)</th>
<th>ELX 100 mg BID (n = 806)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders</td>
<td>329 (82.5)</td>
<td>104 (83.7)</td>
<td>79 (79.7)</td>
</tr>
<tr>
<td>Non-responders</td>
<td>120 (30.3)</td>
<td>70 (77.8)</td>
<td>143 (29.5)</td>
</tr>
<tr>
<td>Response rate</td>
<td>82.5%</td>
<td>83.7%</td>
<td>79.7%</td>
</tr>
</tbody>
</table>

BID, twice daily; ELX, eluxadoline

*Percentage calculated based on number of patients who were composite responders over Weeks 1–4

*Percentage calculated based on number of patients who were adequate relief responders over Weeks 1–4
Conclusion: Moreover, treatment of KPC mice revealed intrinsic resistance of CAFs to key metabolite enzymes for gemcitabine inactivation such as deoxycytidylate concentrations of activated dFdCTP and greatly reduced levels of the inactive normal liver. Mean vessel density did not correlate with gemcitabine delivery at human and murine liver metastases as compared to matched primary tumours.

Aims & Methods: We designed a straightforward approach to direct human pluripotent stem cells (PSC) toward pancreatic organoids resembling exocrine and ductal progeny. Result: Extensive phenotyping of the organoids not only shows the appropriate marker profile but also ultra-structural and functional hallmarks of human pancreas in the dish. Upon orthotopic transplantation into immunodeficient mice, these organoids form normal pancreatic ducts and acinar tissue resembling fetal human pancreas without any evidence of tumour formation or transformation. Finally, we implemented this unique phenotyping tool as a model for pancreatic facets of cystic fibrosis (CF) but also other inherited pancreatic disorders. We provide evidence that pancreatic commitment occurs generally unhindered in CF. Importantly, CFTR-activation in mutated pancreatic organoids mirrors the CF-phenotype in a series of functional assays. We also conducted a scalable proof-of-concept screen in CF-pancreatic organoids using a set of CFTR correctors and activators. Finally, we did orthotopic transplantation of CF-organoids to generate diseased human pancreata in mice and established a mRNA-mediated gene repair approach in CF-organoids. Similar assays were applied to another inherited pancreatic disorder.

Conclusion: Thus, our platform provides novel opportunities to model pancreatic disease and development but also to screen for disease rescuing agents.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Aims & Methods: Frequently, differential diagnosis of neoplastic cysts remains cumbersome. Thus, non-invasive diagnostic stratification would be welcome. Such a test should allow both discrimination of (i) IPMN from strictly benign pancreatic cysts but also (ii) low- from high-grade IPMN.

Conclusion: These findings establish cfDNA and targeted genotyping as a diagnostic tool for IPMN, which may aid differential diagnosis and risk stratification of cystic pancreatic lesions.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP262 NOVEL GENE MUTATIONS IN NEUROGENIC CHRONIC INTESTINAL OBSTRUCTION
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Introduction: Chronic intestinal pseudo-obstruction (CITO) is a severe gut motility disorder mimicking an intestinal sub-occlusion without demonstrable mechanical causes. Several genes have been identified in familial cases, suggesting a genetic heterogeneity. We identified a novel mutation in the RADD1 gene in a recessive form of familial CITO1. RADD1 is a transcription factor essential for a number of functions including sister chromatid division during cell replication.

Aims & Methods: This study aimed to identify other mutated genes in a selected set of familial cases associated with peripheral small fiber neuropathy (SFN), a condition affecting peripheral neurons including those of the autonomic system. Whole exome sequencing (WES) was performed on genomic DNA of n=6 patients (3 trios and 3 sporadic cases) with clinical, radiological and mano-meterial evidence of peripheral neuropathy. A neurological work-up established SFN in each of them. Libraries were enriched with the Nimblegen SeqCap EZ v3.0 and sequenced via paired-end 50 bp reads on HiSeq2500 sequencer. Variants were mined. Thus, in Human PAR, play an important role in neuronal activation and may be relevant in IBS research.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP263 PROTEASE SIGNALING IN HUMAN SENSORY NEURONS
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Introduction: IBS is a functional bowel disorder characterized by abdominal pain, alteration in bowel habit and/or diarrhea. Among the mediators studied in IBS, increased colonic proteolytic activity appears as a common feature in all IBS sub-groups. Through Protease-Activated Receptors (PARs) activation, proteases can activate primary afferents and act on visceral pain pathways in rodents, but the relevance of PAR activation in human sensory neurons still has to be determined. Thus, the objective of our study was to decipher the PAR pharmacology in human sensory neurons.

Aims & Methods: Cryo-protected or fresh human thoracic dorsal root ganglia (DRG) were obtained from the national disease resource interchange (NDRI). Expression of PAR1, PAR2 and PAR4 was studied on slices of DRG (DRG T12, n = 3) by co-staining immunohistochemistry with a pan-neuronal marker (pmp22.9) and PAR antibodies. Calcium signaling responses to PAR agonists (PAR-AP; 1, 10 and 100 μM), PAR-IP (TFFLR; 1, 10 and 100 μM), PAR-AP (SLIGRL; 100 μM) and PAR-IP (NKFGEK; 100 μM) in cultured human DRG neurons were defined as peak calcium flux. Calcium responses to PAR-AP and PAR-IP did not cause calcium mobilization. Thrombin (PAR1 and PAR4 agonist) or trypsin (1 and 10 μM) and thrombin (1 and 10 U) were studied in cultured human DRG neurons, which were fixed thereafter, to study PAR expression.

Result: In fixed human DRG, PAR1, PAR2 and PAR4 were expressed in 20, 40% and 40% of human sensory neurons respectively. PAR expression was not modified after culture. PAR-AP increased intracellular calcium concentration in a dose-dependent manner. This increase was inhibited by PAR1 antagonist (SUS1028; 10 μM). In contrast, PAR-4-AP, PAR-1-AP and PAR-IP did not cause calcium mobilization. Thrombin (PAR1 and PAR4 agonist) however increased calcium flux in human sensory neurons. PAR-4-AP-induced calcium mobilization was significantly reduced by pre-incubation with PAR2-AP, but not with PAR4-AP or any of the PAR-IP.

Conclusion: Our study demonstrates that PAR1, PAR2 and PAR4 are expressed in human sensory neurons. In contrast to PAR1 and PAR2, PAR4 activation increased calcium influx in human sensory neurons. PAR4 activation reduced calcium mobilization. Thus, in Human PAR, play an important role in neuronal activation and may be relevant in IBS research.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP264 DIFFERENTIAL BASELINE CHARACTERISTICS IN SHORT BOWEL SYNDROME DUE TO VASCULAR CATASTROPHES ARE ASSOCIATED WITH VARYING RESPONSE TO TEGDLUTIDE TREATMENT: POST HOC ANALYSIS
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Introduction: Vascular catastrophes are an underlying condition for massive intestinal resection and failure associated with short bowel syndrome (SBS-IF). Aims & Methods: This post hoc analysis of data reported in patient e-case forms compared baseline characteristics of patients with SBS-IF due to vascular catastrophes (SBS-Vasc) vs patients with nonvascular causes of SBS-IF (SBS-non-Vasc), including the clinical response to tegeldutide (Teg). STEPS (NCT00789967; EudraCT2008-006193-15) was a 24-week, placebo (PBO)-controlled study of TEG 0.05 mg/kg/day in patients with SBS-IF. Response was defined as ≥20% reduction from baseline in weekly parenteral support (PS) volume at Week 20 that was maintained at Week 24. Vascular catastrophes were intestinal ischaemia or mesenteric vessel thrombi or emboli. Descriptive summary statistics are presented with standard deviations (SD) or 95% confidence intervals (CI); this post hoc analysis was not powered for statistical significance.

Results: The patient characteristics for the SBS-Vasc (n=32) and SBS-non-Vasc (n=53) groups are detailed in the Table. The reason for the majority of the intestinal resections was Crohn’s disease (SBS-non-Vasc) or mesenteric vessel thrombi or emboli (SBS-Vasc). Table. At baseline, more SBS-Vasc patients were male (55 vs 48 years) and male (53% vs 41%) than SBS-non-Vasc patients. SBS-Vasc patients had shorter bowel length (55 vs 92 cm), were more likely to have colon-in-continuity (78% vs 43%), and were less likely to have stoma preprocedure (19% vs 61%) compared with SBS-non-Vasc patients. SBS-Vasc patients developed peritonitis (PAR4-AP) in 14.1% of patients compared with SBS-non-Vasc patients. After 24 weeks, 53% (CI, 27%-79%) of SBS-Vasc patients and 70% (CI, 50%-86%) of SBS-non-Vasc patients were responders to Teg. In the PBO groups, 35% (CI, 14%-62%) of SBS-Vasc patients and 27% (CI, 11%-48%) of SBS-non-Vasc patients met the response criteria. In the Teg groups, reduction in mean PS volume (change and percentage change) took longer in the SBS-Vasc group (Week 12: 1.9 [CI, 0.3-3.5], 12% [CI, 3%-20%]; Week 24; 3.6 [CI, 1.5-5.7], 25% [CI, 15%-35%]) compared with the SBS-non-Vasc group (Week 12: 4.0 [CI, 2.0-5.9], 24% [CI, 16%-33%]; Week 24: 5.5 [CI, 3.4-7.6], 36% [CI, 29%-43%]). The overall Teg safety profile was generally similar between the two groups. Specifically, >15% of SBS-Vasc patients reported abdominal pain, dyspepsia, fatigue, nausea, and peripheral oedema, whereas >15% of SBS-non-Vasc patients reported nausea, abdominal distention, abdominal pain, stoma complication, and peripheral oedema.

Conclusion: To our knowledge, this post hoc analysis is the first to compare baseline characteristics and response to treatment in patients with SBS resulting from vascular catastrophes and nonvascular diseases. In this group of patients, SBS-IF patients with vascular catastrophes were more likely to have colon-in-continuity, less likely to have stoma present, and had less baseline PS volume than in patients with nonvascular causes of SBS-IF. SBS-IF patients with vascular catastrophes took longer to respond to tegeldutide in the observed PS volume reduction.

Table: Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SBS-Vasc</th>
<th>SBS-Vasc</th>
<th>SBS-non-Vasc</th>
<th>SBS-non-Vasc</th>
</tr>
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<tbody>
<tr>
<td>PS volume reduction (%)</td>
<td>0.05 mg/kg/day</td>
<td>0.05 mg/kg/day</td>
<td>0.05 mg/kg/day</td>
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Tegledutide (TEG), an expanding CD38 inhibitor, has, in Human PAR, play an important role in neuronal activation and may be relevant in IBS research.
patients who underwent small bowel or multivisceral transplants at Chelsea and Westminster Hospital, UK. There were 54 patients, from January 2006 to April 2015. Patients with survival less than 6 months post-transplant (n = 9) and with incomplete data (n = 1) were excluded. This resulted in 44 eligible patients whose weights, BMI and grip strengths (in non-dominant hand) were analysed. Grip strengths were performed by one of two dedicated dietitians.

Result: Patient characteristics: Transplants included 12 isolated small bowel (SBT), 5 liver and small bowel (LSBT), 12 modified multivisceral (small bowel, stomach, pancreas, liver-MVT) and 22 multivisceral (small bowel, stomach, pancreas, liver-MVT). 7 patients were re-transplanted. Recently, donor colon has been included in the graft to help with fluid balance. Mean age at transplant was 43.9 years. Patients were followed up for a median of 30 months, to April 2016 or death (n = 11). Primary outcomes: Out of the 30 long-term survivors, 73.3% (22) of them are maintained on oral diet alone at the end of follow up. The other 5 patients require ONS, 2 require IV fluids and 1 patient continues on PN. Most patients (95.5%; 21/22) who achieved nutritional autonomy were previously dependent on nutritional support (2 ONS; 1 EN; 18 PN). 1 patient was a donor-recipient mismatch, who was listed super-urgently. Of the patients who died, 3 out of 14 were requiring PN. The mean BMI pre-transplant was 21.7 (SD = 3.5). Post-operatively, the majority of patients (86.7%) lost weight (mean 14.3%; range 1–30%) with their nadir weight occurring at a mean of 10.7 months. 11 lost ≥20% of their pre-transplant weight. However more than half (26/44) of the patients weights improved over time. Compared to the time of assessment, their BMI improved by 0.6 kg/m² (SD = 4.3) in the mean (median = 11 months) and increased further by 1.4 kg/m² (SD = 4.3) at the end of the follow up. The most recent mean BMI in 30 survivors were 23.3 kg/m² (SD = 5.2). Further analysis revealed 20 patients have healthy weight (BMI 18.5–25), 4 underweight (BMI < 18.5), 3 overweight (BMI > 25) and 3 obese (BMI > 30). Short bowel syndrome (SBS) patient had a serum creatinine of 2.2 mg/dL at 2 years post-transplant. PN was given for a median of 22 days (range 2-241) and 39.5 days (range 11–262) of EN. At the end of the follow up, those who have nutritional autonomy required a considerably shorter duration of nutritional support post-transplant compared to those who are nutrition dependent (mean of 65.3 vs 120 days). This suggests that the duration on nutritional support post-transplant may predict nutritional autonomy. Of the patients who have colon (graft or continuity), 64% have nutritional autonomy. However those without functioning colon are less likely to (47.4%) (P = 0.36). Handgrip strength was measured in 31 patients pre and post-transplant. At median of 9 months (range from 2-32), there was a slight reduction by 6% of expected value which correlates with their weight loss. 18 patients had further handgrip strength test and they improved with a mean of 7% at last follow up (median 16 months).

Conclusion: The majority of patients achieved nutritional autonomy post-transplant and a colon-containing graft may be beneficial. It is common for patients to lose a moderate amount of weight, up to 30% post-operatively. Therefore timely referral is crucial to allow optimisation of perioperative nutritional status. Disclosure of Interest: All authors have declared no conflicts of interest.

Table Continued

<table>
<thead>
<tr>
<th>SBS- Vasc</th>
<th>SBS- Vasc</th>
<th>SBS- non-Vasc</th>
<th>SBS- non-Vasc</th>
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<tbody>
<tr>
<td><strong>Female</strong></td>
<td>9 (53)</td>
<td>6 (40)</td>
<td>15 (58)</td>
</tr>
<tr>
<td><strong>Body weight, kg</strong></td>
<td>66.6 (12.9)</td>
<td>63.9 (11.2)</td>
<td>58.5 (11.5)</td>
</tr>
<tr>
<td><strong>BMI, kg/m²</strong></td>
<td>23.3 (3.4)</td>
<td>22.6 (3.4)</td>
<td>21.5 (2.8)</td>
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</table>

### SBS history

- **Vascular catastrophe categories**
  - Intestinal ischaemia: 4
  - Mesenteric thrombi or emboli: 13
  - **Unknown vascular cause**: 0

- **Nonvascular causes of SBS-IF, n**
  - Crohn’s disease: 10
  - Injury: 4
  - Volvulus: 6
  - Cancer: 2

- **Other**: 6

- **Colon-in-continuity, n (%)**: 13/76 (76) 12/80 (80) 10/38 (26) 13/48 (29)

- **Stoma presence, n (%)**: 2/12 (16) 4/27 (15) 15/58 (26) 17/63 (27)

- **Jejunostomy**: 1/50 (2) 2/50 (4) 4/26 (15) 9/53 (17)

- **Ileostomy**: 0/1 (0) 1/25 (4) 9/60 (15) 5/29 (17)

- **Colonostomy**: 0/1 (0) 1/25 (4) 1/7 (14) 1/10 (10)

- **Other**: 1/50 (2) 0/7 (0) 0/1 (0)


- **PS duration at baseline, y**: 4.0 (2.9) 7.0 (5.7) 8.7 (7.6)* 9.5 (6.7)*

- **PS days per week at baseline**: 5.4 (1.8) 5.6 (1.6) 6.3 (1.2) 5.6 (1.8)

Data are expressed as mean (SD) unless otherwise noted.

BMI = body mass index; PBO = placebo; PS = parenteral support; SBS-IF = intestinal resection and failure associated with short bowel syndrome; TED = fedglutide.

**SBS- Vasc n = 16 PBO; Nonvascular, n = 24 PBO, n = 24 TED**

Disclosure of Interest: P. B. Jeppesen: Has received grant/research support and served as a consultant, advisory board member, and study investigator for NPS Pharmaceuticals, Inc.

U. Pape: Has received grant/research support and served as an advisory board member or speaker’s bureau for NPS Pharmaceuticals, Inc., Shire plc, and Fresenius Kabi GmbH; served as a study investigator for NPS Pharmaceuticals, Inc.

K. Iyer: Has received grant/research support and served as an advisory board member and consultant for NPS Pharmaceuticals, Inc. and Shire plc.

H. Lee: Employee and stockholder of Shire plc.

C. Olivier: Employee and stockholder of Shire plc.

The clinical trial was funded by NPS Pharmaceuticals, Inc., Bedminster, NJ. NPS Pharmaceuticals, Inc., is a wholly owned indirect subsidiary of Shire plc. This analysis research was funded by Shire plc.

### OP266 SUBANALYSIS OF TEDUGLUTIDE EFFICACY AND SAFETY DATA FROM PATIENTS WITH CROHN’S DISEASE AND ULCERATIVE COLITIS IN THE STEPS STUDY

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Introduction: Inflammatory bowel disease (IBD; Crohn’s disease (CD) and ulcerative colitis (UC)) is a major underlying condition for massive intestinal resection leading to intestinal failure associated with short bowel syndrome (SBS-IF).

Aims & Methods: This post hoc subgroup analysis compared response to teduglutide (TED) in patients with SBS-IF due to IBD (SBS-IF) vs those with noninflammatory causes of SBS-IF (SBS-non-IBD). STEPS (NCT00798967, EudraCT2008-006193-15) was a 24-week, phase III, placebo-controlled study of 0.05 mg/kg/day TED in patients with SBS-IF. Patients with CD were in a clinical remission for ≥12 weeks at baseline. Response was ≥2% reduction from baseline in weekly parenteral support (PS) volume at Week 20 that was maintained at Week 24. Descriptive summary statistics are presented with 95% confidence intervals (CIs); this post hoc analysis was not powered for statistical significance.

Result: The Table details patient characteristics (SBS-IF, n = 19; SBS-non-IBD, n = 67). Patients with SBS-IF had lower colon-in-continuity, higher stool frequency, and higher baseline PS volume than those with SBS-non-IBD. After 24 weeks, 73% (95% CI, 39%–94%) of patients with SBS-IF and 59% (95% CI, 41%–76%) with SBS-non-IBD were responders to TED. In the patients, mean PS volume was reduced by 45% (95% CI, 31%–59%) in patients with SBS-IF and 29% (95% CI, 22%–35%) in those with SBS-non-IBD. Two of 9 (22%) patients with SBS-IBD and 6/30 (20%) patients with SBS-non-IBD achieved a PS reduction of ≥2 days per week. Overall safety profile was similar in both groups (SBS-IF, n = 19; SBS-non-IBD, n = 66). Among patients receiving treatment-emergent adverse events (TEAEs) were reported by 100% of patients with SBS-IBD and 77% of those with SBS-non-IBD. Serious adverse events among those receiving TED occurred in 27% of patients with SBS-IBD and 39% of those with SBS-non-IBD. No TEAEs of CD were reported in either
subgroup. No patients with SBS–IBD and 1/47 (2%) with SBS–non-IBD with a colon experience 1 TcEa (TED) of colitis. **Conclusion:** In this analysis, the subgroup of patients with inflammatory bowel disease (SBS–IBD) had evidence of more severe disease based on a higher frequency of stoma presence, higher PS requirements, and lower colon-in-continuity. Despite this, clinical responses to TED were equally strong.

<table>
<thead>
<tr>
<th>Table: Demographic and Disease History Data</th>
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<tr>
<td>Age, mean (SD), y</td>
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<tr>
<td>Women, n (%)</td>
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<tr>
<td>Body mass index, mean (SD), kg/m²</td>
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<tr>
<td>Stoma present, n (%)</td>
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<tr>
<td>Colon-in-continuity, n (%)</td>
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<tr>
<td>Estimated small bowel L/wk</td>
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<td>Baseline PS, mean (SD), L/wk</td>
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<td>Baseline PS duration, mean (SD), y</td>
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**Disclosure of Interest:** U. Pape: Has received grant/research support and served as an advisory board member or speaker’s bureau for NPS Pharmaceuticals, Inc. and Fresenius Kabi GmbH; served as a study investigator for NPS Pharmaceuticals, Inc. P.B. Jeppesen: Has received grant/research support and served as a consultant, advisory board member, and study investigator for NPS Pharmaceuticals, Inc. A.A. Grimm: Employee of Shire plc. S.J. O’Keefe: Has received research funding support from NPS Pharmaceuticals, Inc. A. J. Butler 2, N. K. Russell 2, S. J. Middleton 1

This clinical trial was funded by NPS Pharmaceuticals, Inc., Bedminster, NJ. NPS Pharmaceuticals, Inc., is a wholly owned indirect subsidiary of Shire plc. This analysis research was funded by Shire plc.

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<tr>
<th>OP267 INDICATIONS AND OUTCOMES OF INTESTINAL AND MULTIVISCERAL TRANSPLANT</th>
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<tbody>
<tr>
<td>1Gastroenterology, Addenbrooke’s Hospital, Cambridge/United Kingdom</td>
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<tr>
<td>2Transplant Surgery, Addenbrooke’s Hospital, Cambridge/United Kingdom</td>
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**Introduction:** Despite a reduction in numbers worldwide, we have seen an increase in adult Intestinal and Multivisceral transplants in the UK in the past 3 years. Some recent transplants have been performed ‘superurgently’ for acute wide-spread splanchnic ischaemia. Longstanding indications include complications of parenteral nutrition in patients with type 3 Intestinal failure (IF-associated liver disease (IFALD), recurrent catheter-related infections and loss of vascular access), cirrhosis with extensive portomesenteric venous thrombosis precluding an isolated liver transplant and the need for extensive evisceration due to benign tumour. Re-transplantation is indicated for loss of previous graft due to rejection, ischaemia or primary non-function.

**Aims & Methods:** We describe here the indications and outcomes for Intestinal and Multivisceral transplant at Addenbrooke’s Hospital, Cambridge, UK Data was collected prospectively on an internal database of all patients transplanted from January 2006 to April 2016. All patients considered for an intestine-containing graft require ratification at a national forum (NASIT). Grafts which include liver or kidney are also discussed at local listing committees. Induction immunosuppression with Campath 6 (Alemtuzumab) and maintenance initially with tacrolimus and steroids. If complications related to tacrolimus occur, patients are switched to ciclosporin or sirolimus. An antimetabolite is added to aid steroid withdrawal post discharge.

**Result:** In the study period, 66 transplants were performed in 61 patients (33 Multivisceral, MVT; 7 Liver/small bowel, LSB; 9 Modified multivisceral, MMV; 17 small bowel, SB). Grafts can also contain colon and pancreas. 26 patients (39%) received a transplant for complications relating to intestinal failure (over IFALD n=11, impending IFALD n=4, recurrent sepsis n=1, loss of vascular access n=10). 14 patients (21%) received a multivisceral graft because an isolated liver transplant was not possible due to extensive portomesenteric venous thrombosis. An increasing indication is that of ‘acute abdominal catastrophe’ – 9 patients were transplanted for this including 5 with widespread splanchnic ischaemia. Less frequent indications included desmoid tumours (h), re-transplant (h), short bowel and renal failure (2). The median length of hospital stay post transplant is 77 days. 7 patients had a proven episode of acute cellular rejection (ACR) within 90 days, 12 patients had an episode between 90 days and 1 year and 7 had ACR after 1 year. The vast majority of episodes were treated with pulsed methylprednisolone (23/26, 88%). Subsequent treatments given were Alemtuzumab (n=9), Infliximab (n=1), second pulse of prednisolone (n=9). 3 grafts required removal due to rejection and all 3 patients have been re-transplanted. Within our cohort, there have been 5 cases of graft versus host disease (GVHD) and 6 cases of post-transplant lymphoproliferative disorder (PTLD). Infections continued to be a problem. We have seen increasing rate of vancomycin resistant enterococcus (VRE) and carbapenem resistant pseudomonas. Cytomegalovirus is the most common viral infection. Overall rates are 37.5% but this increases to 91% when seropositive donor is given to a seronegative recipient. 1 year patient survival for SB recipients is 91%, for MMV is 89% and for MVT/LSB is 69%. 3 year patient survival for SB recipients is 81%, for MMV is 89% and for MVT/LSB is 52%.

**Conclusion:** Transplantation of intestinal-containing grafts is technically challenging and recipients have a higher rate of complications compared to other solid organ transplants. However, with advances in surgical techniques and increasing experience of the management of medical complications, survival is improving. Intestinal or Multivisceral transplant should be considered for certain patients who have suffered an abdominal catastrophe, are unable to have a liver transplant due to extensive portomesenteric thrombosis, or have complications arising from intestinal failure. Timely referral to a transplant centre and careful follow-up is essential to continue improvement in outcomes.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**TUESDAY, OCTOBER 18, 2016 14:00-15:30**

**PROGNOSTIC FACTORS IN LOWER GI CANCER – ROOM LB8**

**OP268 EXPRESSION OF DDR2 CORRELATES WITH HIGH FREQUENCY OF PERITONEAL DISSEMINATION AND POOR PROGNOSIS IN COLORECTAL CANCER**

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**Introduction:** In the previous study, our colleagues identified that discoidin domain receptor 2 (DDR2) is a promising driver gene of peritoneal dissemination in gastric cancer by a comprehensive expression assay. We found DDR2 expression was associated with high frequency of peritoneal dissemination and poor prognosis in gastric cancer, and also revealed that the DDR2 was upregulated by the loss of DNA methylation and that DDR2 knockdown reduced peritoneal dissemination in a xenograft. Furthermore, we found dasatinib, an inhibitor of the DDR2 signaling pathway, suppressed peritoneal dissemination. In colorectal cancer, peritoneal dissemination is second popular site for colorectal cancer metastasis, next to the liver. Its frequency is estimated to be 4–7% of patients with colorectal cancer at primary surgery, and approximately 4–19% of patients during follow-up after curative surgery. Peritoneal dissemination is one of most frequent non-curative clinical factors also in colorectal cancer.

**Aims & Methods:** In this study, we analyzed correlations of DDR2 expression with clinicopathological factors in colorectal cancer, especially peritoneal dissemination. We selected 63 cases with colorectal cancer who had an operation in our hospital between 2009 and 2014. Among them, 13 cases had synchronous or metachronous peritoneal dissemination. We performed immunohistochemical examinations for 63 primary colorectal cancers and 12 peritoneal dissemination lesions in 11 cases with anti-DDR2 antibody. We evaluated histological localization of DDR2 expressions, and compared various clinicopathological factors and overall survival between these two groups.

**Result:** In primary lesions, DDR2 was expressed more preferentially in cancer cells at invasive front of tumors. The group with high DDR2 expression had significantly more proportion of T4, lymph node metastasis, and peritoneal dissemination than the group with low DDR2 expression (p = 0.0025, 0.012, and 0.012, respectively), and the prognosis of the former was significantly poorer than the prognosis of the latter (p = 0.0164). In peritoneal dissemination lesions, 11 out of 12 exhibited intense DDR2 expressions.

**Conclusion:** High DDR2 expression correlates with peritoneal expression and poor prognosis in colorectal cancer as well as in gastric cancer. DDR2 might be one of promising driver genes of peritoneal dissemination universally in gastrointestinal peritoneal dissemination.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

TUMORIGENICITY OF COLORECTAL CANCER THROUGH POLYMORPHISMS IN THE DEVELOPMENT OF COLORECTAL PNEOPLASMS


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Objective: The familial risk of colorectal cancer (CRC) has been established as a relevant factor in the development of CRC. Dysregulated gene expression has been associated with CRC development. The aim of the study was to assess the role of single nucleotide polymorphisms (SNPs) in CRC development.

Aims: To study the risk of colorectal adenomas and colorectal cancer associated with specific SNPs in the development of CRC.

Methods: We performed a genome wide association study in patients with CRC from the population-based CRC registry of the Institute of Cancer Research (Spain). The study sample consisted of 1140 patients with CRC diagnosed in the period 2008-2014. The SNPs were selected based on their functional role and their potential association with CRC risk.

Results: Two SNPs, rs10795668 and rs11255841, were significantly associated with an increased risk of CRC (OR: 2.22, 95% CI: 1.36–3.61 for rs10795668, and OR: 0.35–0.78 for rs11255841), suggesting their possible implication in early stages of CRC development.

Conclusion: Our results suggest that rs10795668 and rs11255841 may be associated with CRC risk and could be potential biomarkers for CRC development.

OP257 PREDICTION OF COMPLETE RESECTIONS AFTER CYTODUCTIVE SURGERY BASED ON THE EXTENT OF COLORECTAL PERITONEAL CARCINOMATOSIS


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Introduction: The extent of colorectal peritoneal carcinomatosis (CDC) is a key determinant of the outcome of cytoreductive surgery (CRS). The aim of this study was to develop a prediction model for complete resection of peritoneal metastases after CRS.

Methods: Patients with peritoneal carcinomatosis from colorectal cancer were included. The extent of CDC was classified as CDC0, CDC1, CDC2, CDC3, and CDC4 based on the number of peritoneal regions involved. The primary endpoint was complete resection of peritoneal metastases after CRS. The secondary endpoints were time to recurrence, overall survival, and progression-free survival.

Results: A prediction model for complete resection of peritoneal metastases after CRS was developed. The model included the following variables: number of peritoneal regions involved, number of lymph nodes, number of liver metastases, number of bone metastases, and number of lung metastases. The model had a good discriminative power with an area under the receiver operating characteristic curve of 0.80. The model was validated in an independent cohort of patients.

Conclusion: A prediction model for complete resections after CRS is developed. The model can be used to predict the likelihood of complete resection and guide patient management.

OP259 GENETIC SUSCEPTIBILITY AND FAMILY HISTORY OF COLORECTAL CANCER RELATIONSHIP WITH SPECIFIC SNPS IN ADENOMAS FROM COLORECTAL CANCER PATIENTS FROM HONG KONG

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Objective: The familial risk of colorectal cancer (CRC) has been established as a relevant factor in the development of CRC. Dysregulated gene expression has been associated with CRC development. The aim of the study was to assess the role of single nucleotide polymorphisms (SNPs) in CRC development.

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Conclusion: Our results suggest that rs10795668 and rs11255841 may be associated with CRC risk and could be potential biomarkers for CRC development.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP260 A NOVEL AMPLIFICATION GENE, PCID2 PROMOTES TUMORIGENICITY OF COLORECTAL CANCER THROUGH DIRECTLY INCREASING A TUMOR SIZE IN PATIENTS WITH CRC


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Methods: Patients with peritoneal carcinomatosis from colorectal cancer were included. The extent of CDC was classified as CDC0, CDC1, CDC2, CDC3, and CDC4 based on the number of peritoneal regions involved. The primary endpoint was complete resection of peritoneal metastases after CRS. The secondary endpoints were time to recurrence, overall survival, and progression-free survival.

Results: A prediction model for complete resections after CRS is developed. The model can be used to predict the likelihood of complete resection and guide patient management.

Conclusion: A prediction model for complete resections after CRS is developed. The model can be used to predict the likelihood of complete resection and guide patient management.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP261 ANALYSIS OF SURVEILLANCE, EPIDEMIOLOGY, AND END-TERM SURVIVAL OF T1 RECTAL CARCINOID TUMORS: AN ANALYSIS OF SURVEILLANCE, EPIDEMIOLOGY, AND END-TERM SURVIVAL OF T1 RECTAL CARCINOID TUMORS

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5United European Gastroenterology Journal 4(5S)

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Introduction: The impact of treatment on survival in rectal carcinoid tumors (RCT) is unknown. The aim of this study was to analyze the survival of patients with T1 RCTs.

Methods: The study included patients with T1 RCTs who were treated at a single institution between 1990 and 2017. The primary endpoint was overall survival (OS). The secondary endpoints were disease-free survival (DFS) and recurrence-free survival (RFS).

Results: A total of 100 patients with T1 RCTs were included. The median follow-up time was 10 years. The 5-year OS, DFS, and RFS rates were 95%, 90%, and 85%, respectively. Multivariate analysis revealed that patients with adjuvant therapy had better survival compared with those who did not receive therapy.

Conclusion: T1 RCTs are associated with excellent survival outcomes. Adjuvant therapy improves survival in patients with T1 RCTs.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP262 PREVALENCE OF LYMPH NODE METASTASIS AND LONG-TERM SURVIVAL OF TI RECTAL CARCINOID TUMORS: AN ANALYSIS OF SURVEILLANCE, EPIDEMIOLOGY, AND END-TERM RESULTS (SEER) DATABASE


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Introduction: Rectal carcinoids are the most common neuroendocrine tumors of the gastrointestinal tract and their incidence is increasing due to colorectal cancer screening. Several previous studies have suggested that local excision (endoscopic submucosal dissection) is effective for ≤10 mm lesions but data on long-term
study described various patterns of a complete response during watch-and-wait ‘watch-and-wait’ approach, limited data exists yet on what we can expect to imaging – mainly MRI – plays an important role. Given the novelty of the once surgery is omitted. In addition to clinical examination and endoscopy, who show a clinical complete response after chemoradiotherapy. An important evidence of recurrence).

Introduction:

Aims & Methods:

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


TUESDAY, OCTOBER 18, 2016
14:00-15:30
GENERAL HEPATOLOGY – ROOM 1.08

OP274 ACCURACY OF A POINT SHEAR WAVE ELASTOGRAPHY TECHNIQUE (ELASTIPQ) IN THE NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS IN A LARGE COHORT OF LIVER PATIENTS


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Introduction: ElastIPQ is a novel point shear wave elastography (PSWE) technique that assesses liver stiffness by measuring liver stiffness (kPa) with few studies published so far. The aim of this study was to determine the accuracy and feasibility of the assessment of liver stiffness in a large cohort of patients undergoing liver biopsy (LB) for various etiologies.

Aims & Methods: Consecutive patients scheduled for LB were studied by using the iU22 Philips ultrasound system with ElastIPQ technique. The correlations between laboratory findings, liver stiffness and the Metavir score were analyzed using Spearman correlation and ROC curve analyses were performed to calculate AUC for F ≥ 2, F ≥ 3 and F = 4.

Results: We enrolled 289 patients (176/113 males/females) who underwent LB for viral chronic (HCV 49%; HBV 27%; HCV+HBV 18%); non-viral chronic liver disease (alcoholic 18%, other 13%). Liver stiffness measurements performed on the right lobe were reliable in all cases but eight patients (due to morbid obesity and narrow intercostal spaces). After univariate and multiple regression analysis PSWE showed a strong correlation with the liver stiffness grade (r ≥ 0.43; p < 0.0001). Moreover, PSWE showed a good correlation with liver stiffness measurements on liver biopsy (r = 0.69; p < 0.0001).

Disclosure of Interest: All authors have declared no conflicts of interest.

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OP275 COMPARATIVE STUDY BETWEEN TWO 2D-SHEAR WAVES ELASTOGRAPHY TECHNIQUES FOR THE ASSESSMENT OF LIVER STIFFNESS IN 2D-SSW VS. 2D-SWE:


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Introduction: Chronic liver diseases are quite frequent encountered in daily practice and several techniques (B or C US, vibration and other conditions) such as chronic alcohol abuse (ASH) and NAFLD. In this conditions, the evaluation of chronic liver disease’s severity is mandatory, for prognosis, for management and for decision regarding therapy.

Aims & Methods: The aim of this study was to compare the feasibility of two 2D-Shear Waves Elastography (2D-SWE) methods for the assessment of Liver Stiffness (LS) and also to compare the methods with a validated one-Transient Elastography(TE). Our study included 130 consecutive patients with chronic hepatopathies (HCV-90%, HBV-6%, other-4%), in which Liver Stiffness (LS) was evaluated in the same session by means of two 2D-SWE techniques: 2D-SWE.GE (LOGIQ E9, GE Healthcare) and 2D-SWE.SSI (Aixplorer, SuperSonic Imagine) and also by an
elastographic reference method: Transient Elastography (TE)- FibroScan, Echosense). Reliable LS measurements were defined as follows: for 2D-SWE: the median value of 10 measurements acquired in a homogeneous area and an interquartile range (IQR) <30% (1), for 2D-SWE: the median value of 3 measurements acquired in an homogeneous area and an interquartile range of <40% (2). Spearman’s rank correlation coefficient (r) was used to assess the correlation of LS measurements by means of 2D-SWE, 2D-SWE.SSI and TE. Result: Valid measurements were obtained in 94.6% (123/130) for 2D-SWE, 90.7% (118/130) for 2D-SWE.SSI, 89.2% (116/130) for TE (p = 0.05). Reliable liver stiffness results were obtained in 107 subjects by means of 2D-SWE.SSI, 2D-SWE.TE and TE. The values ranged from 4.17 to 20.48 kPa for 2D-SWE and 7.83 to 82.4 kPa for 2D-SWE.SSI. The mean LS values by 2D-SWE.SSI were significantly higher than for 2D-SWE: 19.1±12.3 kPa vs. 12.1±3.7 kPa (p <0.0001). There was a significant correlation between 2D-SWE.SSI and 2D-SWE LS values (r = 0.712, p < 0.0001). The correlation between 2D-SWE and TE was r = 0.746, p < 0.0001 and between 2D-SWE.SSI and TE was r = 0.604, p < 0.0001 with no significant differences between them (p = 0.0056). Taking TE as the reference method, both 2D-SWE.SSI and 2D-SWE had a good value to differentiate between stages of liver fibrosis and liver cirrhosis. For 2D-SWE.SSI the best liver stiffness cut-off value to differentiate between liver cirrhosis and other stages of fibosis was >13.7 kPa with 88.37% sensitivity, 75.68% specificity, 87.73% positive predictive value (PPV) and 77.8% negative predictive value (NPV) (AUROC = 0.831, p < 0.0001). For a liver stiffness cut-off value >10.7 kPa, 12.4% of 2D-SWE.SSI had valid measurements for liver stiffness assessment by 2D-Shear Wave Elastography (2D-SWE) and which value should be used: the mean or median?. Med Ultrasound 2013; 15: 268-272. 3. Castil, L., Foucaur, J., Bernard, Ph et al. Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 patients. Hepatology 2010; 51: 828-835. 4. R.L.D. Sirli: Roxana Sirli received speaker fees from Philips for Siemens and received speaker fees from Philips, Siemens and General Electric for invasive liver fibrosis assessment and both have a strong correlation with TE. Both 2D-SWE techniques have a very good feasibility for the non-invasive assessment of liver fibrosis. Conclusion: The AUROC for these measurements with a cut-off value of ≥50% and an interquartile range <30% (3). Pathology, Aomori Prefectural Central Hospital, Aomori/Japan 2. Radiology, Aomori Prefectural Central Hospital, Aomori/Japan 3. Pathology, Aomori Prefectural Central Hospital, Aomori/Japan Contact Email Address: qqqc2@cerley.ocn.ne.jp

OP276

UTILITY OF REAL-TIME SHEAR WAVE ELASTOGRAPHY FOR ASSESSING LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C

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Introduction: A newly developed technique of evaluating liver stiffness, which previously had limited comparability with other non-invasive fibrosis biomarkers. Aims & Methods: This study aimed to compare the utility of SWE, magnetic resonance elastography (MRE), M2BPGi, Fib-4 and platelet count (PLT) for diagnosing liver fibrosis. One hundred thirty-seven patients with biopsy-proven chronic hepatitis C (73 men and 64 women; mean age, 64.6 ± 10.6 years; mean body mass index, 23.6 ± 5.08 kg/m²) were enrolled. Fibrosis was staged according to the median value of the PLT and the diagnostic performances of SWE (GE Healthcare, USA), MRE (GE Healthcare, USA), M2BPGi, Fib-4 and PLT. MRE, M2BPGi, Fib-4, MRE and liver biopsy were performed on the same day, when we also collected blood samples for 2D-SWE.GE and TE. The values ranged from 7.83 to 82.4 kPa for 2D-SWE.SSI. The mean LS values by 2D-SWE.SSI were significantly higher than for 2D-SWE: 19.1±12.3 kPa vs. 12.1±3.7 kPa (p <0.0001). There was a significant correlation between 2D-SWE.SSI and 2D-SWE LS values (r = 0.712, p < 0.0001). The correlation between 2D-SWE and TE was r = 0.746, p < 0.0001 and between 2D-SWE.SSI and TE was r = 0.604, p < 0.0001 with no significant differences between them (p = 0.0056). Taking TE as the reference method, both 2D-SWE.SSI and 2D-SWE had a good value to differentiate between stages of liver fibrosis and liver cirrhosis. For 2D-SWE.SSI the best liver stiffness cut-off value to differentiate between liver cirrhosis and other stages of fibosis was >13.7 kPa with 88.37% sensitivity, 75.68% specificity, 87.73% positive predictive value (PPV) and 77.8% negative predictive value (NPV) (AUROC = 0.831, p < 0.0001). For a liver stiffness cut-off value >10.7 kPa, 12.4% of 2D-SWE.SSI had valid measurements for liver stiffness assessment by 2D-Shear Wave Elastography (2D-SWE) and which value should be used: the mean or median?. Med Ultrasound 2013; 15: 268-272. 3. Castil, L., Foucaur, J., Bernard, Ph et al. Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 patients. Hepatology 2010; 51: 828-835.

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Introduction: The human Toll like receptors (TLRs) family consists of ten receptors and is involved in recognition and response to diverse microbial molecules and enable the innate immune system to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation in various cellular compartments and in this way is able to both stimulate proinflammatorycytokine production leading to liver damage and evade immune responses to establish viral persistence. Aims & Methods: The aim of this work is to investigate the association of TLR SNPs with the outcome of HCV infection. Four SNPs of TLR3 and TLR4 were genotyped by real time PCR using TaqMan® allelic discrimination kit (Applied Biosystem) according to the manufacturer’s protocol. A total 392 families (1176 individuals) were recruited in this study from upper & lower Egypt (east & west delta), we compared the risk of allele carriage of selected markers in different chronic HCV patients. The rs3747308 (C/T) were genotyped by pyrosequencing for TLR3 while rs4967891 (C/T) and rs62522600 (G/A) were genotyped for TLR4. Result: As regard TLR2, The allele of rs12191786 (C/T) is significantly higher in HCV group compared to that control group and spontaneous (spontaneous group) (OR = 2.0571 (95% CI 1.95 to 3.45 P = 0.0001) and 2.635 (95% CI 2.14 to 4.11 P = 0.0001)) respectively. While A allele of rs3747308 (G/A) is highly significant associated with HCV group compared to that control group and spontaneous group (spontaneous group) (OR = 2.2701 (95% CI 1.2056 to 4.004 P = 0.007) and 2.1321 (95% CI 1.5258 to 2.9274 P = 0.0001)) respectively. On the other hand the TLR4 genotyping revealed that the carriers of C allele of rs4967891 was significantly higher in negative and spontaneous (spontaneous group) C group (OR = 0.4834 95% CI 0.3886-0.646 and 0.4449 and 95% CI: 0.2917-0.6787 (p =0.007) simultaneously indicating that the C allele act as protective allele against HCV infection and development of chronic HCV. Linkage Disequilibrium of rs4967891 and rs62522600 SNPs indicating that the carriage of TA haplotype was significantly higher in chronic HCV compared to that chronic group (OR = 2.0571 (95% CI 1.95 to 3.45 P = 0.0001) and 2.635 (95% CI 2.14 to 4.11 P = 0.0001)) respectively. No one of spontaneous group was carriage for TA haplotype, this revealing the role of TA haplotype as a risk indicator for HCV infection. Conclusion: Current study demonstrated that spontaneous clearance of HCV was associated with The allele C of rs4967891 of TLR4 and chronicity of HCV infection is associated with the risk haplotype (TA) of TLR4 & T allele of rs12191786 & A allele of rs5743708 of TLR2. This Research Was Funded By Science, Technology Development Foundation (Sdf), Project No.1784 (Tc-2/health/2009/hep-1.3). All authors have declared no conflicts of interest.
References

OP278 USEFULNESS OF MULTIPOLAR BIPOLAR RADIOFREQUENCY SYSTEM AND VALUE OF 3D SIM-NAVIGATOR
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Introduction: Fusion imaging technology is reportedly useful for radiofrequency ablation (RFA), and various types of ultrasound equipment with integral fusion imaging technology have been developed. Several RFA devices have also become available in Japan. CelonPOWER (Olympus Surgical Technology), a multipolar and bipolar RFA device, was approved for use in Japan in 2012. A single procedure using several applicators simultaneously can ablate an extensive area and reduce the risk of local recurrence sufficiently wide that ablation requires the optimal placement of multiple applicators. The accurate positioning of two applicators can be quite easily visualized by ultrasonography, whereas precise three-dimensional (3D) positioning of three applicators cannot. The 3D Sim-Navigator (HITACHI) is a new navigation system that can be used during real-time virtual 3D Sim-Navigator.

Results: The incidence rate of NODAT within 6 months post liver transplantation was 29% (75/181). There were 214 men and 42 women in the study and the average age was 48.0 ± 9.9 years. Age (54.0 ± 4.1 vs 45.4 ± 6.9, P < 0.001), BMI (23.1 ± 3.0 vs 22.3 ± 3.8, P < 0.014), blood tacrolimus level at 1 month post liver transplantation (10.25 ± 3.30 vs 8.76 ± 1.74, P < 0.001), ADIPOQ rs1501299 (P < 0.007) and rs822396 (P = 0.013) were significantly correlated with NODAT with univariate analyses. Dominant model and recessive model confirmed these risk factors further. Three NODAT prediction models were built containing these risk factors, that we finally found the optimized model (AUROC = 0.743). Metabolic syndrome was also associated with NODAT (21% vs 8%, P = 0.003). The overall survival rate (P < 0.015) and graft survival rate (P < 0.01) for the NODAT patients were lower than those for non-NODAT patients at 5 years. There were no significant differences in the cumulative annual local recurrence rates between NODAT and non-NODAT. The study included 256 patients who underwent liver transplantation on large samples. Our findings demonstrate that recipient rs1501299 genotype polymorphism is associated with NODAT realizing the potential predictive ability of NODAT. The NODAT patients were observed to have a higher BMI, blood tacrolimus level at 1 month after LT are independent risk factors of NODAT. These findings may be beneficial in helping to estimate the risk of NODAT development in liver transplantation and thereby in controlling modifiable risk factors.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

TUESDAY, OCTOBER 18, 2016 15:45–17:15
MANAGEMENT OF REFRACTORY CROHNI’S DISEASE – ROOM A

OP279 ASSOCIATION BETWEEN ADIPOQ GENE POLYMORPHISMS AND THE RISK OF NEW-ONSET DIABETES MELLITUS AFTER LIVER TRANSPLANTATION
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Introduction: New-onset diabetes mellitus (NODAT) is a common metabolic complication after liver transplantation (LT). The prevalence of NODAT stays high and has been reported as 17–36%.1 NODAT contributes to an increased risk of infections, cardiovascular disease, chronic rejection and renal failure, which subsequently lead to a reduced life quality and high mortality.2–3 Recent findings suggest a tight link between ADIPOQ gene polymorphism and glucose metabolism and diabetes mellitus. Several studies have found that serum adiponectin levels are lower in diabetic patients than healthy people.4 In addition, reduced pretransplantation serum adiponectin concentrations could predict the development of NODAT. However, there have been no report to describe the association between ADIPOQ gene polymorphism and new-onset diabetes mellitus after liver transplantation.

Methods: In the current study, we aim to investigate whether single nucleotide polymorphisms of ADIPOQ were correlated with the NODAT and also to compare the overall survival and graft survival between NODAT group and non-NODAT. The study included 256 patients who underwent liver transplants at our center from January 2009 to December 2011. They were divided into two groups: NODAT group and non-NODAT group. We screened independence risk factors of NODAT with univariate and multivariate analyses. We further built three NODAT prediction models containing the risk factors and got optimized model with AUROC curve method. In addition, the association between metabolic syndrome and NODAT was also examined. Overall survival and graft survival were determined by the Kaplan-Meier method and tested by the log-rank statistics.

Results: The incidence of NODAT within 6 months post liver transplantation was 29% (75/181). There were 214 men and 42 women in the study and the average age was 48.0 ± 9.9 years. Age (54.0 ± 4.1 vs 45.4 ± 6.9, P < 0.001), BMI (23.1 ± 3.0 vs 22.3 ± 3.8, P < 0.014), blood tacrolimus level at 1 month post liver transplantation (10.25 ± 3.30 vs 8.76 ± 1.74, P < 0.001), ADIPOQ rs1501299 (P < 0.007) and rs822396 (P = 0.013) were significantly correlated with NODAT with univariate analyses. Dominant model and recessive model confirmed these risk factors further. Three NODAT prediction models were built containing these risk factors, that we finally found the optimized model (AUROC = 0.743). Metabolic syndrome was also associated with NODAT (21% vs 8%, P = 0.003). The overall survival rate (P < 0.015) and graft survival rate (P < 0.01) for the NODAT patients were lower than those for non-NODAT patients at 5 years. There were no significant differences in the cumulative annual local recurrence rates between NODAT and non-NODAT. The study included 256 patients who underwent liver transplantation on large samples. Our findings demonstrate that recipient rs1501299 genotype polymorphism is associated with NODAT realizing the potential predictive ability of NODAT. The NODAT patients were observed to have a higher BMI, blood tacrolimus level at 1 month after LT are independent risk factors of NODAT. These findings may be beneficial in helping to estimate the risk of NODAT development in liver transplantation and thereby in controlling modifiable risk factors.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
regain clinical response. Detailed documentation of disease activity was retrieved.

**Result:** In 98/376 patients ADA directed against IFX and in 61,226 patients ADA against ADL were detectable. From all 159 ADA positive patients, 17 patients had received an IM, either a thiopurine or MTX, because of secondary loss of response. Seven patients received MTX, ten a thiopurine (4 azathioprine, 4 mercaptopurine and 2 6-TG). In 7 out of 8 patients treated with IFX, addition of an IM resulted in an increase of serum drug levels accompanied with a decrease of ADA till they were undetectable. The median time for ADA to IFX to become undetectable was 11 months (IQR 6–28). For patients treated with ADL, an increase of the serum drug concentrations, together with a decrease of ADA levels, was reached in 6 out of 7 patients after addition of an IM. The median time for the ADA levels to be undetectable was also 11 months (IQR 2–37). All patients receiving MTX responded clinically which resulted in continuation of the ongoing anti-TNF treatment.

**Conclusion:** Addition of an IM to IFX or ADL monotherapy in IBD patients with secondary loss of response due to ADA formation, led to a decrease of ADA levels and an increase in serum drug concentrations in the majority of the patients. Patients who regained response due to this strategy could continue the current anti-TNF treatment and switching to another agent was not necessary.

**Disclosure of Interest:** G.R. van den Brink: G. van den Brink has received consulting and lecture fees from AbbVie, Coviden, Dr. Falk, Ferring Pharmaceuticals, Merck Sharp & Dohme and Ferring Pharmaceuticals. He has received research grants from AbbVie laboratories, Merck Sharp & Dohme and Ferring Pharmaceuticals. M. Lowenberg: M. Löwenberg has served as speaker for AbbVie, Coviden, Dr. Falk, Ferring Pharmaceuticals, Merck Sharp & Dohme, Receptos, Takeda, Tillots and Tramedico. He has received research grants from AbbVie, Merck Sharp & Dohme, CMS, healthcare and Ferring. G. D’Haens: G. D’Haens reports having received consulting fees from AbbVie, Boehringer, Ferring, Jansen Biologics, Merck Sharp & Dohme, Takeda, Pfizer, Tillots Pharma and reports receiving research grants from AbbVie Laboratories, Jansen Biologics, MSD, Dr. Falk Pharma, and Ferring. All other authors have declared no conflicts of interest.

**OP281 POST-OPERATIVE COMPLICATIONS IN ELDERLY-ONSET INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY**

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**Introduction:** Inflammatory Bowel Diseases (IBD) diagnosed after the age of 60 are increasing and seems to have a milder course compared to younger patients. However, the intestinal surgery rates are similar to those in the young adult population. Data on post-operative complications (POC) in elderly-onset IBD are scarce. We reported the incidence and factors associated with POC in general population.

**Aims & Methods:** Among 841 elderly-onset population-based EPIMAD Cohort (1), 139 patients underwent surgery. Among those, 100 had Crohn’s Diseases (CD) and 39 Ulcerative Colitis (UC). Medical charts for early (within 30 days of surgery) and late (>30 days of surgery) POC (POC) have been reviewed according to Dindo’s classification (2). Associated factors have been tested by Cox regression models.

**Result:** After a median follow-up of 7.3 years [Q1 = 3–Q3 = 12], 50 patients (36%) had at least one POC. No significant difference was observed for POC frequency of UC and CD. Thirty-two early POC were found in 23 patients (16.5%); 52% were severe (defined by a Dindo’s grade >2) and 47% infected. Among the 37 late complications observed in 33 patients (23.7%), 42 were severe (grade >2) and 56% were mechanical (bile, evisceration, anastomotic stricture). The cumulative probability of POC was 7.4% at 6 months (95% CI: 3.9–11.9) and 10.9% at 1 year (6.5–18.1). 22.8% at 5 years (16.0–32.0) and 30.5% at 10 years (21.8–41.4). In multivariate analysis, emergency surgery (HR = 4.46 [1.75–11.36]) and acute severe ulcerative colitis (HR = 7.84 [2.15 – 28.52]) were significantly associated with POC. Recent PO, recent PO intake and co morbidities (Charison’s index) were not independently associated with an increased risk. Female gender (HR = 2.10 [1.01 – 4.37]) and time between diagnosis and surgery >3 months (HR = 2.09 [1.01 – 4.31]) were significantly associated with late POC.

**Conclusion:** In elderly onset IBD patient who underwent surgery, POC were frequent. The early POC were more severe than the late POC. Emergency surgery and acute severe ulcerative colitis were significantly associated with early complications when female gender and delay between diagnosis and surgery was associated with late POC. These results reinforce the need for specialized and dedicated management of these at-risk elderly patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**TUESDAY, OCTOBER 18, 2016 15:45-17:15 FROM GUIDELINES TO CLINICAL PRACTICE: H. PYLORI – ROOM D**

**OP282 PAN-EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT AH-EUREG: INTERIM ANALYSIS OF THE SINGLE-CAPSULE BISMUTH QUADRUPLE TREATMENT (PYLERA®)**


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**Introduction:** The most novel treatment used in H. pylori management in Europe is the single-capsule bismuth quadruple treatment (Pylera®), but there is still very little evidence of its efficacy and efficacy on routine clinical practice. Pylera® is still not nationally/commercially available in most countries in Europe and, in most of those available, it has just recently reached pharmacies.

**Aims & Methods:** We aimed to evaluate the use and outcomes of Pylera® in the European Registry on H. pylori Management (Hp-Eureg). Methods: A systematic prospective registry of the clinical practice of European gastroenterologists regarding H. pylori infection and treatment (31 countries and 280 recruiting investigators). A local coordinator was selected from each country. Each coordinator selected a representative group of recruiting investigators from its country. An electronic clinical research file (e-CRF) was created on AEG-REDCap to systematically register all adult patients infected with H. pylori. Variables included: Patient’s demographics, previous eradication attempts, prescribed eradication treatments, adverse events, and outcomes (cure rates, compliance, follow up, etc.). Patients with both eradication definitive test and with less than one year follow-up have been considered ongoing and were excluded from the analysis.

**Results:** Up to now, 15,660 patients have been included, and 12,921 have finished follow up (59% females, 88% Caucasian). Mean age was 55 years. Pylera® was used in 175 patients (1.2% of all treatments registered: 44% in first-line, 27% in second, 22% in third, and 8% in following rescues). Omeprazole was used in 69% of cases and esomeprazole in 24%. Overall efficacy was 76% (95%CI = 66–86%) by ITT and 78% (69–87%) by PP. In first line, efficacy was 93% (84–100%) both by ITT and PP. Second line efficacy was 68% (51– 85%) by ITT and 74% (58–90%) by PP. Compliance with treatment was 98%. Adverse events were reported in 14% of cases and did not cause treatment discontinuation in any patient.

**Conclusion:** Experience with single-capsule bismuth quadruple therapy (Pylera®) is still limited. Wide confidence intervals do not allow drawing conclusions for rescue regimens; however, our preliminary data suggests that given its safety profile, compliance rates and efficacy, it may be an acceptable option as first-line treatment in Europe.

**Disclosure of Interest:** A.G. McNicholl: Speaker for Allergan

A. Perez Aisa: Speaker for Allergan


All other authors have declared no conflicts of interest.
small bowel diseases. Secondary objectives: procedural success, - time of main intervention, therapeutic efficacy and adverse events. Patients with occult gastro-intestinal bleeding (OGB) or indeterminate iron-deficiency anemia (IDA) or positive findings of small bowel imaging examinations were included in a two-center prospective clinical trial. In total 132 cases were enrolled to determine the overall efficacy. A rate of 0.1% would be considered as clinically efficacious under consideration of a two sided non-inferiority margin of 20% in comparison to conventional enteroscopy. A novel reusable endoscope (Olympus Corp.) with an integral motor was used for rotating a disposable short spiral overtube mounted on the insertion of the small bowel capsule to “peel” or “unpeel” the tube either on or off the insertion tube as the spiral rotates in a clockwise or counter-clockwise direction. All procedures were performed under general anesthesia.

Result: Thirty patients (12 f 18 m; mean age [range]: 62 [20-92] years with positive findings of video capsule endoscopy or other small bowel imaging modality (angiectasia n = 18, jejunal/ileal polyps n = 3, thickening of wall/stricture n = 3, other n = 1) have so far been included in the trial. 27 of 30 patients had IDA. NMSE could be performed in 29 of the 30 patients with advancement of the endoscope beyond the ligament of Treitz. In one case further insertion was not be performed because of a bradycardia which caused discontinuation of the procedure. Mean insertion time to the jejunum was 6.4 [2-19] min. and to the deepest point of insertion distal from ligament of Treitz 22.6 [7-52] min. The mean insertion depth from ligament of Treitz was 393 [0–600] cm. Panenteroscopy to secum could be achieved in one patient from the oral route. The diagnostic yield of NMSE was 83.4% corresponding to no findings in 5 cases, at least one angiectasia in 18 cases, one or more benign polyps in 6 and no other findings in 12 patients. Thirty-two interventions were performed in 22 patients (biopsies n = 8, APC n = 17, tattooing n = 3, clipping n = 3, EMR n = 2). Mean withdrawal time without interventions was 14 [7-55] min. Mild mucosal trauma in the esophagus or duodenum was registered in 6 cases. There were no serious adverse events.

Conclusion: First clinical data of an ongoing large prospective trial demonstrate that NMSE can be effectively and safely performed for diagnostic and therapeutic enteroscopy. The procedure offers advantages over traditional methods in terms of procedural duration and ease of use.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP286 THE ENZYME ACTIVITY OF SMALL INTESTINAL MUCOSA IN ADULT PATIENTS WITH CELIAC DISEASE

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Introduction: Some patients with celiac disease (CD), who have followed gluten-free diet (GFD) and have a normal histological structure of small intestine mucosa, may still have symptoms of bloating, rumbling and diarrhea. These symptoms may be associated with changes of the activity of the small intestine enzymes. Objective: To determine the activity of enzymes (glucoamylase, maltase, sucrase and lactase) in CD patients.

Aims & Methods: Thirty patients with newly diagnosed CD: 9 women and 4 men (mean age 41.96 ± 18.46 years) were observed in the group A and 20 patients with previously diagnosed CD: 22 women and 8 men (mean age 38.68 ± 16.75 years) were included in the group B.

Result: In patients with newly diagnosed CD, the activity of all enzymes was decreased in 92.3% in the group of patients followed GFD - in 36.5% (p < 0.005). It was found that the total atrophy (Marsh IIIc) was associated with a reduced activity of all enzymes in 92.3% in the group of patients followed GFD - in 36.5% (p < 0.005), group B from 260 to 204 (p = 0.002), group B from 263 to 145 (p < 0.0001), p = 0.0247, group B vs. A. In group A 10% reached remission, in group B 25% (p = 0.0408). All subscases independently significantly and only abdimal pathophysiologic abnormality (SF-36 physical health score improved in group B (p = 0.0081), but not in group A. Patients in group B were significantly more satisfied with pain relief (p = 0.0132), but it was also more challenging to follow their diet (p = 0.0008).

Conclusion: Patients with celiac disease and IBS-symptoms showed significant improvement in abdominal symptoms and physical health from a low FODMAP diet for 6 weeks. A gluten-free diet with reduced FODMAP content was more effective than a more strict gluten-free diet, and should be offered to coeliac patients with refractory IBS-symptoms on a gluten-free diet.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
COELIAC DISEASE FOR THE CLINICIAN – ROOM F2

OP287 FODMAP RESTRICTION OF A GLUTEN-FREE DIET IN PATIENTS WITH COELIAC DISEASE: A RANDOMIZED, CONTROLLED CLINICAL STUDY

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Introduction: In 30% of coeliac patients on gluten free diet still have irritable bowel syndrome (IBS) symptoms. A low FODMAP (fermentable oligo-, di-, mono-saccharides and polyols) diet is effective to reduce symptoms in IBS patients.

Aims & Methods: We wanted to investigate the benefit from restricting the FODMAP content of the diet in patients with coeliac disease, who are still symptomatic on a gluten-free diet. 40 patients with coeliac disease and IBS symptoms confirmed by the Rome III-criteria and of at least 8 weeks were randomized to an intervention group and a control group.

Result: The mean total IBS-SSS score was significantly reduced: Group A from 260 to 145 (p = 0.0081), group B from 263 to 145 (p < 0.0001), p = 0.0247, group B vs. A. In group A 10% reached remission, in group B 25% (p = 0.0408). All subscases independently significantly and only abdimal pathophysiologic abnormality (SF-36 physical health score improved in group B (p = 0.0081), but not in group A. Patients in group B were significantly more satisfied with pain relief (p = 0.0132), but it was also more challenging to follow their diet (p = 0.0008).

Conclusion: Patients with celiac disease and IBS-symptoms showed significant improvement in abdominal symptoms and physical health from a low FODMAP diet for 6 weeks. A gluten-free diet with reduced FODMAP content was more effective than a more strict gluten-free diet, and should be offered to coeliac patients with refractory IBS-symptoms on a gluten-free diet.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
PATHOPHYSIOLOGY OF IBS – ROOM N2

OP288 ADDITIVE EFFECT OF PATHOPHYSIOLOGICAL FACTORS ON PATIENT REPORTED OUTCOMES IN IBS

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Introduction: Both central and peripheral pathophysiological factors are thought to contribute to the symptoms of IBS. Psychological symptoms reflect CNS dysfunction, while abnormal GI sensorimotor function reflects mainly peripheral dysfunction; both have been associated with symptoms in IBS. These factors may have additive effects on patient reported outcome (PRO) measures in IBS. Our aim was to study whether these pathophysiological alterations have additive effect on PROs in patients with IBS. To achieve this, we included 407 patients fulfilling the Rome II or Rome III IBS criteria (74% females; mean age 36 ± 12 years). The following pathophysiological factors were measured in all subjects: colonic transit time (radiopaque markers); compliance, allodynia (low pain threshold) and hyperalgesia (increased pain intensity) (rectal barostat); and anxiety and depression (HAD scale). Abnormal findings on the physiology assessments were defined based on the 5th and 95th percentiles in healthy controls, and on the HAD scale by score > 7. The patients also completed questionnaires to assess IBS symptom severity (IBS-SSS or GSRS-IBS), and bowel habit (stool diary). To be included in the analysis, a pathophysiological factor had to be associated with severity of ≥ one IBS-related symptom. As PRO measures we used z-scores of IBS symptom severity (IBS-SSS or GSRS-IBS) total score and somatic symptom severity (SCCL-90 somatization subscale or PHQ-15), and quality of life (IBSQOL).

Result: Allodynia was seen in 40% of patients, hyperalgesia in 17%, accelerated colonic transit in 18%, delayed transit in 7%, anxiety in 52% and depression in 24% - these factors were associated with severity of at least one IBS related symptom. As PRO measures we used z-scores of IBS symptom severity (IBS-SSS or GSRS-IBS) total score and somatic symptom severity (SCCL-90 somatization subscale or PHQ-15), and quality of life (IBSQOL).

Conclusion: At least 3 pathophysiological abnormalities were relevant for symptoms were present in 20% of patients, 2 in 30%, 1 in 31%, and 0 in 30% of patients. The number of pathophysiological abnormalities that were not associated with age (p = 0.15), gender (p = 0.12) or IBS subgroup (p = 0.21). With increasing number of pathophysiological abnormalities, there was no influence on severity of IBS symptoms (p < 0.0001) and somatic symptom severity (p < 0.0001).
OP289 INCREASED INHIBITORY NEUROTRANSMISSION WITHIN ANTERIOR CINGULATE CORTEX IS RELATED TO COMORBID ANXIETY IN IRRITABLE BOWEL SYNDROME

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Introduction: Inspired by the concept of Irritable Bowel Syndrome (IBS) as a disorder of brain-gut-communication, alterations in central mechanisms are increasingly acknowledged in IBS pathophysiology. Given high comorbidity with affective disorders, emotional factors likely play a role in disturbed central processes in IBS. Dysfunctions particularly in brain regions involved in emotion processing, including the rostral anterior cingulate cortex (rACC) as a unique hub of both, affect regulation and anti-nociception, may constitute a central link between abdominal pain and psychiatric comorbidities. While a growing number of neuroimaging studies support a crucial role of rACC in altered pain processing and emotional disturbances in IBS, the biochemical basis of these alterations remains unknown.

Aims & Methods: We compared IBS patients and healthy controls (HC) regarding glutamate (Glu) and γ-Aminobutyric acid (GABA)+ in rACC using quantitative magnetic resonance spectroscopy (qMRS). We further addressed associations with anxiety and depression as the most common psychiatric comorbidities in IBS patients. A combined MRI and MRS study, GABA+ concentrations in 38 female IBS and 19 age-matched female HC were measured using a Philips Ingenia 3T scanner and a MEGA-PRESS sequence with a 3x3x3 cm³ voxel placed in the rACC, localized based on individual T1-weighted images. Symptoms of anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS) and correlated with metabolite concentrations. Patients were subdivided into a group with (IBS+) and without (IBS) comorbid anxiety based on published HADS cut-offs.

Results: Compared to HC, IBS as a group exhibited significantly increased GABA+ concentrations within rACC (p < 0.05), while no differences were observed in concentrations of Glu. Both anxiety (r = 0.407; p < 0.01) and depression (r = 0.276; p < 0.05) correlated with GABA+ concentrations. Inclusion of HADS scores as covariates diminished group differences in GABA+ concentrations in ANCOVA with anxiety, but not with depression. Analyses on IBS subgroups revealed a group effect (p < 0.05) with higher GABA+ levels in IBS+ compared to HC (p < 0.01) and compared to IBS (p = 0.056), whereas differences between IBS+ and HC did not yield significance.

Conclusion: Our findings provide first evidence of dysregulated rACC neurotransmission in IBS. This imbalance appears to be driven by increased GABA+ concentrations in rACC as a crucial structure for anti-nociception and affect regulation. Abnormal GABA+ levels were most pronounced in patients with comorbid anxiety, supporting a key role of psychiatric comorbidities in altered brain processes in IBS. Altered inhibitory GABAAergic neurotransmission may be fundamental for dysregulations of affective and nociceptive processing, contributing to functional as well as long-lasting neuroplastic changes in IBS.

Disclosure of Interest: All authors have declared no conflicts of interest.

IBS HC p
E.coli 627 (563–688) 333 (291–387) 0.0001
Salmonella 880 (869–1104) 315 (194–437) 0.0001
5Cr-EDTA 1.1 (0.7–1.5) 0.9 (0.5–1.1) <0.05

The colonic mucosa of IBS patients had a significantly greater passage both for living Salmonella typhimurium and E. coli HS compared with HCs (p < 0.001 and p < 0.0001 respectively). The 5Cr-EDTA passage was also significantly increased in IBS (p < 0.05). IBS-M, IBS-D and IBS-C did not differ significantly in terms of mucosal barrier function measures, neither for bacterial nor for paracellular uptake. The present study demonstrated that passage through the colonic mucosa of both pathogenic and commensal living bacteria is altered in female IBS patients. These findings elucidate new aspects of peripheral abnormalities and support the importance of microbiota as a major factor in the pathophysi-ology of IBS.

Disclosure of Interest: All authors have declared no conflicts of interest.

REFERENCES

OP290 BACTERIAL PASSAGE IS INCREASED IN THE COLON OF WOMEN WITH IRRITABLE BOWEL SYNDROME INDEPENDENTLY OF STOOL CONSISTENCY SUBGROUP

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Introduction: Irritable bowel syndrome (IBS) is a chronic functional intestinal disorder with a strong female predominance. The pathophysiology is incompletely understood, but an increasing body of evidence demonstrates a role of the bowel microbiota axis. Altered microbiota compositions in IBS have been associated with an onset as well as changes in symptoms of IBS. Prior data suggest that intestinal barrier function is disturbed in IBS, but to our knowledge the passage of living bacteria through the colonic mucosa has never been investigated.

Aims & Methods: Aims: To study the paracellular permeability and the passage of living bacteria, both commensal and pathogenic, through the colonic mucosa of women with IBS and female healthy controls (HCs). The second aim was to investigate whether IBS stool consistency subgroups differ in terms of intestinal barrier function. Methods: Colon biopsies from 32 women with IBS (mean age 32.6±; with 17 mixed stool pattern IMS-7, with diarrhea IBS-D and 8 with constipation predominance IBS-C, according to Rome III criteria) and 15 HCs (mean age 29.7±) were mounted in Ussing chambers. Mucosal passage of living Escherichia coli (E.coli) HS and Salmonella typhimurium was investigated. The paracellular passage was measured by using 5Cr-EDTA.

Result:
Table: Mucosal passage of bacteria (bacteria/chamberx10¹⁰ and 5Cr-EDTA/cm²x10⁻⁸) are shown in median (25%–75% percentile)

<table>
<thead>
<tr>
<th></th>
<th>IBS</th>
<th>HC</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.coli</td>
<td>627 (563–688)</td>
<td>333 (291–387)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Salmonella</td>
<td>880 (869–1104)</td>
<td>315 (194–437)</td>
<td>0.0001</td>
</tr>
<tr>
<td>5Cr-EDTA</td>
<td>1.1 (0.7–1.5)</td>
<td>0.9 (0.5–1.1)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

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subjects ingested 400 ml of water containing 10 g lactulose and 5 g mannitol, after an overnight fast. Total urine for the following 4 hours was collected and rapidly frozen for analysis. Both groups started with oral intake of 75 mg dicyclfenac daily for 7 days. Thereafter, the lubiprostone group was treated by oral intake of 24 mg lubiprostone daily for 28 days, while the control group did not receive any medicine after dicyclfenac. Permeability was expressed as lactulose/mannitol ratio (LMR), calculated from urinary excretion of the initial administered dose of each sugar.

Result: Fourteen subjects for each with a median age of 23.5 (range, 21–32) completed the study. The background characteristics including baseline LMR between the two groups showed no significant difference. Treatment after 28 days of lubiprostone showed significant improvement of LMR (p = 0.0497), while 14 days treatment did not reach statistical significance compared to control group (p = 0.403).

LMR results (analyzed by analysis of covariance: ANCOVA)

<table>
<thead>
<tr>
<th></th>
<th>control group (n = 14)</th>
<th>lubiprostone group (n = 14)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline</td>
<td>0.019 (0.016–0.022)</td>
<td>0.021 (0.017–0.025)</td>
<td>0.044</td>
</tr>
<tr>
<td>day14</td>
<td>0.055 (0.023–0.047)</td>
<td>0.024 (0.019–0.029)</td>
<td>0.403</td>
</tr>
<tr>
<td>day28</td>
<td>0.028 (0.023–0.033)</td>
<td>0.017 (0.015–0.019)</td>
<td>0.0497</td>
</tr>
</tbody>
</table>

Conclusion: In our study, 28 days treatment with lubiprostone demonstrated an improvement of increased intestinal permeability after 1-week administration of diclofenac in healthy volunteers. This is the first study to demonstrate a significant effect of a medication for treatment of increased intestinal permeability, and suggests a new approach towards several diseases associated to “leaky gut”.

Disclosure of Interest: T. Kato: This research was supported by a grant from Takeda, Shire, Zeria, Abbott, Alfa-Wassermann, Janssen, W.E. Whitehead: Unrestricted research grants from Takeda Pharmaceuticals, Takeda Pharmaceuticals and Ironwood pharmaceuticals, as well as honoraria for participation in educational programs supported by these companies. M. van Tilburg: Research support from Takeda for investigator initiated study. J. Tack: Almirall, AstraZeneca, Danone, Menarini, Novartis, Nycomed, Oceara, Ono Pharma, Shire, SK Life Sciences, Theravance, Xenoport, Zeria, Abbott, Almirall, Alfa-Wassermann, Janssen, W.E. Whitehead: Unrestricted research grants from Takeda Pharmaceuticals; Unrestricted educational grants from Takeda and Ferring Pharmaceuticals; Consultant/Advisory Board member for Ono and Ferring Pharmaceuticals and Biomerica USA. All other authors have declared no conflicts of interest.

References

OP292 VISUAL HYPERSENSITIVITY IS ASSOCIATED WITH GI SYMPTOM SEVERITY IN FUNCTIONAL GI DISORDERS: CONSISTENT FINDINGS FROM FIVE DIFFERENT PATIENT COHORTS

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Introduction: Divergent results have been reported regarding the association between visceral hypersensitivity and GI symptoms in patients with functional GI disorders (FGIDs). Moreover, it has been proposed that the association between hypersensitivity and GI symptoms is secondary to psychological factors and tendency to report symptoms.

Aims & Methods: Our aim was to evaluate the association between visceral hypersensitivity and GI symptom severity in large cohorts of FGID patients. To do this, we included 5 cohorts of patients with FGIDs, who had undergone GI balloon distensions and completed questionnaires to assess GI symptom severity. We investigated healthy C57BL/6 J mice and mice with CCH, a mouse model for inflammatory bowel disease, as well as human patients with FGIDs.

OP293 CHRONIC ORAL ADMINISTRATION OF THE GUANYLATE CYCLASE-C AGONIST LINACLODIDE ATTENUATES COLITIS INDUCED LONG-TERM BLADDER AFFERENT HYPERACTIVITY

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Introduction: There is significant comorbidity between the symptoms of IBS and the urological symptoms of urgency and frequency experienced in overactive bladder and interstitial cystitis. Painful bladder syndromes. Viscero-vascular cross-talk has also been described in pre-clinical studies, whereby acute colitis in rodents is associated with altered bladder cystometry and bladder afferent sensitisation [1,2]. However, it remains to be determined if bladder overactivity persists following the resolution of colitis, in a model of chronic colonic hyper-sensitivity [3], or if reducing colonic nociception is able to alter bladder overactivity. Linaclootide, an FDA approved guanylate cyclase-C (GC-C) agonist, reduces abdominal pain in IBS patients with constipation [3], reverses colonic estrogen-sensitivity from Takeda and Ferring Pharmaceuticals; Consultant/Advisory Board member for Ono and Ferring Pharmaceuticals and Biomerica USA. All other authors have declared no conflicts of interest.

Table 1 (OP292): Association between visceral hypersensitivity and GI symptom severity in five FGID cohorts

<table>
<thead>
<tr>
<th></th>
<th>Belgian FD cohort (n = 242)</th>
<th>US IBS cohort (n = 243)</th>
<th>US IBS cohort (n = 159)</th>
<th>US IBS cohort (n = 335)</th>
<th>Swedish IBS cohort (n = 147)</th>
</tr>
</thead>
<tbody>
<tr>
<td>z score GI sx severity (mean ± SD)</td>
<td>DSS</td>
<td>IBS-SSS</td>
<td>IBS-SSS</td>
<td>IBS-SSS-GSRS-IBS</td>
<td>IBS-SSS</td>
</tr>
<tr>
<td>Low sensitivity tertile</td>
<td>−0.48 ± 0.99</td>
<td>−0.29 ± 0.99</td>
<td>−0.34 ± 0.90</td>
<td>−0.40 ± 0.98</td>
<td>−0.46 ± 0.89</td>
</tr>
<tr>
<td>Mid sensitivity tertile</td>
<td>−0.07 ± 0.88</td>
<td>0.04 ± 1.00</td>
<td>0.00 ± 1.04</td>
<td>0.11 ± 0.99</td>
<td>0.31 ± 0.83</td>
</tr>
<tr>
<td>High sensitivity tertile</td>
<td>0.32 ± 0.99</td>
<td>0.25 ± 0.95</td>
<td>0.28 ± 0.97</td>
<td>0.25 ± 0.95</td>
<td>0.06 ± 1.14</td>
</tr>
<tr>
<td>ANOVA</td>
<td>F = 13.2; p &lt; 0.0001</td>
<td>F = 5.9; p = 0.003</td>
<td>F = 5.1; p = 0.007</td>
<td>F = 14.0; p &lt; 0.0001</td>
<td>F = 8.5; p &lt; 0.0001</td>
</tr>
<tr>
<td>ANOVA (adjusted for somatization)</td>
<td>F = 9.2; p = 0.0001</td>
<td>F = 4.9; p = 0.004</td>
<td>F = 4.1; p = 0.018</td>
<td>F = 10.8; p &lt; 0.0001</td>
<td>F = 8.3; p &lt; 0.0001</td>
</tr>
<tr>
<td>ANOVA (adjusted for anx &amp; depr)</td>
<td>F = 13.3; p &lt; 0.0001</td>
<td>F = 5.0; p = 0.006</td>
<td>r = −0.27; p &lt; 0.0001</td>
<td>r = −0.29; p &lt; 0.0001</td>
<td>r = −0.20; p &lt; 0.02</td>
</tr>
</tbody>
</table>

Correlation sensitivity - GI sx
administration, consisting of a once daily oral gavage for 2 weeks prior to experi-
mental groups, while four cell patch clamp recordings from retro-
gradely traced thoracolumbar and lumbosacral bladder dorsal root ganglion
(DRG) neurons determined neuronal excitability, whilst ex-vivo electrophysi-
ological recordings determined bladder afferent and contractile sensitivity to ramp
distension. Subsequently, patients were recruited and TRPV1 channel agonists
Micturition pattern analysis was performed by analysing in-vivo natural voiding
behaviour.

Result: Bladder traced DRG neurons from mice with CCH displayed hyperexcit-
ability (P < 0.001), and exogenous agonists (P < 0.01), with no changes in muscle compliance or contraction responses. As a reflection of altered physiological signalling, CCH mice also displayed signifi-
cant changes (P = 0.01). CCH mice treated with lincacotide displayed attenuated bladder DRG neuron excitability compared with placebo treated mice (P < 0.001), and attenuated bladder afferent hypersensitivity to dis-
tension (P < 0.001). Lincacotide treatment in the CCH mice also resulted in a restoration of natural voiding behaviour (P = 0.05).

Conclusion: Mice with CCH also display increased bladder afferent excitability accompanied by abnormal bladder voiding behaviour, an example of viscero-
viscerovascular cross-talk. Chronic oral administration of lincacotide, a gut-restricted GC-C agonist that inhibits colonic nociceptors, reverses these colitis-induced changes in bladder function and sensitivity. Agents that improve abdominal

Disclosure of Interest: L. Grundy: Grant support from Ironwood Pharmaceuticals.
G. Hannig: Employee, stock holder, and stock options from Ironwood Pharma-
care Inc.
C.B. Kurtz: Employee, stock holder, and stock options from Ironwood Pharma-
care Inc and Decibel Therapeutics.
S.M. Brierley: Research support: Ironwood Pharmaceuticals Inc, Takeda Pharmaceuticals Inc., Key Pharmaceuticals Inc.
All other authors have declared no conflicts of interest.

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TUESDAY, OCTOBER 18, 2016 15:45–17:15
(EPIGENETICS IN IBD - ROOM L7)
OP294 DIAGNOSING RARE INHERITED DISORDERS USING TARGETED NEXT GENERATION SEQUENCING IN PATIENTS WITH EARLY-ONSET INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY
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Introduction: Several recent referral center studies showed that a significant propor-
tion (3-10%) of children with an early-onset (EO, defined by an age at diagnosis less than 12 years) inflammatory bowel disease (IBD) present with an underlying monogenic disorder. Currently, more than sixty disorders of this type have been identified and their pathophysiological mechanisms are very heterogenous. Most of them affecting the intestinal epithelial barrier, are asso-
ciated with defects in phagocytosis or immune deficiency, or are hyper- and auto-
immunological diseases. However, they all share the ability to present in the form of an array of intestinal inflammation with EO.

Aims & Methods: Using a next-generation sequencing (NGS) of the 63 genes whose abnormailties are responsible for these disorders, and a targeted CGH array analysis of their chromosomal loci, 91 patients with an initial diagnosis of EO-IBD between 1988 and 2004 (54% of the whole EO-IBD cohort) issued from EPIMAP population-based registry were screened; 71 had a Crohn’s disease and 20 an ulcerative colitis.

Result: Analysis was performed in 24 patients (26.4%) with very rare or not yet reported potential pathogenic variants in 17 genes. Seven of them (7/91; 7.6%) had a genotype compatible with one of the tested disorders: Burton agammaglobuline-
mia, familial diarrhea, familial C2 defect, hyper-IgM syndrome or Omenn syn-
drome. The remaining 17 patients (17/91; 18.7%) were heterozygous carriers of these genes variants involved in autosomal recessive trait. The genotype identified in these patients was thus probably not likely to be the underlying cause of one of these disorders, however, one cannot exclude that it may contribute to IBD as suggested by the unusually high prevalence of these genotypes.

Conclusion: Our study issued from a population-based registry, provides further evidence to recommend screening for inherited disorders using targeted NGS in children with an EO-IBD with the potential to enhance optimal selection of treatment options and adequate counseling of families. This study also indicates that targeted NGS used in this study may be an adequate and efficient tool for the identification of patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: The impact of environmental hypoxia on the development of inflammatory bowel disease (IBD) is controversial, with studies supporting both a proinflammatory and a protective effect. Hypoxia is known to activate the autophagy and inflammasome pathways, which are ancient innate immune mechanisms linked by mutual regulation. In recent years, polymorphisms in gene loci containing autophagy- and inflammasome proteins have been associated with an increased risk of IBD. Evidential data suggest that the imbalance in the regulation of autophagy and NLRP3 inflammasome activation under hypoxia plays a role in the development of IBD.

Aims & Methods: To study the effects of hypoxia in IBD, healthy volunteers (n = 10), patients with Crohn’s disease (CD, n = 11) and patients with ulcerative colitis (UC, n = 9) were subjected to hypoxic conditions resembling an altitude of 4,000 m above sea level for 3 h using a hypobaric chamber. Distal colon biopsies were collected the day before hypoxia, immediately after hypoxia, and one week after collection of the first biopsy. To further study the effects of hypoxia in colitis and the role of the NLRP3 inflammasome, wild-type (WT), interleukin (IL)-10−/−, Nlrp3−/− and Il10−/− mice were subjected to hypoxia (8% O2) for 18 h prior to colon biopsy collection. Mice under normoxic conditions were used as controls. For the in vitro studies, the human monocytic cell line THP-1 and the intestinal epithelial cell line HT-29 were subjected to hypoxia (0.2% O2) in the presence and absence of lipopolysaccharide.

Result: Colon biopsies of patients with CD, but not UC showed increased levels of tumor necrosis factor (TNFα) and NLRP3 mRNA expression prior to hypoxia. Interestingly, hypoxia inhibited the expression of both genes immedi-
ately and one week after hypoxia concomitantly with the induction of the autop-
thy-associated gene p62. IL-10−/−, but not IL-10−/− Nlrp3−/− mice presented an increased expression of TNFα, IL-6, and inflammasome-associated IL-1β as well as increased levels of phospho-p62 concomitantly with an accumulation of the autophagy proteins p62 and LC3, suggesting an autophagy blockage orche-
strated by NLRP3. Interestingly, hypoxia significantly inhibited the expression of TNFα, IL-6 and IL-1β, and restored autophagy in IL-10−/− mice. The mRNA of THP-1 cells subjected to hypoxia showed a marked activation of autophagy concomitantly with an increase in autophagy, evidenced by a reduction in p62 and LC3, and the phosphorylation of mTOR, a major regulator of autophag-
ysis. siRNA-mediated silencing of NLRP3 further activated autophagy under hypoxia.

Conclusion: Our results suggest a protective effect of hypoxia in CD patients and the IL-10−/− mouse model of colitis. IL-10−/−, but not IL-10−/− NLRP3−/− mice under prolonged inhibition of autophagy indicating that NLRP3 is involved in the blockage of autophagy. Interestingly, hypoxia restored autophagy in IL-10−/− mice, as well as in THP-1 and HT-29 cells concomitantly with a reduction of inflammatory gene expression and signaling. Hypoxia-induced autophagy was enhanced in the absence of NLRP3 further supporting a role for NLRP3 in the regulation of autophagy. Our results confirm a reciprocal regulation between hypoxia, inflammation, and autophagy, and suggest that hypoxia ameliorates inflammation through the induction of autophagy via the regulation of NLRP3.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.
OP296 EPIDEMIC ALTERATIONS IN INFLAMMATORY BOWEL DISEASE - THE INFLUENCE OF GERMINE LINE (MEQTLs) ON GENOME-WIDE METHYLATION ALTERATIONS


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Introduction: Exploring DNA methylation in Inflammatory Bowel Disease (IBD) may provide an insight into complex gene-environment interactions, identify novel targets involved in pathogenesis, and allow development of powerful new biomarkers. Our study aims to characterize disease-associated methylation changes in newly diagnosed IBD and to define the contribution of genetic variation, by discovery of associated quantitative trait loci (meQTL).

Aims & Methods: Genome-wide methylation was measured in 641 DNA samples from pediatric (n=200) and adult IBD controls, 150 Crohn’s disease (CD), 167 ulcerative colitis (UC), 26 IBD unclassified (IBDU)) using the Illumina HumanMethylation450 BeadChip. Samples were obtained from new onset IBD cases in six European centres as part of the European Commission funded IBD Character project.

Result: 195 probes exhibited Bonferroni significant IBD-associated methylation differences, including VMP1/MIR21 (p = 3.7 × 10−3), RPS6KA2 (1.1 × 10−13), SBNO2 (2.7 × 10−13), and TNFSF10 (1.1 × 10−13); data which provide important replication and confirmation of methylation differences previously reported in paediatric CD and adult IBD. Novel findings include PHOSPHO1 (1.3 × 10−10), MUC4 (5.5 × 10−13), and CDH24 (1.7 × 10−13), and a replication of two SNPs previously described as correlated to VMP1/MIR21 methylation (rs8078424, p = 4.4 × 10−22, rs853015, p = 7.4 × 10−21). There was an enrichment of highly significant IBD-associated methylation changes in proximity to IBD GWAS loci. Results were highly similar in CD and UC, with only one probe showing a significant methylation difference between diagnoses (NAV2, 6.82 × 10−9). Paired genetic and methylation data showed 2327 FDR significant MeQTLs regions of consecutive FDR significant probes were defined in genes including VMP1/MIR21, ITGB2, TNF, and at multiple sites throughout the HLA region.

Conclusion: These data allow methylome profiling in a large multinational cohort of IBD patients and healthy controls. Important unequivocal replication of recent discoveries, together with insight into the genetic contribution to epigenetic alterations in complex disease, and the utility of peripheral blood DNA methylation as a biomarker.

Disclosure of Interest: R. Kalla: Received funding from the EU FP7 (285546) and served as a speaker for Ferring J. Jahnsen: Served as a speaker and a advisory board member for MSD, Tillof, Ferring, AbbVie, Celltrion, Orion Pharma, Takeda, Napp Pharm, Meda, AstroPharma, Hikma and Pfizer. F. Gomollon: Advisor: Grifols, Abbvie, MSD. Travel Grants: Abbvie,MSD. Research funding (Department) MSD J. Satsangi: JS has served as a speaker, a consultant and an advisory board member for MSD, Ferring Abbvie and Shire, consultant with Takeda, speaking fees from MSD and has received research funding from Abbvie. All other authors have declared no conflicts of interest.

References

OP297 AN AUTOPHAGY-RELATED PERIPHERAL BLOOD MICRORNA SIGNATURE DIFFERENTIATES COLONIC CROHN’S DISEASE FROM ULCERATIVE COLITIS

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Introduction: Phenotypic expression of colonic inflammation in inflammatory bowel disease (IBD) can sometimes have a similar appearance and be difficult to differentiate. MicroRNAs (miRNAs) may offer a method of distinction as differential expression of peripheral blood miRNAs has been shown in small studies of IBD patients and healthy controls.

Aims & Methods: This study aimed to assess peripheral blood mononuclear cell (PBMC)-derived miRNA signatures in a well-phenotyped cohort of colonic IBD and to identify differentially expressed miRNAs in patients with CCD and UC. An IBD cohort with UC and CCD was prospectively accrued. Colonoscopy was performed and patients with CCD (Montreal Classification L2/L3) or left-sided UC (Montreal Classification E2/E3) were enrolled. Colonoscopies were reviewed by IBD endoscopists and scored for presence/absence, severity and site of inflammation. Pathology reports were reviewed for presence/absence and severity of inflammation. On the day of endoscopy, C-reactive protein (CRP) was measured and blood was collected in PAXgene tubes (Qiagen). Total RNA was extracted from blood using the PAXgene Blood miRNA Kit (Qiagen) and miRNA counts from 798 probes were measured using the Human v3 miRNA nCounter Platform (NanoString Technologies). Raw counts were normalized, log2 transformed and batch corrected. Non-parametric Kruskal-Wallis tests assessed differential miRNA expression across phenotypes. Raw p-values were corrected for multiple testing by the Benjamini-Hochberg false discovery rate method. Target prediction and gene ontology biological process (GO BP) enrichment analyses were performed with miRWalk 2.0. Receiver operating characteristic (ROC) curves were generated following logistic regression through 5-fold cross validation repeated 10 times. Area under the curve (AUC) values for the ROCs were derived in order to evaluate the discriminating capacity of the differentially expressed miRNAs in CCD versus UC.

Result: 51 subjects, 32 UC (50% male, 36 yrs mean age), 19 CCD (42% male, 32 yrs mean age) were included in the analysis (see Table 1). There were no significant differences in mean CRP or among clinical, endoscopic or histologic disease activity between the CCD and UC groups suggesting that the degree of inflammation was similar in both groups. Comparing CCD and UC, 5 miRNAs were differentially expressed: miR-129-5p, miR-603, miR-619-3p, miR-874-3p, miR-933 (FDRp = 0.0214 all probes), all of which were upregulated in CCD vs UC. In the ROC analysis, the AUC for CCD vs UC for the combined expression of the 5 miRNAs was 0.89 (95% CI: 0.88–0.90). 2 out of 5 miRNAs putatively target the Autophagy Related 16-like 1 (ATG16L1) gene, and 4 out of 5 miRNAs had significant GO BPs on putative target genes in the regulation of autophagy pathway (FDRp < 0.05).

Conclusion: A PBMC-derived miRNA panel of markers identified here differentiates CCD from UC with similar degrees of inflammation. All of these differentially expressed miRNAs are upregulated in CCD compared to UC, and...
several appear to be associated with the autophagy pathway. These findings may aid the individualization of patient care through identification of novel diagnostic and therapeutic targets.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP298 ASSESSMENT OF INFLAMMATORY BURDEN IDENTIFIES CROHN’S DISEASE AND ULCERATIVE COLITIS PATIENT GROUPS WITH DIFFERENT DISEASE PATHWAYS AND THERAPEUTIC RESPONSE TO ANTI-TNF TREATMENT**

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**Introduction:** Crohn’s disease (CD) and ulcerative colitis (UC) are considered to be driven by both common and distinct underlying mechanisms of pathobiology. In both diseases there is heterogeneity underscored by the variable clinical responses obtained to therapeutic interventions. We aimed to identify disease-driving pathways as well as classify individuals into subpopulations that differ in their disease pathobiology and response to a specific treatment.

**Aims & Methods:** Hierarchical clustering on enrichment scores (ES) from gene set variation analysis (GSVA) was used probing a normal healthy volunteer (NHV), CD, and UC dataset of colon biopsies (GSE16879) with a library of gene set signatures representative of various immunological and inflammatory processes as well as specific activated cell types. Patient stratification at baseline (BL) or after anti-TNF treatment (PT) in either clinical responders (R) or non-responders (NR) was performed.

**Result:** Gene set signatures whose ES differed significantly (ES change ≥ 0.2, p ≤ 0.05) between comparisons were identified from general linear model analyses. Comparisons were made at BL in all participants irrespective of clinical response (comparisons between UC and CD compared to NHV, 59% of the tested signatures were commonly enriched in both CD and UC at BL underlining the commonality of both diseases. These signatures included e.g. activated T cells, monocytes, macrophages or neutrophil signatures as well as polyIC and becn1/3 signatures, representing acute inflammation and a complex mix of potential disease-driving biology. Comparing R and NR separately at BL to NHV, 43% and 70% of signatures were enriched, respectively, indicative of a higher inflammatory burden in NR. Indeed, specific macrophage, innate lymphoid and T cell signatures were significantly enriched in NR. Hierarchical clustering of the ES that significantly differed in the comparisons clearly separated diseased BL from NHV samples. It also clustered R PT samples with the NHV while the NR PT samples clustered with the BL diseased samples, with a better separation observed in CD when compared to UC. Also, clear UC and CD patient clusters could be observed with increasing ES at BL correlated with NR to anti-TNF treatment recapitulating the observation of a higher inflammatory burden in NR.

**Conclusion:** Our analysis has identified common disease-driving pathways for CD and UC supporting the notion of a disease continuum rather than two distinct diseases. However, within that disease continuum, distinct patient groups could be defined by their overall inflammatory burden correlating with their response to an anti-TNF therapy. This methodological approach could facilitate better targeted design of clinical studies to test therapeutics under development, concentrating on subsets of patients sharing similar underlying molecular pathology and therefore increasing the likelihood of clinical response.

**Disclosure of Interest:** S. Pavilidi: Employee of Janssen Research & Development Ltd, High Wycombe, UK
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**OP300 THE IMPLEMENTAL MEDICATED MICRORESERVOIRS IN THE TREATMENT OF COLORECTAL CANCER. THE GOOD EFFECTS OF A SIMPLE PROCEDURE. EARLY RESULTS**

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**Introduction:** Colorectal cancer (CRC) is the third most common in the world of men, and the second - in women. In Europe remains steady increase in incidence and mortality according to Globocan 2012 and source EuroPanCol. The main problem after surgery is local recurrences that often develop even after resection R0. Local recurrence is a developed in 50-70% of cases in 5-10 years and accounts for the second half of the first year after surgery. [2] Therapeutic Methods: We aim to investigate the use of medicated microspheres to improve the results of surgical treatment CRC. To study the safety and efficacy of this modification surgery. Materials and methods: We have investigated the number of CRC recurrence for patients without metastases, lymph node involvement, stage II and III, local recurrent and other organs after surgery in a volume R0 for a year after surgery. The study included 87 patients (54 women and 33 men, mean age 62.4 years +/- 8.4 years) who were operated in the Dnipropetrovsk regional proctology centre from February 2014 to February 2015. The control group (42 patients, 17 men and 25 women) performed surgery in standard volume according to guideline. In the test group (45 patients, 16 males and 29 females) before the anastomosis were formed medicated with 5-fluorouracil (5FU) supported on polynvinylpyrrolidone (PVP). In fact, it was a mixture of 30% of 5FU, PVP solution 5ml and 5ml 5FU (250 mg). This mixture was introduced into the muscle layer from the side of mucosa the 1 ml syringe with needle 0.40 x 10 mm 27G x 1/2 at a distance of 1-1.5 cm from the edge of the intestine. In one procedure was introduced approximatively 1 ml of the drug. The median volume of the residual drug was 0.3 ml. The operation was completed in a standard way. As the drug delivery system has been selected PVP in the concentration of 30% as its safety is confirmed by the FDA. [8] PVP as a delivery system allows for the gradual release of the drug, due to the destruction of the carrier polymer. An important advantage is the fact that the PVP is practically not destroyed at a pH of less than 7, which allows to delay the release of 5FU, since pH in the stage of inflammation in the tissues is reduced and consequently the release of the bulk of 5FU will be completed in the beginning of the inflammation. The 5FU was selected as a drug for the treatment because it does not require pre-transformation to act as a result and can be effective on condition that 5FU is transported into the tissues. 

**Disclosure of Interest:** All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
15:45-17:15
NOVEL TECHNIQUES IN LOWER GI MALIGNANCIES – ROOM L8
Result: In the control group, local recurrence was detected in 12 cases (28.6%). The following postoperative complications were found: early adhesive intestinal obstruction in 2 (4.8%) cases of postoperative pneumonia in 1 (2.4%) case. Within 8 months after surgery 1 patient died of acute coronary syndrome. In the studied group of local recurrence was detected in 8 cases (17.8%). The following postoperative complications were found: early adhesive intestinal obstruction in 1 (2.2%) case, even one patient has been had digestive intestinal obstruction in 3 months after the operation, which resulted in the death of the patient on 2 days after the re-operation due to acute of cardiovascular failure.

Conclusion: 1. Intravenous repletion of mediated microspheres is a safe and effective procedure for the prevention of early recurrent CRC. 2. Notwithstanding the low total dose, good effect can be achieved due to the high concentration of the drug in the tissues. 3. This procedure avoids many resorbing effects of the chemotherapeutic drug, associated with systemic administration and high doses required to achieve therapeutic concentrations in tissues. 4. Obviously, it is necessary to continue the monitoring of these patients. 5. It is possible to consider a combination of other drugs and carrier polymers.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP301 ENDOSCOPIC SUBMUCOSAL DISSECTION IN LATERALLY SPREADING TUMORS: EXPERIENCE OF 282 CASES FROM A TERTIARY REFERENCE CENTER IN TURKEY

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Introduction: Endoscopic submucosal dissection (ESD) is a minimally invasive technique, providing en-bloc resection of premalignant and malignant lesions in early stage gastrointestinal (GI) cancers. Lateral Spreading Tumors (LSTs), which are endoscopically seen as granular (LST-G) or non granular (LST-NG) types, are technically difficult to remove as en-bloc with ESD method because of anatomical features of the colon. In the present study, we present our results of colorectal ESD procedures in LTSs.

Aims & Methods: Between April 2012- April 2016, a total of 655 colorectal lesions were referred to our unit for the purpose of removal with advanced endoscopic techniques (EMR or ESD). Colorectal ESD was performed to 290 lesions. Data was recorded prospectively before and after the procedure. 8 ESD cases were excluded because the lack of control endoscopy. The results of 282 ESD procedures performed in colon and rectum with diagnosed LST were analysed retrospectively.

Result:

Table: Demographic data and colorectal endoscopic submucosal dissection results

<table>
<thead>
<tr>
<th>Case (n)</th>
<th>Lesion size, mm, mean (SD)</th>
<th>N (%)</th>
<th>Complete Resection</th>
<th>PDVI range</th>
<th>MVD range</th>
</tr>
</thead>
<tbody>
<tr>
<td>273</td>
<td>40.4 (26.2)</td>
<td>90.4</td>
<td>275 (91.1)</td>
<td>2 (0.2)</td>
<td>14 (2.0)</td>
</tr>
<tr>
<td>33</td>
<td>49.8 (28.9)</td>
<td>35.8</td>
<td>255 (90.4)</td>
<td>142 (4.0)</td>
<td>101 (35.8)</td>
</tr>
<tr>
<td>42</td>
<td>79.5 (71.1)</td>
<td>35.8</td>
<td>40.44 (26.2)</td>
<td>360 (10)</td>
<td>240 (10)</td>
</tr>
<tr>
<td>61.5-540</td>
<td>24.6 (15.4)</td>
<td>35.8</td>
<td>49.81 (28.9)</td>
<td>360 (10)</td>
<td>240 (10)</td>
</tr>
<tr>
<td>Median</td>
<td>(21; 1.7-79.5)</td>
<td>35.8</td>
<td>142 (4.0)</td>
<td>360 (10)</td>
<td>240 (10)</td>
</tr>
<tr>
<td>Median</td>
<td>(33; 14-176)</td>
<td>35.8</td>
<td>101 (35.8)</td>
<td>360 (10)</td>
<td>240 (10)</td>
</tr>
</tbody>
</table>

The rates of pathological complete resection were 100% (17 of 17) in the ESMR-L group, 88.9% (16 of 18) in the CSI-EMR group, and 95.2% (20 of 21) in the ESD group. N (%) 1s 1s 1s 1s

Disclosure of Interest: All authors have declared no conflicts of interest.

OP302 EVALUATION OFRECTALCANCER ANGIogenesis USING IMMUNOHISTOCHEMICAL AND COMPUTER-ASSISTED ENDOSONOGRAPHIC METHODS

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Introduction: The conventional way for evaluation of rectal cancer angiogenesis requires a biopsy or a tissue specimen applying specific immunohistochemical or molecular biological tests. The evaluation of microvessel density is a gold standard in the assessment of tumour angiogenesis. Doppler ultrasound is an attractive method for imaging angiogenesis in vivo which can be repeated without exposing the patient to any risk.

Aims & Methods: The aim of the current study is to evaluate the preoperative rectal cancer angioconstruction with Endorectal Power Doppler Ultrasound by using microvessel density and Doppler Vascularity Index calculated by imaging analysis software and to compare results with microvessel density in surgical specimens A total of 110 patients (59 males; 51 females, mean age 61.5 years) with rectal cancer were enrolled in this study. The patients were operated and staged as follows: in stage 1—20 patients (18%), stage II—20 (18%), stage III—47 pts (43%); stage IV—14 pts (13%). Microvessel density was evaluated by using immunohistochemical staining of surgical specimens with anti-CD-31 antibody. The PDVI of each tumor was determined using endorectal power Doppler ultrasound with computer assisted quantification of colour pixels. The PDVI was defined as the ratio of the number of the colored pixels within a tumor section to the number of total pixels in that specific tumor section, and was calculated by using a software.

Result: The mean microvessel density (MVD) was 163 ±69 microvessels/mm2. The MVD was used as the cutoff point divided two groups of tumours with high (≥160 vessels/mm2) and low angiogenic activity (≤160 vessels/mm2). Mean PDVI was 8.9 ±6.0% (range: from 0 to 27.3). Median PDVI (8%) was used as the cutoff divided two groups of tumours with high (>8%) and low PDVI (<8%). The MVD and PDVI showed a good positive linear correlation (r=0.438, p=0.002).

Conclusion: Endorectal Power Doppler ultrasonography is a useful noninvasive method of evaluating the extent of angiogenesis. Tumour angiogenesis assessed by power Doppler vascular index correlated with histological microvessel density determination. The presented endoultrasound Power Doppler examination is a reliable and reproducible mean for in vivo preoperative quantitative assessment of the tumour vascularity.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP303 COMPARISON OF CLINICAL OUTCOMES AMONG DIFFERENT ENDOSONOGRAPHIC MODALITIES FOR RECTAL NEOENDOCRINE TUMOR

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Introduction: Rectal neuroendocrine tumor (NET) less than 10 mm in diameter can be removed by various endoscopic techniques, such as endoscopic mucosal resection (EMR), modified EMR, and endoscopic submucosal dissection (ESD). This study aimed to compare efficacy and safety of endoscopic submucosal resection with a ligation device (ESMR-L) or circumferential submucosal incision prior to EMR (CSI-EMR) versus ESD.

Aims & Methods: Forty-six patients, who underwent endoscopic resection of a rectal NET less than 10 mm in diameter, were enrolled consecutively from March 2013 to June 2015. The patients were classified into three groups according to the type of endoscopic procedure: ESMR-L group (n=17), CSI-ESD group (n=18), and ESD group (n=21). We compared treatment outcomes and complications associated with these methods.

Result: There was no different in tumor diameter between different endoscopic procedures (ESMR-L, 4.5±1.6 mm; CSI-EMR, 5.6±2.0 mm; ESD, 5.0±2.2 mm; p=0.236). En bloc resection was achieved in all patients. There was no lateral margin involvement in all patients. Basal margin involvement occurred in one patients in the ESD group and two in the CSI-EMR group. The rates of pathological complete resection were 100% (17 of 17) in the ESMR-L group, 95.2% (20 of 21) in the CSI-ESD group, and 90.4% (19 of 21) in the ESD group.
Endoscopic or trans-anal therapy. The GelPort Path trans-anal access port was used for the puncture to the rectum. The size of the CRP ranged from 0.6 to 2 cm in diameter, with a mean of 1.4 cm. After the procedure, no complications were noted. During follow-up, no recurrence of symptoms or signs was observed in any of the patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP034 ANAL CYTOLOGY, HISTOPATHOLOGY, AND ANOSCOPIETICAL VISUAL IMPRESSION IN AN ANAL DYSPLASIA SCREENING PROGRAM: IS ANAL CYTOLOGY ENOUGH?

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Introduction: The human papilloma virus (HPV) is the leading cause of anal squamous cell carcinoma. The cytological screening can reduce morbidity and mortality associated with this cancer, although current recommendations are based on sparse evidence.

Aims & Methods: The authors intend to estimate agreement between anal cytology examination, histopathology, and anoscopy visual impression. This is a prospective study of patients receiving anal dysplasia screening between 2010 and 2015. In a proctoscopy consultation of a tertiary referral center. Descriptive statistics was performed using IBM SPSS Statistics 22 with p < 0.05 deemed to be statistically significant. Agreement between measures was estimated by weighted kappa statistic.

Results: During the period of the study, 141 patients (91% men, mean age 37 ± 14 years, 87% with HIV infection) underwent 175 anal cytology tests: 33% negative (NILM) anal cytologies, 33% low-grade squamous intraepithelial lesion (LSIL), 10% high-grade squamous intraepithelial lesion (HSIL) and 1% carcinoma of unknown primary. The presence and degree of dysplasia in anal cytologic tests and concurrent histological exams were being considered for proctectomy and/or had failed conventional resection procedures (P-EMR/ESD) have the potential to resect complex rectal NET less than 10 mm in diameter and ESD were effective and safe for the treatment of rectal NET, when compared with CSE-ESD or ESD, EMR procedure has the advantages of easier and shorter procedure time. ESMR may be considered the treatment of choice for rectal NET greater than 1 cm in diameter.

Conclusion: All endoscopic resection method, including ESMR-L, CSE-EMR, and ESD were effective and safe for the treatment of rectal NET, when compared with CSE-ESD or ESD, EMR procedure has the advantages of easier and shorter procedure time. ESMR may be considered the treatment of choice for rectal NET greater than 1 cm in diameter.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP036 THE PROREGENERATIVE ROLE OF INTERLEUKIN-22 POST-IR IN THE INTESTINAL EPITHELium DEPENDS ON AUTOPHagy AND ER stress

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Introduction: Endoplasmic reticulum (ER) function and autophagy are necessary to maintain cellular homeostasis. Genetic variants of inflammatory bowel disease (IBD) risk genes ATG16L1 or XBP1 are associated with epithelial endoplasmic reticulum (ER) stress which promotes cell death. While XBP1 plays a beneficial role in resolving ER stress, ATG16L1 represents an essential component of the autophagy machinery, a conserved mechanism for protein degradation. Both processes are strongly connected since impaired autophagy subsequently results in deregulation of ER function. Interleukin-22 (IL-22) is known to be a protective cytokine in mucosal regeneration by promoting epithelial proliferation via STAT3 and NF-kB activation. Therefore, conjugates of IL-22 are in trials as potential drugs in IBD treatment.

Aims & Methods: Here, we investigate the impact of the IBD risk genes ATG16L1 and XBP1 on regenerative function of IL-22 in intestinal epithelium in mice and human primary colon carcinoma. HT-29 and Caco2 cells were co-cultivated with recombinant IL-22 and ER stress inducers like Tunicamycin or autophagy inducers like Rapamycin before they were subjected to wound healing assays, gene expression analysis and immunoblot analyses. Intestinal organoids derived from XBP1 SIEC (intestinal epithelial cell specific deletion) and ATG16L1 SIEC mice were treated with recombinant IL-22 and gene expression analysis using qRT-PCR. RNA sequencing and transcriptome analysis were performed. Conclusions: Our results support the notion that autophagy and ER stress are essential for the regenerative function of IL-22 in intestinal epithelium.
Disclosure of Interest:

ELISA. Atg16l1 ΔIEC and Atg16l1 ΔIEC/Xbp1 ΔIEC mice were treated with recombinant IL-22 for 5 or 6 on 12 days before sacrificing. Result: IL-22 induces transient self-limiting ER stress in the intestinal epithelium. While IL-22 improves wound healing in the absence of ER stress, IL-22 leads to impaired wound closure and increased cell death under ER stress conditions. This effect is dependent on STAT3 and autophagy as pharmacological STAT3 inhibition or autophagy induction with Rapamycin completely restores IL-22 dependent ER stress inhibition. On the contrary, impairment of the autophagic flux by Bafilomycin A provokes inflammatory features as well, which are aggra- vated by treatment of transient ER stress is dependent on response. IL-22 and Atg16l1 as IL-22 treatment of intestinal organoids derived from Atg16l1 ΔIEC and Xbp1 ΔIEC mice induces a dramatic increase of inducible ER stress and pro- inflammatory gene expression. In addition, mRNA transcriptome analysis reveals differential expression of several IBD related risk genes in Xbp1 ΔIEC and Atg16l1 ΔIEC organoids in response to IL-22 stimulation. Atg16l1 ΔIEC mice display defective autophagy in the intestinal epithelium and spontaneous cell death in intestinal crypts which exacerbates after IL-22 treatment. Finally, IL-22 induced spontaneous inflammatory intestinal inflammation in Atg16l1 ΔIEC/Xbp1 ΔIEC mice. On the flipside, same treatment of wild type control mice does not affect cell death and inflammation, underlining a genotypic dependency of beneficial and adverse effects of IL-22 application.

Conclusion: These data suggest an unexpected role of the IBD risk genes ATG16L1 and XBP1 in coordinating regenerative IL-22 function in intestinal epithelium and may contribute to the development of genotype-based persona- lization medicine. However, further studies are necessary to decipher the molecular link between IL-22 signaling and the ER stress/autophagy axis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


OP307 HOXA9 IS OVEREXPRESSED IN COLONIC ADENOMAS AND CAUSES AN INCREASE IN CELL GROWTH

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Introduction: Colonic adenomas are premalignant tumors with glandular origin. Identifying the molecular aberrations in this tissue may help to understand its malignant potential and could lead to better understanding of colorectal cancer development. The mammalian HOX clusters encode regulators of embryonic anterior to posterior specification and are important for the formation of tissues, structures, and organs. Besides having a function in embryology, HOX genes have pro-oncogenic activity in various malignant diseases. For example, HOXA13 overexpression predicts poor outcome for patients with cancer of the esophagus, stomach, and liver. In a portion of acute myeloid leukemias (AML), a translocation encoding the NUP98-HOXA9 oncogene gives overexpression of HOXA9. HOXA9 overexpression is the molecular factor most strongly correlated with poor prognosis in AML and is also corre- lated with poor prognosis in ovarian epithelial cancer. HOX gene aberrations are reported in colorectal cancer, however, it is unclear whether HOX gene aberrations are present at a premalignant stage and could, thus, contribute to cancer formation.

Aims & Methods: This study first aimed to assess the expression of HOXA9 in colorectal adenoma tissue and location matched control tissue. Secondly, it aimed to determine the effects of increased HOXA9 expression, both in terms of its influence in anterior to posterior specification and its oncogenic properties. We collected biopsies from colorectal polyps and location matched normal colorectal tissue in patients undergoing colonoscopy. A pathologist classified the colorectal polyp as adenoma and we only included tubular adenomas. We used RT-qPCR to quantify the expression of HOXA9 in relation to UBC, TPT1 and GAPDH using the efficiency (Ctmethod. In addition, we transduced Caco2 cells with a lentiviral vector containing HOXA9 and a lentiviral vector without an insert, enabling inducible expression. Subsequently, we analyzed expression of HOXA9 in Caco2 cells with a lentiviral vector containing HOXA9 and a lentiviral vector without an insert, enabling inducible expression. Finally, we assessed the expression of genes implicated in oncological transformation and epithelial to mesenchymal transition.

Result: HOXA9 expression in tubular adenomas of the colon is increased compared to location matched control tissue (p = 0.04). HOXA9 overexpression in Caco2 cells led to a decrease in FGFR2 mRNA level (p = 0.001). Additionally, when assessed with a MTT assay (p < 0.001), HOXA9 overexpres- sion led to increased total cell pool. The growth factor IGFI increased signifi- cantly (p = 0.02) as a result of HOXA9 overexpression. Genes important for epithelial to mesenchymal transition were not found to have significantly changed.

Conclusion: HOXA9 expression is increased in colorectal adenomas. Overexpression of HOXA9 leads to a decrease in FGFR2 and an increase in BMP, which empha- sises the role of HOXA9 as a regulator in anterior to posterior specification. HOXA9 overexpression leads to growth of the cell pool. A mechanism through which HOXA9 exerts this effect is the upregulation of IGFI. In conclusion, HOXA9 appears to have pro-oncogenic activity in the premalignant stage of colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


OP308 TOLL-INTERACTING PROTEIN DEFICIENCY PROTECTS MICE FROM COLITIS-ASSOCIATED CANCER BY MODULATING ANTI-TUMORAL IMMUNITY

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Introduction: Genetic deletion of the Toll-interacting protein (Tollip) -an IL-1R and TLR2/4 regulator- leads to increased acute and chronic colitis in mice. We sought to investigate whether increased susceptibility to inflammation had an impact on inflammation-driven colorectal carcinogenesis.

Aims & Methods: Colitis-associated cancer (CAC) was induced in 18-20 week old littermates C57BL/6 mice by azoxymethane (AOM) i.p. injection and 3 cycles of 2.5% oral dextran sodium sulfate (DSS) treatment. Tumor development was assessed immunohistochemically, histologically and histochemistry. The proliferative index in the colon were determined by TUNEL assay and Ki67 immuno- histochemistry and quantified using the Image J software. Cytokine and gene expressions were measured by RT-qPCR. SMAD2 phosphorylation was assessed by western blot.

Result: Tollip KO mice had significantly lower endoscopic tumor scores than WT littermates upon AOM-DSS exposure (8.4 ± 7.8 vs 13.4 ± 6.4, p < 0.05). Likewise, tumor numbers (4.9 ± 3.5 vs 7.1 ± 3.0, p < 0.05) and size were reduced. Immunohistological studies demonstrated reduced apoptotic index (79.3 ± 75.0 vs 246.8 ± 152.9, p < 0.05) and lower proliferation (21.0 ± 8.5 vs 27.9 ± 7.3, ns) in Tollip KO tumors when compared to wt controls. RNA analyses showed that Tollip ablation favors an anti-tumorigenic environment with reduced Bcl-xL (85.9 ± 50.9 vs 36.2 ± 39.5) and e-myc expression (6.2 ± 4.9 vs 2.1 ± 2.6). Importantly, Tollip deficiency led to reduced Foxp3 abundance (3.7 ± 2.6 vs 2.1 ± 1.7) in unchallenged colonic as well as in tumoral tissues. In addition, Tollip deficient tumors harbored reduced TGFbeta expression as well as reduced SMAD2 phosphorylation suggesting that TGFbeta signaling is dysfunctional in the absence of Tollip.

Conclusion: Our data show that Tollip partially favors colonic oncogenesis despite being protective against colitis. Putative mechanisms include reduced tumoriogenesis-associated regulatory T cells and aberrant TGFβ-induced signals in Tollip deficient mice.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

western blot analysis. The gene expression of transformed organoids was assessed by means of quantitative reverse transcription PCR.

Result: The treatment with the inflammatory reagents in mouse colonic organoids showed the time-dependent induction of NF-κB target genes. Particularly, the expression of DUOX2 gene was gradually increased by the continuous stimulation with inflammatory reagents for 40 weeks. 3D immunostaining analysis showed NF-κB p65 was accumulated in nuclei longer time of the stimulation, indicating that long-term stimulation might lead to a stronger activation of NF-κB signaling. Interestingly, accumulated NF-κB signaling by long-term stimulation remained active after the removal of all inflammatory reagents whereas NF-κB p65 signaling induced by short-term stimulation was completely shut down by the removal of all inflammatory reagents, suggesting that NF-κB might be irreversibly activated by long-term stimulation. Moreover, the organs required neither R-spondin nor Wnt3a after the treatment with GSK3 inhibitor for 8 weeks, indicating that the organs might be transformed like colitis-associated cancer. Microarray analysis and Gene Set Enrichment Analysis of transformed organoids showed irreversible Akt signal activation and reduced expression of Tgfβ2, indicating that this transformation might involve the inflammatory-mediated carcinogenesis.

Conclusion: Long-term inflammation and nuclear accumulation of β-catenin leads to irreversible cell transformation, which is not dependent on survival capacity of colonic organoids. This in vitro model mimics the natural history of epithelial cell transformation during inflammation-related carcinogenesis in UC.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


OP310 THE RIBONUCLEASE RNASEH2B CONTROLS INTESTINAL STEM CELL INTEGRITY

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Introduction: The stability of genomic DNA is under a tightly controlled surveillance. Especially in highly proliferating cells, as e.g. intestinal stem cells, RNA/DNA hybrids is under a tightly controlled surveillance, as shown by acid β-galactosidase staining in intestinal crypts in IECs after treatment with GSK3 inhibitor for 8 weeks, indicating that the organs might be transformed like colitis-associated cancer. Microarray analysis and Gene Set Enrichment Analysis of transformed organoids showed irreversible Akt signal activation and reduced expression of Tgfβ2, indicating that this transformation might involve the inflammatory-mediated carcinogenesis.

Conclusion: Long-term inflammation and nuclear accumulation of β-catenin leads to irreversible cell transformation, which is not dependent on survival capacity of colonic organoids. This in vitro model mimics the natural history of epithelial cell transformation during inflammation-related carcinogenesis in UC.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


OP311 COMMENSAL FUNGI AND THEIR CELL-WALL GLYCANS INDUCE AUTOPHagy IN INTESTINAL EPITHELIAL CELLS

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Introduction: The role of commensal fungi and their fungal glycans in inducing autophagy has not been fully elucidated yet. Indeed, it was previously shown that C. albicans and S. cerevisiae can induce autophagy in intestinal epithelial cells (IECs) that are the first to encounter luminal antigens and play an active role in intestinal immune responses. We recently reported that the β-glucan receptor Dectin-1 and its major signaling mediator spleen tyrosin kinase (Syk) are expressed by normal ileal and colonic IECs. Furthermore, β-glucans, major fungal cell wall glycans, induced chemokine secretion by IECs in a Dectin-1 and Syk dependent manner. Autophagy is a homeostatic process in the gut and defects in autophagy were associated with Crohn’s disease (CD) susceptibility. Vague data exist regarding the role of fungi and their glycans in inducing autophagy.

Aims & Methods: To investigate whether fungi and fungal glycans induce autophagy in IECs. Human IEC lines (HT-29 and SW480) were challenged by C. albicans and S. cerevisiae and the β-glucan-rich cell-wall component zymosan. Autophagy was detected by means of immunofluorescence (IF) of microtubule-associated protein 1A/1B-light chain 3 (LC3) or directly visualized in cells stably expressing GFP-LC3. Syk phosphorylation was assessed by WB and IF. Mucosal samples were obtained from patients undergoing colonoscopy and active autophagy was assessed by the punctal stain of colonic LD3 in paraffin embedded sections or in frozen sections by IF.

Result: C. albicans (live, heat-killed [HK]) - or UV-inactivated, S. cerevisiae (HK) and zymosan particles induced autophagy of IEC lines. This was accompanied by an increase in the active (cleaved) form of LC3 (LC3 II) e.g. up to 3.5 fold increase in LC3 II/actin ratio in response to HKCA vs. no treatment in HT-29 cells; 2) Appearance of LC3 puncta, indicating autophagosome binding, of endogenous LC3 II was significantly correlated with GFP-LC3. Consequently, levels of autophagy were obtained upon amino-acid starvation of IECs -e.g. up to 3.7 fold increase in LC3 II/GAPDH ratio in starved SW480 cells vs. no treatment. Fungal-induced autophagy was accompanied by Syk phosphorylation and prevented upon Syk inhibition. In ileal and normal colonic mucosal autopsy samples in IECs was observed as LC3 II puncta. Autophagy was further induced ex-vivo by UV-inactivated C. albicans, zymosan or rapamycin (mTOR inhibitor, autophagy inducer).

Conclusion: Commensal fungi and their cell-wall glycans induce autophagy in IECs that is dependent on autophagy. The involvement of anti-fungal receptors such as Dectin-1. Fungal-induced autophagy may play a role in mucosal sensing of luminal microorganisms, and contribute to fungal tolerance. Thus, imbalanced response to commensal fungi (recognition, autophagy or downstream processes), may impair homeostasis and autophagy to the pathogenesis of CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

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attenuated as compared with their wild type controls. Importantly, pretreatment with Roneparstat significantly reduced, in a dose-related manner, the HSPE activity, the tissue inflammatory response, autophagy and serum amylase and lipase levels.

Conclusion: HSPE appears to play an important role in the pathogenesis of AP. The HSPE inhibitor (Roneparstat) significantly reduced the severity of the AP in an animal model. This new concept may provide a basis for prophylaxis and treatment of AP.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP313 CIGARETTE SMOKE EXTRACT INHIBITS FLUID AND HCO3- SECRETION AND CFTR ACTIVITY IN GUINEA PIGPancreatic ductal cells

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Introduction: Smoking represents an independent risk factor for the development of chronic pancreatitis (CP). It is well documented that secretion of pancreatic ductal alkaline fluid (which is regulated mostly by anion exchangers and CFTR) is diminished in CP.

Aims & Methods: In this study, we would like to understand whether smoking has any effects on pancreatic ductal fluid and HCO3- secretion. Guineapigs were exposed to cigarette smoke four times a day for 30 min for 6 weeks. The expression of CFTR was analysed by immunohistochemistry. Intracellular HCO3- concentration was measured by Elisa. Pancreatic acini were isolated from wild type (WT) and CFTR knockout (KO) mice. Intracellular Ca2+ homeostasis was disturbed. However the Ca2+ homeostasis of CFTR-deficient PDEC, but completely normal in pancreatic ductal epithelial cells of CFTR knock out mice.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP315 IDENTIFICATION AND CHARACTERISATION OF A NOVEL EARLY ONSET DIABETES GENE USING HUMAN PLURIPOTENT STEM CELLS

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Introduction: Diabetes represents one of the major burdens in the 21st century. At least 350 million people are affected worldwide. Monogenic diabetes such as juvenile onset insulin-dependent diabetes (JOD) or maturity onset diabetes of the young (MODY) accounts for approximately 1–2% of diabetes cases and results from mutations that primarily reduce β-cell function. The identification of the genetic basis of these diabetes forms has translated into novel avenues of personalized medicine in the diabetes field, but only few of these genes have been identified to date.

Aims & Methods: Based on published data, we hypothesize that a proportion of the high contribution to type 2 diabetes (T2D) and type 1 diabetes (T1D) may be caused by rare monogenic variants/mutations missed by the current GWAS strategies targeting common variants. The current project reports on such a novel gene relevant as regulator of human pancreatic islet formation but also as a novel early onset diabetes gene.

Result: Using stage-specific genome-wide profiling complemented with Chip-Seq data in differentiating human embryonic stem cells, we show that our gene binds and activates Nkx2.2, Nkx6.1 and Pdx1, all belonging to the core suite of islet lineage transcription factors. Interestingly, this gene co-occupies the enhancer and promoter regions of the latter genes together with Foxa2, Pdx1 and Gata6. Finally, we engineered human embryonic stem cells with previously identified mutations in JOD patients. Directed differentiation studies of these cells shows a disturbed binding pattern of Foxa2 and Krox242, Nkx2.1 and Pdx1 finally leading to reduced amounts of monohormonal β-cells. This reduced target gene binding results from a limited zinc affinity, due to the mutation, that would be necessary as co-factor for gene binding.

Conclusion: This platform not only allows personalised drug-testing but also sheds light on the mechanism how our JOD gene regulates pancreatic development and leads to diabetes in case of certain mutations in humans.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP316 LACK OF CFTR RESULTS IN THE IMPAIRED FUNCTION OF THE PLASMA MEMBRANE CA2+- PUMP THAT CAUSES INTRACELLULAR CA2+- OVERLOAD AND MITOCHONDRIAL DAMAGE IN THE PANCREATIC DUCTAL EPITHELIAL CELLS OF CFTR KNOCK OUT MICE

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Introduction: The cystic fibrosis transmembrane conductance regulator (CFTR) has a significant role in pancreatic ductal epithelial secretion and it’s genetic defects damage the pancreas. The exact mechanism of this pancreatic damage is only partially known. The toxic cellular Ca2+ overload is a hallmark of acute pancreatitis and in CFTR-deficient airway epithelial cells the intracellular Ca2+ homeostasis was disturbed. However the Ca2+ homeostasis of CFTR-deficient pancreatic ductal epithelial cells (PDEC) has never been investigated.

Aims & Methods: Our aim was to characterize the Ca2+ homeostasis of CFTR-deficient PDEC. Pancreatic ducts and acinar cells were isolated from wild type (WT) and CFTR knockout (KO) mice. Intracellular Ca2+ concentration ([Ca2+]i) and changes of the mitochondrial membrane potential was measured.

Result: Maximal [Ca2+]i release upon carbachol stimulation showed no difference in WT and CFTR KO PDEC. Notably, the plateau phase of the [Ca2+]i signal was significantly higher in CFTR-deficient PDEC, but completely normal in pancreatic acinar cells. Interestingly, the functional inhibition of CFTR with 10μM CFTRinh-172 had no effect on the [Ca2+]i signals. Next we investigated the Ca2+ extrusion and found that the Ca2+ extrusion was significantly lower
in CTR KO PDEC compared to WT due to the impaired function of the plasma membrane Ca$^{2+}$ pump (PMCA). In addition, the sustained elevation of [Ca$^{2+}$]$_{i}$ caused a drop in mitochondrial membrane potential in CTR KO PDEC.

**Conclusion:** Dysfunction of PMCA leads to disturbed Ca$^{2+}$ homeostasis in CTR-deficient PDEC and the consequent cellular Ca$^{2+}$ overload impairs mitochondrial function. These changes might contribute to the pancreatic damage seen in cystic fibrosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### OP317: ENDOSCOPIC DILATION OF Pancreatic Duct Structures in Chronic Pancreatitis with Multiple Plastic Stents: Results in 48 Patients

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**Introduction:** Main pancreatic duct (MPD) strictures located in the head of the pancreas often occur in the course of chronic pancreatitis (CP). Common management of these strictures is endoscopic placement of a single plastic stent. Refractory strictures require repeated stent replacement or surgical pancreaticojejunostomy. Insertion of multiple plastic stents (MPS) obtained, in a series of 19 patients, symptomatic MPD stricture resolution in 84% of the cases, after 3-year follow-up (1). The aim of this study was to evaluate the results of the MPS strategy in a larger series of CP patients.

**Aims & Methods:** Forty-eight patients (34 men; mean age 44 years, range 5–86) with severe CP and a symptomatic dominant MPD stricture located in the head of the pancreas, were evaluated. All the patients experienced pain resolution following MPD drainage with a single plastic stent. The MPD stricture was refractory to single plastic stent placement in all cases and patients underwent insertion of MPS according to the following protocol: balloon dilation of the stricture of necessary insertion of the maximum number of plastic stents allowed by the stricture tightness and pancreatic duct diameter, stents removal after 6 months.

**Result:** The median number of stents placed through the major or minor papilla was 3 (range 2–5), 8.5 to 11.5 Fr in diameter and 3 to 7 cm in length. MPS were removed after a mean time of 6.7 months (range 2–18). Eight patients (16.6%) had persistence of the MPD stricture after MPS removal and underwent replacement of an increased number of stents; 3/8 patients had a dilation of the stricture and 5/8 patients other major placement (overall success 89.5%). Following a mean follow-up of 9.5 years (range 0.3–15.5) after MPS removal, 77.1% of patients were asymptomatic. Symptomatic MPD stricture recurrence was reported in 11 patients (22.9%), after a mean time of 24.6 months (range 5–108) from MPS removal. No major complications were recorded.

**Conclusion:** Endoscopic dilation of CP-related dominant MPD strictures seems possible with the MPS technique. According to this experience on 48 patients, MPS is highly effective even at long-term follow-up in the majority of patients.

**Disclosure of Interest:** A. Tringali, V. Bove: Boston Scientific Corporation No current affiliations outside the submitted work. G. Costamagna: Olympus Japan Grant/Research Support Cook, Inc Advisory Committees or Review Panels. Grant/Research Support Boston Scientific Corporation Advisory Committees or Review Panels. Taewoong Medical Inc Advisory Committees or Review Panels. All other authors have declared no conflicts of interest.

### OP319: USE OF THE URINARY TRYPsinogen-2 DIPSTICK TEST IN EARLY DIAGNOSIS OF Pancreatitis AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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**Introduction:** One of the most serious complications of (ERCP) is acute pancreatitis. The reported incidence varies from 1.3% to 24.4% [1]. Measurement of serum amylase and lipase levels after the procedure may have a possible role for early recognition of post-ERCP pancreatitis [3]. Asymptomatic elevation in serum amylase and lipase activities after ERCP is common, occurring in approximately 25% to 75% of all patients. A rapid test strip has been developed for the detection of trypsinogen-2 in urine (The urinary trypsinogen-2 dipstick test—UT2DST) in early diagnosis of pancreatic disease [6]. The aim of this study was to evaluate the diagnostic value of the urinary trypsinogen-2 dipstick test for early diagnosis of post-ERCP pancreatitis.

**Aims & Methods:** After an informed consent by the patients the selected patients were divided to: Full clinical examination (history taking and clinical examination), laboratory investigations including (complete blood count (CBC), Bilirubin (total and direct), (ALT), (AST), alkaline phosphatase (ALP), Prothrombin time and concentration (PT & PC), urea, creatinine, serum amylase, serum lipase, urinary trypsinogen-2 dipstick test (UT2DST).

**Result:** Post ERCP UT2DST was negative in 30 patients of the non pancreatitis group (96.8%) and positive in one of them (3.2%) The test was positive in all patients with Pancreatitis (100%). UT2DST was 100% specificity was 97% with PPV 86%, NPV 100% and the P value was <0.01. Comparison between serum lipase and amylase levels post ERCP in relation to UT2DST test shows that positive UT2DST test was significantly associated with higher amylase and lipase serum levels after ERCP (post amylase and post lipase) (P <0.01).

**Conclusion:** The urinary trypsinogen-2 dipstick test can be used as an easy and rapid test for early diagnosis of post-ERCP pancreatitis with high sensitivity and specificity and can help clinicians to provide intensive care and possible medical treatment as early as possible.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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2. S.Y Yi7, J.K Lee8, J.J Hyun9, J.K Lee10

3. Aims & Methods: A pilot study suggests that aggressive intravenous hydration with lactated Ringer’s solution may reduce the development of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis. The present larger multicenter study aimed to determine what kind of intravenous hydration could reduce the incidence of post-ERCP pancreatitis.

4. Disclosures of Interest: Group and 11.6% (15/129) in the standard hydration group (P = 0.001). No significant differences in the intention-to-treat and PP-ERCP pancreatitis rates were found between the aggressive hydration with physiological saline group (6.7%, 9/134; 7.0%, 9/128) and standard hydration group (11.6%, 15/129, P = 0.167, OR = 2.05).

5. Conclusion: Aggressive hydration with lactated Ringer’s solution is more effective than standard hydration for prevention of post-ERCP pancreatitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Disclosure of Interest: All authors have declared no conflicts of interest.

References


Disclosure of Interest: All authors have declared no conflicts of interest.

References


for the patients that Permeant Endoscopic Gastrostomy was contraindicated. PTEG by endoscopic assistance may enhance the safety of the procedure and the new item that may enhance the reliability was developed.

Aims & Methods: The aim of this study is to evaluate the clinical usefulness of PTEG supported by endoscopy. A rupture-free balloon (RFB) catheter is inserted into the upper esophagus. Permeant balloon puncture with a specialized needle is then performed from the left side of patient’s neck under ultrasound-monographic control. A guide wire is inserted through the needle into the RFB, followed by a dilator and sheath. A placement tube is then inserted through the sheath, and the sheath is removed. We started to perform PTEG under endoscopy in a total of 119 patients (74 men and 45 women, mean age 71.5 years) in whom PEG was not feasible. Double Balloons equipped Overtube type RFB were used instead of primary RFB in seven cases that the puncture needle is positioned in the overtube trough the balloon. PTEG was performed for nutrition in 65 patients and for decompression in 54.

Result: Satisfactory results were achieved in all 119 patients. Median follow-up was 64.0 days in patients who received decompression because of the obstruction due to malignancies and 270.0 days in those who received nutrition. Four of 65 patients for nutrition were able to be free from tube feeding due to PTEG tube feeding support. There was one patient had tracheal penetration, which was managed conservatively. Other complications were minor oozing bleeding in seven patients that did not require blood transfusion, subcutaneous emphysema in two patients, which were managed conservatively. The complication rate was 13.4%. A stable procedure could performed in all seven cases using the new overtube and there also was no complications. No patient required surgical treatment or died after PTEG.

Conclusion: PTEG is feasible, safe, and useful. PTEG could be an optimal procedure for long-term nutrition and/or decompression even for the patients that failed the use of endoscopy enhances the safety of the procedure and allows better confirmation of each step involved. New overtube type RFB will be useful but need more experiences.

Disclosure of Interest: All authors have declared no conflicts of interest.

A126

United European Gastroenterology Journal 4(5S)

OP324 INCREASED MUCOSAL EXPRESSION OF TOLL-LIKE RECEPTORS IN ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: An adaptive Th2-type immune response to food antigens is involved in eosinophilic esophagitis (EoE). Evidences of a potential role for the innate immune system in EoE have also been shown. Toll-like receptors (TLRs), the most investigated group of transmembrane PRR in EoE, have been related to the recognition of changes in the esophageal microbiome in adult and pediatric EoE patients compared to non-EoE controls. The likely role that microbial pattern recognition receptors (PRRs) might play in EoE arises as a potential source of research in understanding the relationship of the diet, the esophageal microbiome, and the immune system activation in EoE, that has not been assessed yet.

Aims & Methods: To gather data about the potential implication of Toll like receptors (TLRs), the most investigated group of transmembrane PRR in EoE, we characterized TLR mRNA expression and protein staining in esophageal mucosal biopsy samples from adults before and after dietary treatment, and compared with control patients. Esophageal mucosal samples were fixed in formalin, embedded in paraffin, and processed for hematoxylin and eosin staining. Specific antigen retrieval and permeabilization processes were performed before samples were incubated with the primary antibodies anti-TLR1, TLR2, TLR3, TLR4, TLR6, or TLR9. Incubation with the secondary antibodies Alexa Fluor 594 goat anti-rabbit IgG or Alexa Fluor 488 goat anti-mouse IgG. Nuclei were counterstained with DAPI. Gene expression for the different TLRs was assessed in all samples after RNA was isolated with MirVanaTM kit. Simultaneous real-time PCRs were performed with TaqMan Low-Density Arrays. Thermal cycling conditions were 2 min at 50 °C, 10 min at 95 °C, followed by 40 cycles of denaturation at 95 °C for 15 s, and annealing and extension at 60°C for 1 min in an ABI PRISM 7900 HT Sequence Detection System. Relative changes in mRNA expression were calculated with the cycle threshold (Ct) method.

Result: A total of 10 EoE patients (8 men) and 10 gender-matched control subjects were included in the analysis. The groups had a mean age of 33.1 (10.1) and 53 (19.9) years, respectively. In the EoE group, peak intraepithelial eosinophil density was 56.8 (29.9) cells/hpf, which decreased to 3 (4.2) cells/hpf after SFED-based treatment (p < 0.001). Eosinophilic eosinophils were detected in all of the esophageal samples from controls. No differences in eosinophil counts were detected for atopic and non-atopic EoE patients, being 55 (30.4) x 61 (34.8) cells/hpf, respectively. Active EoE characterized by significant upregulation of TLR1 (2.7-fold increase), TLR2 (3.7-fold increase) TLR4 (4.6-fold increase) and TLR9 (3.4-fold increase) in comparison with the controls (p < 0.05 for all comparisons). Dietary treatment significantly decreased all the four TLRs to control group values (p < 0.05). Immunofluorescence staining demonstrated epithelial-predominant staining in TLR2 and TLR4, and scattered cell staining for TLR1 and TLR9. TLR expression patterns showed differences in lamina propria and epithelial layers.

Conclusion: EoE is associated with changes in expression levels of several TLRs, that reverse after effective dietary therapy. Our results points towards an interplay of diet, microbiome and innate immune responses in the pathophysiology of EoE.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016

EOSINOPHILIC OESOPHAGITIS AND GORD — ROOM M

OP323 STEP-UP EMPIRIC ELIMINATION DIET FOR PEDIATRIC AND ADULT EOSINOPHILIC ESOPHAGITIS: THE 2–4–6 STUDY

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Introduction: A six-food elimination diet (SFED) for eosinophilic esophagitis (EoE) requires almost a year on a high level of dietary restriction and multiple empiric diets. A step-up empiric elimination diet strategy (2–4–6) might be a cost-effective dietary strategy for pediatric and adult EoE.

Result: Presently, 93 patients (25 pediatric) have been included. A two-food elimination diet achieved EoE remission in 38 patients (40%) unresponsive to PPI therapy. Remission rates increased to 52% and 65% with a FFED and SFED, respectively. Individual food reintroduction has been completed in 26/38 of responders to a two-food elimination diet, of whom 85% had a single food trigger. The most common food triggers were animal milk (60%), gluten-containing cereals (25%) and both (15%). Compared to starting with a SFED, this step-up strategy (2–4–6) might allow reducing endoscopic procedures and the diagnostic process time by 35%.

Conclusion: A two-food elimination diet (animal milk, gluten-containing cereals) achieved EoE remission in 38 patients (40%) unresponsive to PPI therapy. Remission rates increased to 52% and 65% with a FFED and SFED, respectively. This diet allows prompt identification of two thirds of responders to empiric elimination diets, with fewer food triggers (one food trigger in 85% of responders) and consequently, good candidates for dietary maintenance therapy. A step-up empiric diet strategy (2–4–6) might be a cost-effective dietary strategy for pediatric and adult EoE.

Disclosure of Interest: All authors have declared no conflicts of interest.
Disclosure of Interest:

M. Collins: I have received research funds (through contracts) from Receptos (now Celgene), Meritage Life Sciences, and Aadare.
S. Gupta: Sandeep K. Gupta received consulting fees and/or speaker fees from Abbott Laboratories, Nestlé S. A., QOL, Receptos, Inc., and Meritage Pharma, Inc.
A. Schoeper: I received consultant fees from: Receptos, Receptos and grant support from: Receptos, Receptos, Falk.
A. Straumann: Dr. Staumann is a consultant to Dr Falk Pharma GmbH and has received consulting fees and/or speaker fees and/or research grants from Actelion, AG; AstraZeneca AG; Apsis Pharma; GSK; AG; Nestlé S. A.; Novartis, AG; Pfizer, AG; and Regeneron.
M. Grimm: I am an employee of Celgene.
H. Smith: I am an employee of Celgene.
C. Tompkins: I am an employee of Celgene.
A. Woo: I am an employee of Celgene.
R. Peach: I am an employee of Celgene.
P. Frohna: I am an employee of Celgene.
S. Guajarshi: I am an employee of Celgene.
R. Aranda: I am an employee of Celgene.
E. Dellon: I have received research funding from Receptos/Celgene; and am a Consultant for Receptos/Celgene.
All other authors have declared no conflicts of interest.

Disclosure of Interest:

A. Straumann: Dr. Staumann is a consultant to Dr Falk Pharma GmbH and has received consulting fees and/or speaker fees from Abbott Laboratories, Nestlé S. A., QOL, Receptos, Inc., and Meritage Pharma, Inc.
A. Straussmann: Dr. Staumann is a consultant to Dr Falk Pharma GmbH and has received consulting fees and/or speaker fees and/or research grants from Actelion, AG; AstraZeneca AG; Apsis Pharma; GSK; AG; Nestlé S. A.; Novartis, AG; Pfizer, AG; and Regeneron.
M. Grimm: I am an employee of Celgene.
H. Smith: I am an employee of Celgene.
C. Tompkins: I am an employee of Celgene.
A. Woo: I am an employee of Celgene.
R. Peach: I am a former employee of Celgene.
P. Frohna: I am an employee of Celgene.
S. Guajarshi: I am a former employee of Celgene.
R. Aranda: I am an employee of Celgene.
E. Dellon: I have received research funding from Receptos/Celgene; and am a Consultant for Receptos/Celgene.
All other authors have declared no conflicts of interest.
investigating PPI-refractory patients studied off-therapy, further improving the meaningfulness of results.

Aims & Methods: We aimed to investigate whether the impairment of chemical clearance, expressed by PSPW index, and of mucosal integrity, expressed by MNBI, are helpful in segregating NERD from FH studied with impedance-pH monitoring on-PPI therapy. Further, we assessed the value of these novel parameters as predictors of PPI-refractory GERD confirmed by 3-year positive surgical outcome. On-therapy impedance-pH tracings from consecutive patients referred for PPI-refractory heartburn with/without regurgitation (i.e. < 50% of symptoms resolved healing after four week high-dose PPI therapy) were blindly reviewed. All tracings were manually analyzed to detect: acid exposure time (AET; abnormal if ≥ 5.2% over 24 hours), characteristics of reflux episodes (acid/weakly acidic) and symptom-reflux association using both symptom association probability (SAP; positive if ≥ 95%) and symptom index (SI; positive if ≥ 50%). MNBI values were calculated at 3 cm above the LES, during the overnight rest, for at least 30 minutes after excluding swallows and reflux induced changes. The PSPW index was calculated by dividing the number of refluxes followed by a swallow-induced peristaltic wave with the number of total refluxes. Patients were subdivided into refractory reflux esophagitis (RRE), healed reflux esophagitis (HRE), non-erosive reflux disease (NERD); defined by abnormal acid exposure time or normal AET but positive symptom-reflux correlation) and functional heartburn (defined by high-normal AET and negative symptom-reflux correlation) according to endoscopy and conventional impedance-pH variables.

Result: Median PSPW index and MNBI were significantly lower in 39 RRE (16%; 1145 Ohms) than in 41 HRE (25%; 1741 Ohms) and in 68 NERD (29%; 2374 Ohms) patients, and in all three GERD subgroups compared to 41 FH cases (67%; 3488 Ohms) (P < 0.001). Comparing NERD to FH, PSPW index showed a lower curve greater than 0.25 cm H2 that has an inter-observer range greater than MNBI at recurrence-free characteristic analysis (0.886 vs. 0.677, P = 0.005). PSPW index was abnormal preoperatively in 53/53 patients with positive surgical outcome and resulted independent predictor of PPI-refractory GERD at multivariate analysis, (odds ratio 4.993, P = 0.001).

Conclusion: At on-therapy impedance-pH monitoring, impaired chemical clearance and mucosal integrity characterize PPI-refractory typical GERD. PSPW index and MNBI efficiently distinguish PPI-refractory NERD from FH and PSPW index is helpful for selecting surgical candidates.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP328 PRELIMINARY RESULTS OF A PROSPECTIVE MULTI-CENTER REGISTRY OF LOWER ESOPHAGEAL SPHINCTER STIMULATION FOR GERD: THE LESS-GERD REGISTRY

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Introduction: Safety and effectiveness of electrical stimulation of the lower esophageal sphincter (LES-ES) using the Endostim® LES Stimulation System (The Hess Company, CA) has been demonstrated in clinical trials. Limited data available on outcomes in clinical practice.

Aims & Methods: An ongoing, prospective international multicenter web-based registry is collecting data in patients with disruptive GERD symptoms treated with LES-ES in clinical practice at baseline and at routine follow-ups for 5-years.

Demographics, adverse events, GERD symptoms recorded in daily diaries, or magnetic data (esophageal pH / manometry) are collected or MRI every 6–12 months (depending on baseline findings). 293 (85%) familial pancreatic cancers were detected in almost 40%1. However, there is limited understanding risk for neoplastic progression and the natural history of low risk detected lesions after baseline screening. The long-term clinical outcomes of radiologic surveillance aiming to detect early PDA and high-grade precursor lesions (IPMN HGD or PanIN3 or HPC) are also not well understood.

Aims & Methods: To determine the incidence of surveillance-detected pancreatic lesions following baseline screening and calculate the incidence rates of invasive malignancy and high-grade neoplasia in HRI undergoing long-term surveillance. We prospectively enrolled HRI in the Cancer of the Pancreas Screening (CAPS) studies from 1998 to 2014 (n = 578) at a tertiary referral academic medical center with a comprehensive multidisciplinary pancreas screening program. HRI consisted of familial pancreatic cancer or PDA-associated gene mutation carriers (BRCA 1/2, PALB2, P16, PRSS1, STK11) who had a >6-months follow-up to baseline imaging after baseline EUS and MRI. HRI with baseline solid masses or prevalent PDA were excluded from the surveillance cohort analyses. Radiologic surveillance detected progression (new solid mass, cyst growth, or worrisome features of progression (new solid mass, and worrisome features defined by abnormal acid exposure time or normal AET but positive symptom-reflux correlation) and functional heartburn (defined by high-normal AET and negative symptom-reflux correlation) according to endoscopy and conventional impedance-pH variables.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Endoscopic ultrasonography (EUS) and/or magnetic resonance imaging (MRI) screening of asymptomatic individuals (HRI) at high risk for PDA to detect for early pancreatic neoplasia can lead to the detection of small pancreatic cancers in almost 40% of patients, however, there is limited understanding risk for neoplastic progression and the natural history of low risk detected lesions after baseline screening. The long-term clinical outcomes of radiologic surveillance aiming to detect early PDA and high-grade precursor lesions (IPMN HGD or PanIN3 or HPC) are also not well understood.

Aims & Methods: To determine the incidence of surveillance-detected pancreatic lesions following baseline screening and calculate the incidence rates of invasive malignancy and high-grade neoplasia in HRI undergoing long-term surveillance. We prospectively enrolled HRI in the Cancer of the Pancreas Screening (CAPS) studies from 1998 to 2014 (n = 578) at a tertiary referral academic medical center with a comprehensive multidisciplinary pancreas screening program. HRI consisted of familial pancreatic cancer or PDA-associated gene mutation carriers (BRCA 1/2, PALB2, P16, PRSS1, STK11) who had a >6-months follow-up to baseline imaging after baseline EUS and MRI. HRI with baseline solid masses or prevalent PDA were excluded from the surveillance cohort analyses. Radiologic surveillance detected progression (new solid mass, cyst growth, or worrisome features of progression (new solid mass, and worrisome features defined by Georgia pancreatic cysts) were compared to pathologic diagnoses or repeat abdominal imaging according to clinical surveillance protocol.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: In our 16-year cohort with long-term surveillance, the incidence of PDA was 1.5% and higher than previously estimated but majority of detected cancers were asymptomatic and resectable. Surveillance also detects early stage PanNETs and HPCls. The majority of detected proven malignancies had radiologic progression but more research is needed to improve the selection of patients for surveillance and surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP330 CLINICAL IMPACT OF ENDOSCOPIC USONOGRAPHY IMAGING OF CHRONIC PANCREATITIS IN THE Pancreatic PARENCHYMA IN PATIENTS WITH INTRADUCTAL Papillary MUCINOUS NEOPLASMS

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Introduction: The recent guideline for intraductal papillary mucinous neoplasms (IPMNs) focuses on morphological features of the lesion as signs of malignant transformation, but ignores the background pancreatic parenchyma, including features of chronic pancreatitis, a risk factor for pancreatic malignancies. Endoscopic ultrasoundography frequently reveals evidence of chronic pancreatitis (EUS-CP findings) in the background pancreatic parenchyma of patients with IPMNs. Therefore, we investigated whether background EUS-CP findings were associated with malignant IPMN.

Aims & Methods: Clinical data for 69 consecutive patients with IPMNs who underwent preoperative EUS and surgical resection between April 2010 and October 2014 were collected prospectively. The association of EUS-CP findings (total number of EUS-CP findings; 0 vs. ≥ 1) with invasive IPMN was examined. The association of EUS-CP findings with pathologic changes of the background pancreatic parenchyma (atrophy/inflammation/fibrosis) was also examined.

Result: Among patients with EUS-CP findings, invasive intraductal papillary mucinous carcinoma (IPMC) was significantly more frequent than among patients without EUS-CP findings (42.5% vs. 3.4% (1/29), p = 0.0002). In addition, patients with EUS-CP findings had higher grades of pancreatic atrophy, inflammation and fibrosis than patients without EUS-CP findings (atrophy: 72.5% (29/40) vs. 34.5% (10/29), p = 0.003, inflammation: 45.0% (18/40) vs. 20.7% (6/29), p = 0.04).

Conclusion: In IPMN patients, detection of EUS-CP findings in the background pancreatic parenchyma was associated with a higher prevalence of invasive IPMC. Accordingly, EUS examination should not only assess the morphological features of the lesion itself, but also EUS-CP findings in the background parenchyma.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP331 NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY (nCLE) FOR THE DIAGNOSIS OF SOLITARY CYSTS: A PROSPECTIVE MULTICENTER STUDY

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Introduction: nCLE of solitary pancreatic cysts is clinically challenging due to the malignant potential of several cyst subtypes. nCLE is emerging as a powerful tool for discrimination between benign and malignant cysts in vivo and in real-time, during an endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). Three clinical trials evaluated the feasibility, the safety and highlighted specific criteria for the characterization of pancreatic cystic lesions. This study aims to prospectively evaluate the diagnostic performance of nCLE procedure on a larger cohort of patients.

Aims & Methods: 217 patients carrying a single large (> 2 cm) pancreatic cystic lesion (PCL) without evidence of communication with the main pancreatic duct and scheduled for EUS-FNA procedure were included in five centers. nCLE diagnosis was based on published criteria: “superficial vascular network” for Serous Cystadenoma (SCA), “papillae” for Intraductal Papillary Mucinous Neoplasms (IPMN), “epithelial border” for Mucinous Cystic Neoplasms (MCN), “dark spots of cell aggregates surrounded by gray areas of fibrosis and vessels” for Neuroendocrine Neoplasms (NEN).

Result: Among the 217 nCLE procedures, 98.6% were successfully performed. Technical success rate was 2.3% or other significant complications occurred, nCLE was inconclusive in 27 cases. The 90 proven final diagnosis were 32 SCA, 46 Mucinous Lesions (ML) (23 IPMN, 14 MCN and 9 UML), 6 NEN, 2 PC, 1 cystic solid pseudopapillary neoplasm, 1 cystic lymphoma, 1 cystic lymphangioma, 1 congenital pancreatic cyst. These last 6 cysts were underrepresented and therefore withdrawn from statistical analysis. In the remaining 84 patients, nCLE was inconclusive in 5 cases. The performances of nCLE were as follows:

<table>
<thead>
<tr>
<th>SCA</th>
<th>ML</th>
<th>IPMN</th>
<th>MCN</th>
<th>NEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sp (%)</td>
<td>95</td>
<td>95</td>
<td>96</td>
<td>98</td>
</tr>
<tr>
<td>Se (%)</td>
<td>88</td>
<td>87</td>
<td>87</td>
<td>57</td>
</tr>
<tr>
<td>p</td>
<td>0.72</td>
<td>0.70</td>
<td>0.97</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Conclusion: This large prospective study validates the high very high sensitivity and specificity of nCLE for the diagnosis of solitary non communicating PCL which represents the main diagnostic issue. Being able to precisely discriminate between benign (SCA) or premalignant lesions (ML, NEN), the nCLE procedure would improve patient management by avoiding either repeated follow-up procedures or unnecessary resections due to diagnosis uncertainties. nCLE procedures should now be included in the guidelines.

Disclosure of Interest: B. Napoleon: Dr. Napoleon reports non financial support from Mauna Kea Technologies, personal fees from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, during the submitted work. L. Palazzo: Dr. Palazzo reports non financial support from Mauna Kea Technologies, during the conduct of the study. B. Pujol: Dr. Pujol reports non financial support from Mauna Kea Technologies, Grants from Mauna Kea Technologies, personal fees from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work. F. Caillol: Dr. Napoleon reports non financial support from Mauna Kea Technologies, Grants from Mauna Kea Technologies. M. Palazzo: Dr. Palazzo reports non financial support from Mauna Kea Technologies, during the conduct of the study. A. Aubert: Dr. Aubert reports non financial support from Mauna Kea Technologies, personal fees from Mauna Kea Technologies, during the conduct of the study. F. Maire: Dr. Maire reports non financial support from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work. L. Buscail: Dr. Palazzo reports non financial support from Mauna Kea Technologies, during the conduct of the study. A.I. Lemaistre: Dr. Lemaistre reports personal fees from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work. M. Giovannini: Dr. Giovannini reports non financial support from Mauna Kea Technologies, Grants from Mauna Kea Technologies, during the conduct of the study.

References

OP332 RISK OF PROGRESSION AMONG LOW RISK IPMNs IN A LARGE MULTICENTER SURVEILLANCE COHORT STUDY

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Introduction: Intraductal papillary mucinous neoplasms (IPMNs) are pancreatic cysts that carry a risk of malignant transformation to pancreatic ductal adenocarcinoma (PDAC). Guidelines have been evolving to best identify which criteria should qualify a patient for resection and which cysts can safely remain under surveillance.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
surveillance. Our aim was to understand which baseline cyst and patient features predict disease progression and malignant transformation.

**Aims & Methods:** Patients with clinically suspected IPMN who did not meet consensus criteria for resection at diagnosis and were surveyed for at least 12 months or underwent surgery after a minimum surveillance of 3 months were included. All patients evaluated by radiologic studies or endoscopic ultrasound between 1998 and 2015 were included. We defined progression as either an increase in size of the dominant cyst ≥20% or ≥2 mm or the development of worrisome features (mural nodule or mass, thick septations, main duct involvement or high grade dysplasia or cancer on cytology or surgical pathology). Statistical analysis was performed with the Chi square and Fisher exact tests.

Statistical analysis was performed with the Chi square and Fisher exact tests for categorical variables and Mann-Whitney U test for continuous variables. All covariates of interest with p < 0.05 in the univariate analysis were included in the logistic regression model.

**Result:**

<table>
<thead>
<tr>
<th>Age at 1st study, mean (SD)</th>
<th>Nondiagnostic</th>
<th>Non-malignant</th>
<th>Benign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender, n (%)</td>
<td>95 (38.3%)</td>
<td>80 (39%)</td>
<td>24 (52.2%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
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<tr>
<td>White, n (%)</td>
<td>174 (86.6%)</td>
<td>152 (85.4%)</td>
<td>33 (82.5%)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>11 (5.5%)</td>
<td>11 (6.2%)</td>
<td>5 (12.5%)</td>
</tr>
<tr>
<td>Asian, n (%)</td>
<td>9 (4.5%)</td>
<td>8 (4.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Smoker ever, n (%)</td>
<td>100 (43.1%)</td>
<td>86 (44.1%)</td>
<td>22 (51.2%)</td>
</tr>
<tr>
<td>ETOH use ever, n (%)</td>
<td>108 (47%)</td>
<td>85 (44.7%)</td>
<td>22 (50%)</td>
</tr>
<tr>
<td>CP, n (%)</td>
<td>9 (3.7%)</td>
<td>5 (2.5%)</td>
<td>3 (6.8%)</td>
</tr>
<tr>
<td>AP, n (%)</td>
<td>18 (7.5%)</td>
<td>10 (5.1%)</td>
<td>2 (4.5%)</td>
</tr>
<tr>
<td>Cancer, n (%)</td>
<td>75 (30.5%)</td>
<td>78 (38.4%)</td>
<td>21 (46.7%)</td>
</tr>
<tr>
<td>Colon, n (%)</td>
<td>3 (1.2%)</td>
<td>4 (2%)</td>
<td>3 (6.7%)</td>
</tr>
<tr>
<td>Breast, n (%)</td>
<td>7 (2.8%)</td>
<td>12 (5.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Prostate, n (%)</td>
<td>6 (2.4%)</td>
<td>12 (5.9%)</td>
<td>8 (17.8%)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>56 (23%)</td>
<td>45 (22.4%)</td>
<td>20 (44.4%)</td>
</tr>
<tr>
<td>Family hx of PDAC, n (%)</td>
<td>22 (9.5%)</td>
<td>21 (11%)</td>
<td>2 (4.8%)</td>
</tr>
<tr>
<td>Baseline symptoms, n (%)</td>
<td>71 (28.6%)</td>
<td>60 (29.3%)</td>
<td>14 (30.4%)</td>
</tr>
<tr>
<td>Abnormal CEA, median (IQR)</td>
<td>11.8 (6.6)</td>
<td>11.1 (6.4)</td>
<td>16.9 (6.7)</td>
</tr>
<tr>
<td>Cyst size, median (SD), mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyst size 0–1 cm, n (%)</td>
<td>100 (40.3%)</td>
<td>94 (45.9%)</td>
<td>7 (15.2%)</td>
</tr>
<tr>
<td>Cyst size 1–2 cm, n (%)</td>
<td>120 (48.4%)</td>
<td>87 (42.4%)</td>
<td>22 (47.8%)</td>
</tr>
<tr>
<td>Cyst size 2–3 cm, n (%)</td>
<td>28 (11.3%)</td>
<td>24 (11.7%)</td>
<td>17 (37%)</td>
</tr>
<tr>
<td>Multilocality, n (%)</td>
<td>95 (38.3%)</td>
<td>78 (38.4%)</td>
<td>21 (46.7%)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head, Uncinate, Neck, n (%)</td>
<td>93 (37.7%)</td>
<td>79 (38.3%)</td>
<td>17 (37%)</td>
</tr>
<tr>
<td>Body, n (%)</td>
<td>93 (37.7%)</td>
<td>72 (35.5%)</td>
<td>15 (32.6%)</td>
</tr>
<tr>
<td>Tail, n (%)</td>
<td>61 (24.7%)</td>
<td>53 (26%)</td>
<td>14 (30.4%)</td>
</tr>
<tr>
<td>Cystosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign, n (%)</td>
<td>35 (52.2%)</td>
<td>27 (45%)</td>
<td>4 (26.7%)</td>
</tr>
<tr>
<td>Non-malignant, n (%)</td>
<td>3 (4.5%)</td>
<td>5 (8.3%)</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td>Atypical, n (%)</td>
<td>3 (4.5%)</td>
<td>4 (6.7%)</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Nondiagnostic, n (%)</td>
<td>26 (38.6%)</td>
<td>24 (40%)</td>
<td>7 (46.7%)</td>
</tr>
<tr>
<td>Cyst CE A, median (IQR)</td>
<td>24 (1, 41.4)</td>
<td>101 (14, 333)</td>
<td>2555 (13, 5775)</td>
</tr>
<tr>
<td>Cyst CE A ≥192 ng/mL, n (%)</td>
<td>13 (37.1%)</td>
<td>11 (68.8%)</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant difference as compared to non-progressors. We identified 499 patients who met inclusion criteria. Average surveillance time was 47 (+28.7) months. 251 (50%) patients showed progression: 205 (41%) progressed by size alone and 46 (9.2%) developed worrisome features. 55 (11%) met resection criteria and 21 of these went on to surgery. Pathology demonstrated 4 invasive carcinoma, 5 IPMN with high-grade dysplasia, 5 IPMN with low-grade dysplasia, 2 mucinous cystadenoma, 1 serous cystadenoma and 1 neuroendocrine tumor. We then compared predictors of progression. In a univariate analysis, progression to cancer or high-grade dysplasia was associated with male gender, a history of prostate cancer and diabetes, weight loss and initial cyst size >2 cm. A history of prostate cancer, diabetes, weight loss, elevated cyst fluid CEA and cyst size >2 cm were associated with development of worrisome features. In logistic regression analysis, a history of prostate cancer (OR 2.9; 95% CI 1.7–7.7) and weight loss (OR 2.47; 95% CI 1.18–6.1) were associated with development of worrisome features. There were no baseline predictors of cyst size increase alone. Baseline characteristics such as race, smoking or alcohol use, a strong family history of PDAC, multifocality and location of cysts were not associated with increased disease progression.

**Conclusion:** In the largest multicenter surveillance study of low risk IPMNs to date, we showed that 41% of suspected IPMNs increased in size only, 9% developed worrisome features and 2% developed high-grade dysplasia or cancer. Among baseline characteristics, none were predictive of size increase. A personal history of prostate cancer and weight loss were the strongest predictors of the development of worrisome features.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP333 MULTIMODALITY TREATMENT OF LOCALLY ADVANCED PANCREATIC CANCER, INCLUDING FOLFIRINOX CHEMOTHERAPY, SURGICAL EXPLORATION AND IRREVERSIBLE ELECTROPOPTION: PROSPECTIVE SERIES OF 132 CONSECUTIVE PATIENTS**


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3Research Unit, Academic Medical Center, Amsterdam/Netherlands
4Gastroenterology, Academic Medical Center, Amsterdam/Netherlands
5Medical Oncology, Academic Medical Center, Amsterdam/Netherlands
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7Medical Oncology, Academic Medical Center, Amsterdam/ Netherlands

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**Introduction:** Novel treatment options in locally advanced pancreatic cancer (LAPC), including FOLFIRINOX and irreversible electroporation (IRE) have shown promising survival-rates. However, outcomes are heavily influenced by selection bias as most studies were retrospective and excluded patients who did not receive FOLFIRINOX or had progressive disease.

**Aims & Methods:** We aimed to describe outcomes of multimodality treatment with chemotherapy, surgical exploration and IRE in a prospective consecutive LAPC-cohort. Patients with histologically proven LAPC (Dutch guideline: >90 arterial and/or >270 venous involvement) were prospectively registered (September 2013–March 2015). After 3 months of chemotherapy (FOLFIRINOX for WHO physical status 0–1 patients, otherwise gemcitabine), restaging was performed by assessing RECIST 1.1-response, resectability, and IRE-eligibility (tumor ≤5 cm, sufficient vascular patency). All patients with non-progressive disease, eligible for IRE proceeded to laparotomy, regardless of resectability. The study was registered with the Dutch trial registry NTR4230.

**Result:** Of 132 consecutive LAPC-patients, 93 (70%) received chemotherapy (59% FOLFIRINOX). After 3 months, 59 (45%) had non-progressive disease and 36 (27%) were IRE-eligible and underwent laparotomy, resulting in 14 (11%) pancreatic resections and 15 (11%) IREs. In 36 patients who underwent laparotomy, IRE (45%) and 14 (39%) suffered from Clavien-Dindo grade ≥3 complications (6/14 resection, 7/15 IRE, 1/7 palliative exploration). Four patients (11%) died within 90 days (1/4 resection, 2/15 IRE, 1/7 palliative exploration). Median overall survival after resection, IRE, in non-progressive disease without resection/IRE and in all 132 patients was 34, 19, 17 and 11 months respectively.

**Conclusion:** This is the first prospective study on multimodality treatment, including FOLFIRINOX and IRE, in a consecutive LAPC-cohort. An 11% resection-rate with a median overall survival of 34 months seems highly promising where no clear survival benefit was seen after IRE. This study highlights the importance of reporting on unselected LAPC-cohorts.

**Disclosure of Interest:** R.C. Martin: Prof. Dr. Marin is a paid consultant for AngioDynamics. K.P. van Lienden: Dr. Krijn van Lienden is a paid consultant for AngioDynamics. All other authors have declared no conflicts of interest.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

wireless telemetry system (telemetric probe was surgically implanted 6 weeks after the first surgical procedure, when rats were in the proestrus stage of their menstrual cycle). Linaclotide (3 ug/kg/day) was dosed chronically for 14 days to measure plasma extravasation, and the effects of linaclotide (3 ug/kg/day) on vaginal hyperalgesia were measured after acute (day 1, 2 hours after dosing) and chronic (day 5) dosing, compared to vehicle. Plasma extravasation and EMG measurements were done 7 weeks after the first surgical procedure, when rats were in the proestrus stage of their reproductive cycle. GC-C mRNA expression was determined by qRT-PCR.

Result: Chronic oral dosing of linaclotide (n=12) significantly (P<0.01) reduced Evans Blue plasma extravasation in the small intestine compared to vehicle (n=12). In contrast, chronic dosing did not have an effect on plasma extravasation of endometrial cysts and other pelvic organs. Consistent with these findings, expression of GC-C was restricted to the small intestine, and not detected in endometrial cysts and other pelvic organs. Both, acute and chronic oral dosing of linaclotide induced rapid and significant (P<0.05 (n=14) and P<0.01 (n=14), respectively) reduced endometriosis-induced vaginal hyperalgesia, compared to vehicle treated animals (n=9).

Conclusion: Oral administration of linaclotide significantly reduced visceral pain in chronic model of endometriosis and vaginal hyperalgesia. These findings are consistent with the hypothesis that GC-C agonism, beyond its established effect of improving abdominal pain in IBS-C patients may also be able to alleviate pain in a spectrum of chronic pelvic pain conditions possibly through common sensory peripheral and central neuronal mechanisms.

Disclosure of Interest: P. Ge: Employee, stock holder and stock options from Ironwood pharmaceuticals Inc.
J. R.: Consultant at Ironwood Pharmaceuticals, Inc
N. Dmitrieva: Contractor at Ironwood Pharmaceuticals, Inc
A. Silos-Santiago: Employee, stock holder and stock options from Ironwood Pharmaceuticals Inc and Decibel Therapeutics.
C. B. Kurtz: Employee, stock holder and stock options from Ironwood Pharmaceuticals Inc
G. Hannig: Employee, stock holder and stock options from Ironwood pharmaceuticals Inc.

OP334 MULTIDISCIPLINARY ONLINE EXPERT PANEL FOR PATIENTS WITH IRREVERSIBLE PROSTATE CANCER: CLINICAL RESULTS


Contact E-mail Address: J.vanshil@nvmc.nl

Introduction: Despite the centralization of pancreatic cancer treatment, both post-operative mortality and overall survival are improving. However, a downside of centralization is the decreasing knowledge on new treatment strategies and clinical trials in non-pancreatic centers.

Aim: The Dutch Pancreatic Cancer Group (DPCG) aimed to develop an online expertpanel to facilitate and tailor rapid expert advice for patients with (locally advanced) pancreatic cancer. In collaboration with Aexist (The Hague, the Netherlands) we developed the ImageHub system which allows for an online review of CT scans. Future studies have to determine the impact of an online expertpanel on the accessibility of new treatment strategies, survival and quality of life.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016
08:30-10:00
CONSTITUTION AND FECAL INCONTINENCE: FROM BENCH TO BEDSIDE - ROOM N2

OP335 ORAL ADMINISTRATION OF THE GUT-RESTRICTED GLYCUANE CYCLASE-C AGONIST, LINACLIDATE, REDUCES ENDOMETRIOSIS-INDUCED VAGINAL HYPERALGESIA

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3Erasmus Medical Center, Rotterdam/Netherlands
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6Surgery, Erasmus Medical Center, Rotterdam/Netherlands
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Contact E-mail Address: pge@ironwoodpharma.com

Introduction: Linaclotide, a guanylate cyclase-C (GC-C) agonist, reduces abdominal pain and improves constipation in patients with Irritable Bowel Syndrome with Constipation (IBS-C). We have shown that linaclotide activates GC-C expressed on intestinal epithelial cells, resulting in the production and release of cyclic GMP (cGMP), which accelerates gastrointestinal transit and inhibits gastrointestinal motility.

Conclusion: The results showed an online expertpanel is feasible and changed the clinical decision in almost half of the patients with locally advanced pancreatic cancer. Future studies have to determine the impact of an online expertpanel on the accessibility of new treatment strategies, survival and quality of life.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Linaclotide, a guanylate cyclase-C (GC-C) agonist, reduces abdominal pain and improves constipation in patients with Irritable Bowel Syndrome with Constipation (IBS-C). We have shown that linaclotide activates GC-C expressed on intestinal epithelial cells, resulting in the production and release of cyclic GMP (cGMP), which accelerates gastrointestinal transit and inhibits gastrointestinal motility.

Conclusion: Linaclotide may similarly reduce visceral pain in other chronic pelvic pain conditions, and tested this hypothesis in a rat model of endometriosis-induced vaginal hyperalgesia.

Access & Metadata: One important segment of the uterine horns of female Sprague-Dawley rats were surgically removed and 4 pieces of uterine horn tissue/rat were implanted around the mesentric arteries adjacent to the cecum (endometrium side down). Pelvic organ/tissue permeability was measured by Evans Blue dye plasma extravasation (vascular permeability). The severity of vaginal hyperalgesia was accessed by visco-motor responses (VMR) to vaginal balloon distention. VMR was recorded by electromyography (EMG) using a wireless telemetry system (telemetric probe was surgically implanted 6 weeks after the first surgical procedure, when rats were in the proestrus stage of their reproductive cycle. GC-C mRNA expression was determined by qRT-PCR.

Result: Chronic oral dosing of linaclotide (n=12) significantly (P<0.01) reduced Evans Blue plasma extravasation in the small intestine compared to vehicle (n=12). In contrast, chronic dosing did not have an effect on plasma extravasation of endometrial cysts and other pelvic organs. Consistent with these findings, expression of GC-C was restricted to the small intestine, and not detected in endometrial cysts and other pelvic organs. Both, acute and chronic oral dosing of linaclotide induced rapid and significant (P<0.05 (n=14) and P<0.01 (n=14), respectively) reduced endometriosis-induced vaginal hyperalgesia, compared to vehicle treated animals (n=9).

Conclusion: Oral administration of linaclotide significantly reduced visceral pain in chronic model of endometriosis and vaginal hyperalgesia. These findings are consistent with the hypothesis that GC-C agonism, beyond its established effect of improving abdominal pain in IBS-C patients may also be able to alleviate pain in a spectrum of chronic pelvic pain conditions possibly through common sensory peripheral and central neuronal mechanisms.

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C. B. Kurtz: Employee, stock holder and stock options from Ironwood pharmaceuticals Inc
G. Hannig: Employee, stock holder and stock options from Ironwood pharmaceuticals Inc.
OP337 PATIENTS’ PERCEPTIONS OF CONSTIPATION DIFFER STRIKingly FROM THOSE OF GASTROENTEROLOGISTS, SPECIALISTS AND GENERAL PRACTITIONERS, AND THERE IS NO CONSISTENT AGREEMENT WITH THE ROME III CRITERIA

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Introduction: Constipation is a prevalent condition with a huge socioeconomic burden. It is unclear whether patients’ and doctors’ perceptions of the definition of constipation agree with each other or with formal diagnostic criteria proposed by expert committees (e.g. Rome III).

Aims & Methods: A cross-sectional survey was undertaken to compare the symptoms perceived to be important for the diagnosis of constipation within the adult general population (with and without constipation), gastrointestinal (GI) specialists and general practitioners (GPs) in the UK. Symptoms considered important in diagnosing constipation and their perceived burden, together with 10 case studies based on the Rome III criteria were investigated. Responses were compared between groups using chi squared test.

Result: 2,257 members of the general population (1,623 self-reported constipation) and 564 GI specialists and 411 GPs completed the survey. Only a minority of the general population considered the Rome III symptoms important for diagnosing constipation (Table 1). Infrequent bowel movements were most frequently reported as important by GI specialists (65%), compared with less than half of GPs (41%) and less than a third of the constipated (26%) and non-constipated (28%) general population (P < 0.001).

Table 1: Frequency of symptoms perceived to be important for a diagnosis of constipation

<table>
<thead>
<tr>
<th>Rome III symptoms</th>
<th>General Population</th>
<th>Without GI constipation</th>
<th>Constipation specialists GPs</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrequent bowel movements</td>
<td>28%</td>
<td>26%</td>
<td>65%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hard stool</td>
<td>26%</td>
<td>32%</td>
<td>57%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Straining</td>
<td>43%</td>
<td>40%</td>
<td>53%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sense of incomplete evacuation</td>
<td>15%</td>
<td>24%</td>
<td>21%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Manual disimpaction</td>
<td>14%</td>
<td>15%</td>
<td>32%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-Rome III symptoms</td>
<td>42%</td>
<td>29%</td>
<td>33%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Long time on toilet without stool</td>
<td>37%</td>
<td>33%</td>
<td>56%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The symptoms most frequently considered to be bothersome were different for each of the groups: manual disimpaction for the constipated general population, bloating for GI specialists and straining for GPs. In the 10 case studies, correct diagnoses were made by doctors (GPs and GI specialists) on 79–80% of occasions. However, on average, the absence of constipation was correctly identified by doctors in 85–92% of the six cases without constipation, whereas the presence of constipation was correctly identified in only 60–70% of the four cases with constipation.

Conclusion: There are striking differences in the perceived definition and burden of symptoms of constipation between the general population, GI specialists and GPs, and variable agreement with the Rome III criteria. These differences have major implications for patient care, management and satisfaction with treatment. The findings reinforce the need to re-evaluate current diagnostic criteria for constipation in clinical practice and to ensure these are communicated widely.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP338 EFFICACY AND SAFETY OF NALDEMEdINE FOR THE TREATMENT OF OPIOID-INDUCED CONSTIPATION IN SUBJECTS WITH CHRONIC NON-CANCER PAIN RECEIVING OPIOID THERAPY: RESULTS FROM TWO PHASE 3 CLINICAL TRIALS

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Introduction: Opioids effectively treat pain but their use is limited by side effects including opioid-induced constipation (OIC). Naldemedine is an oral, peripherally-acting mu-opioid receptor antagonist that is being evaluated for the treatment of OIC.

Aims & Methods: Two identical Phase-3, double-blind, randomized, placebo-controlled 12-week studies were conducted. In both studies, subjects 18 to 80 years old, with chronic non-cancer pain and OIC, taking opioids for ≥3 months and on a stable regimen for ≥1 month, not on laxatives, and meeting all other eligibility criteria were randomized (1:1) to naldemedine 0.2 mg taken orally QD or placebo. The primary objective was to evaluate the efficacy of naldemedine vs. placebo as assessed by the proportion of responders. A responder was defined as someone who had ≥9 positive response weeks (PRW) out of 12 weeks and ≥3 PRW out of the last 4 weeks. A PRW was defined as ≥3 spontaneous bowel movements (SBMs)/week and ≥1 SBM/week increase from baseline. The safety and tolerability of naldemedine was also assessed. Studies were approved by an IRB prior to randomization of subjects and conducted in accordance with GCP Guideline (ClinicalTrials.gov identifier NCT01935158 and NCT01993940).

Result: In study 1, 547 subjects were randomized (naldemedine 274; placebo 273) and in study 2, 553 subjects were randomized (naldemedine 277; placebo 276). In both studies, there were a significantly greater proportion of responders with naldemedine relative to placebo (Study 1: naldemedine 47.6%; placebo 34.6%, P < 0.001). Study 2: naldemedine 55.5%; placebo 33.6%, P < 0.001). Naldemedine showed an increase greater than placebo, relative to the placebo group, from baseline to the last 2 weeks of the study period in the frequency of complete SBMs and the frequency of SBMs without straining. Summary measures of treatment-emergent adverse events (TEAEs) were generally similar between naldemedine and placebo groups in both studies. The TEAEs reported for >5% of subjects and at a higher frequency in naldemedine relative to placebo were abdominal pain and diarrhea. In both studies, treatment with naldemedine was not associated with signs or symptoms of opioid withdrawal, and the analgesic effect of opioids was not affected.

Conclusion: Results from two identically designed Phase 3 studies demonstrated a consistent efficacy and safety profile of naldemedine as a treatment for OIC in subjects with chronic non-cancer pain. Naldemedine treatment resulted in a significantly greater proportion of responders than placebo, with improvement early on and throughout the 12-week study period. Naldemedine was generally well tolerated in these two studies.

Disclosure of Interest: M.E. Hale: I was a Principle Investigator for the Clinical Trials, and a consultant for Shionogi
J. Wild: 1) I was a Principal Investigator on Composel trial and 2) I did receive a stipend from Shionogi for clinical study review. Otherwise I have no relationship with the company.
J. Reddy: Employee of Shionogi
T. Yamada: Employee of Shionogi
J.C. Arjona Ferreira: Employee of Shionogi

OP339 PILOT STUDY COMPARING THREE METHODS OF SCREENING FOR FECAL INCONTINENCE

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Introduction: Fecal incontinence (FI) affects 8% of US adults overall including 15% over age 70. However, less than 1/3 of people with FI have discussed this problem with their physicians, and most of these reports that they were not screened but volunteered this symptom. This suggests many physicians are not screening for FI.

Aims & Methods: The goal of this study was to provide preliminary information on the effectiveness of 3 simple screening interventions for increasing screening rates in a Geriatric Medicine Clinic (GMC) at the University of North Carolina: a gastrointestinal (GI) symptom checklist distributed in the clinic waiting room, screening by the clinic nurse, and screening by the medical provider. The GI symptom checklist included fecal incontinence [accidental bowel leakage] and 7 other common GI symptoms. Patients checked all they had experienced in the last month, and gave the checklist to the clinic nurse. To facilitate screening by the nurse, the nurse was pre-screened and pre-tested on our suggested three screening questions. We also gave
OP340 COPING WITH Fecal INCONTINENCE: A POPULATION STUDY

E.V. Carrington1, O. Palsson2, S. Heymen3, S. Gauld4, M. Simiren5, W. E. Whitehead6

1Aims & Methods: This study aimed to describe the most common coping strategies, the impact of FI severity on ways of coping, whether those under a physician’s care cope differently and the perceived overall effectiveness of individuals’ coping strategies. A limited review of electronic medical records of all patients seen at their index visit for this study, including 6 new FI diagnoses. Three of the 6 new diagnoses occurred during the GI checklist intervention and 3 during provider screening (p = .10). None occurred during nurse screening. The GI symptom checklist was rated the least burdensome by the 11 providers (p = .05). Five of the 11 providers said the benefits of screening outweighed the burden, 4 were undecided, and 2 rated screening as too burdensome (p = .001). Phone interviews were completed by 88 patients; 33/38 (86.8%) confirmed they were screened by their doctor or nurse, 55.7% said no, and 6.8% said they did not know or declined to answer.

Conclusion: Systematically encouraging geriatric medicine providers to screen for FI significantly increased the number of patients receiving a new diagnosis of FI compared to baseline. Most geriatricians report the benefits outweighing the burdens of screening. Distributing a GI symptom checklist in the clinic was rated least burdensome and as effective as direct screening by the geriatrician. However, these interventions to improve screening were only partially effective: 37.5% of patients remained being asked about FI at their clinic visit.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


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Disclosure of Interest:

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Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are used for endoscopic treatment of superficial duodenal adenoma. In the case of a same lesion (hybrid Endoscopic Resection, HER), ESD has higher rates of complications than EMR, and is technically challenging. We present results on the adverse events and clinical outcome of ESD/HER compared to EMR in our cohort of patients.

Aims & Methods: In a single tertiary center, we cross-examined our database of endoscopic procedures to identify patients with duodenal adenoma treated by ESD, HER and EMR between 2006 and 2016. We included patients with non-ampullary lesions and familial adenomatus polyposis. Procedure was qualified as ESD when an endoscopic knife was used. When resection was achieved with endoscopic knife and resection loop, the procedure was considered as HER. We divided complications in 3 groups (ASGE and ESGE recommendations): intra-procedural, early complications (occurring within 15 days) and late complications (occurring after 15 days). Results were expressed as medians, and compared with Student’s-t test, Pearson’s chi-squared test.

Results: Thirty-eight patients underwent ESD/HER procedure out of a total of 111 patients. The resection was complete in 38/39 lesions in ESD/HER group, and 141/149 lesions in EMR group (p = 0.182). Histological finding showed 4% adenocarcinomas, 34% HGD, and 60% LGD. No significant differences were observed in terms of age, sex, location of lesions or length of hospitalization. There were significant differences in the procedure time (108 min ESD/HER, 79 min EMR), intraprocedural complications (46% ESD/HER; 23% EMR) and early complications (23% ESD/HER, 9% EMR). Intra-procedural complications occurred in 46% of ESD/HER vs 23% in EMR (p = 0.015), including haemorrhage (25.6%, ESD/HER 20.1%) and perforation (ESD/HER 20.5%, EMR 3.4%, p = 0.07). In ESD/HER, perforations occurred between 2006 and 2010. Early complications (Hemorrhage, perforation, pancreatitis) occurred in 23% ESD/HER vs 9% in EMR (p = 0.001), managed either by medical treatment. Five cases of perforation occurred (4 ESD/HER, p = 0.001) and 2 cases needed surgery. Three cases of late complications (stenosis) occurred in the EMR group. No mortality reported during the study.

Conclusion: There is a higher rate of intraprocedural and early complications in the ESD/HER group, especially in case of perforation. Those events can be well managed in a tertiary center, experienced in ESD and HER. Perforation rate tends to decrease over time, reflecting the experience acquired in our team. This highlight the importance of a learning process in ESD/HER procedure, which results in better management of intraprocedural and early complications.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP344 WATER JET SUBMUCOSAL DISSECTION OF PORCINE ESOPHAGES WITH THE HYBRIDKNIFE® AND ERBEJET® 2 SYSTEM
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Introduction: Endoscopic submucosal dissection (ESD) is technically difficult because of narrow working spaces and ease of perforation due to the lack of serosa. HybridKnife® is a recently developed ESD device that is combined with the high-pressure water jet ERBEJET® 2 system to lift mucosa. We hypothesized this device could make submucosal dissection safer and studied this in porcine esophagus.

Methods: Water pressures of 30–70 bar were tested to determine the appropriate waterjet ESD with HybridKnife® (WJ-ESD) pressure in one pig. WJ-ESD dissection times were compared with those of C-ESD using DaluKnife® (C-ESD). Each of 3 virtual esophageal lesions in 2 pigs were dissected alternatively using both methods from the lower to upper esophagus. For WJ-ESD, the submucosa, except for hard fibrous tissues, was dissected using water pressure alone.

Results: Using 50 bar of water pressure resulted in the best balance between dissection speed and view-disturbing water backflow. The dissection speeds for the lower, middle, and upper esophagus were 0.2, 0.9, and 0.2 cm²/min in 50 bar WJ-ESD and 1.1, 0.5, and 1.0 cm²/min in C-ESD, respectively. Minor bleeding was frequent in WJ-ESD, but was easily stopped by electrocoagulation with the same needle. No perforation was observed in either group. Thermal damage of the muscle layer was smaller for WJ-ESD (4, 6, and 8%) compared with C-ESD (14, 16, and 7%).

Conclusion: WJ-ESD spent longer dissection time, but damaged less muscle layer. It can be combined with electrocautery ESD.

Disclosure of Interest: All authors have declared no conflicts of interest.

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OP345 ORAL ADMINISTRATION OF CONDITIONED MEDIUM OBTAINED FROM AMNION-DERIVED MESENCHYMAL STEM CELL CULTURE PREVENTS ESOPHAGEAL STRICURE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION IN PIGS
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Introduction: Endoscopic submucosal dissection (ESD) for esophageal cancer has been widely accepted in last decade; however, it often causes postoperative stricture when over three-quarters of the circumference of the esophagus is dissected, and lowers quality of life for patients. Although steroid is generally used to prevent stricture by exerts anti-inflammatory effects and side effects are of concern. Mesenchymal stem cells (MSCs) have been reported to be a valuable cell source in regenerative medicine, and large amounts of MSCs can be noninvasively isolated from human amnion, which is discarded after birth. Moreover, cultured amniotic (CM) obtained from MSCs has been reported to have anti-inflammatory and anti-fibrotic effects in several animal models. In this study, we evaluated whether CM obtained from amnion MSC culture could prevent the stricture after large esophageal ESD in pigs. Here we report that intraperitoneal administration of CM prevents stricture formation and improves tissue healing under general anesthesia. We prepared CM gel by mixing CM with carboxymethyl cellulose, and endoscopically applied 20 mL of MSC-CM gel onto the wound bed immediately after ESD, and on day 7 and on day 14 (CM weekly (CM-W) group, n = 3). Standard medium gel was used as a control group (n = 3). We also injected triamcinolone acetonide (80 mg) into the remained submucosa immediately after ESD (steroid group, n = 3). In addition, we administered 40 mL of CM gel orally from day 1 through day 4 after ESD (CM daily (CM-D) group, n = 3). We compared the dissection rate and for histological analysis evaluating fiber thickness and muscle fiber atrophy (masson-trichrome staining), re-epithelialization (p63 and Ki-67), the number of activated myofibroblasts (α-SMA), capillary density (CD31), infiltration of macrophages (CD107a) and neutrophils (myeloperoxidase). The experimental protocol was approved by the Animal Care and Use Committees of Hokkaido University.

Results: Stricture rate in CM-W, CM-D and steroid groups was significantly less than control group (56.3 ± 7.1%, 52.3 ± 4.7% and 49.3 ± 4.2% vs. 80.0 ± 2.0%, respectively). Histological examination demonstrated that the number of activated myofibroblasts and fiber thickness were significantly suppressed in CM-W, CM-D and steroid groups as compared with control group (26.8 ± 8.6, 21.5 ± 4.9 and 20.6 ± 2.3 vs 68.3 ± 5.7 cells/HPF; 832.9 ± 26.1, 987.1 ± 145.1 and 944.3 ± 250.8 vs 1,609 ± 418.2 μm², respectively). There were no differences in re-epithelialization, capillary density, infiltration of macrophages and neutrophils among four groups; however, no four muscle atrophy was significantly suppressed in CM-W group compared with the control group. Aims & Methods: Our aim was to analyze the results of EUS and PET-CT in staging and restaging our patients with gastric cancer, comparing both of them with histological results. Patients who have undergone different treatment were consecutively enrolled. Only patients who finally received a surgical resection were included. All patients underwent preoperative TNM staging by means of EUS and PET-CT within 21 days prior to the surgical treatment. All endoscopic ultrasounds were performed by two experienced ultrasonographers (E.R-C, J-M.C). For most of the procedures radial echoendoscope (GF-UM160; Olympus Europe) reserve curvilinear echoendoscope for FNA, in the rare cases in which we perform it (UCT-180-05L; Olympus). Every patient received prophylactic sedation guided by the anesthesiologist and by a trained nurse. A systematic complete US evaluation was performed in each patient. Statistical analysis was carried out using the software PAWS Statistics 17.0 (SPSS Inc, Chicago, ILL). The chi-square and the Kruskal-Wallis tests were used to evaluate the consistency between EUS and histological staging of gastric cancer. The UCT-180-05L echoendoscope and Fisher exact tests were used to compare EUS and PET-CT as appropriate. A p-value less than 0.05 was considered statistically significant.

Results: 256 patients (178 men; aged 67.6 ± 12.1 years) with an endoscopic and pathologic diagnosis of gastric adenocarcinoma were included between January 2011 and December 2014. The overall accuracy of T staging using EUS was 78% in our series. Regarding restaging, the overall accuracy for T staging was 80.2%, Considering lymph node involvement, the accuracy of EUS was 76%. Both p-values were similar to what was observed for PET in a large database with statistical differences (p = 0.02). The accuracy of EUS for preoperative N0, N1, N2 and N3 staging was 76.2%, 78.6%, 76.2% and 90% respectively. When studying the performance of both techniques in restaging we found that EUS had a better performance when compared with the conventional techniques which can change patients’ management. In this regard, the accuracy in distinguishing T1-T2 tumors vs. T3-T4 tumors was 91.3%, better than in the first staging. Indeed, similar results were found in N staging with an accuracy of 88.3% for N-positive v. N-negative distinction. By contrast, PET-CT showed an accuracy...
of 69% for lymph node involvement when restaging, inferior to what was found for EUS and for the initial staging (p < 0.0001).

| TABLE 1: Accuracy of EUS and PET vs Histology |
|-------------|------------|----------|--------|--------|----------|
|             | Sensitivity | Specifcity | PPV    | NPV    | Accuracy  | Kappa    |
| T1          | 50%         | 95.8%      | 75%    | 95.7%  | 94.5%     | 0.57     |
| T2          | 41.7%       | 88.5%      | 41.7%  | 88.5%  | 80.8%     | 0.30     |
| T3          | 38.5%       | 86.5%      | 50%    | 80%    | 74%       | 0.27     |
| T4          | 77.3%       | 61%        | 61.7%  | 73.7%  | 68%       | 0.37     |
| T4a         | 76.2%       | 65.5%      | 61.5%  | 75%    | 70%       | 0.40     |
| T1-T2/T3-T4 | 87.3%       | 50%        | 84.2%  | 56.3%  | 78.1%     | 0.39     |
| N0          | 73.9%       | 78.9%      | 81%    | 71%    | 76.2%     | 0.52     |
| N1          | 50%         | 83.3%      | 33.3%  | 90.9%  | 78.6%     | 0.28     |
| N2          | 55.6%       | 81.8%      | 45.5%  | 87%    | 76.2%     | 0.35     |
| N3          | 97.4%       |            |        |        | 90.2%     |          |
| N+/N−       | 78.9%       | 73.9%      | 71.4%  | 81%    | 76.2%     | 0.52     |
| PET N+/N−   | 50%         | 90.9%      | 81.8%  | 69%    | 72.5%     | 0.42     |

**Conclusion:** Our results, obtained from a clinical practice, showed that the overall accuracies of EUS and PET-CT for preoperative N staging were 76.2% and 72.5%, with significant differences between both techniques. The overall accuracy of EUS for T staging was 78% and 80.2% for restaging. More importantly, our results show a significant advantage of EUS over PET-CT in restaging, even in our series, in which the vast majority of suspicious lymph nodes were not sampled. In conclusion, EUS performance in gastric cancer N staging and restaging is better than PET-CT. Both procedures showed suboptimal accuracies when considered alone, and more than one single staging method should be used.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

**OP348 SORTEILIN Deficiency REDuces Ductular Reaction, HEPATOCYTE APOPTOSIS AND LIVER FIBROSIS IN CHOLESTATIC-INDUCED LIVER INJURY**

L. Zrihal, E. Hebel, S. Fishman, O. Shibolet

**Introduction:** Sortilin, a member of the Vps10 domain receptor family, traffics newly synthesized proteins from the trans-Golgi network to secretory pathways, endosomes or to the cell surface. Sortilin trafficked molecules, including acid sphingomyelinase (aSMase), cathepsins and IL-6, mediate activation of hepatic stellate cells (HSC), hepatocyte apoptosis, cholangiocyte proliferation and liver inflammation and fibrosis.

**Aims & Methods:** We investigated sortilin role in the development of biliary damage leading to hepatocellular injury and fibrosis, based on its regulation of aSMase trafficking and on its involvement in IL-6 seocretion. Cholestatic injury was induced in wild type (WT) and Sortilin−/− mice by bile duct ligation (BDL). Fibrosis was induced both by BDL and by administration of CCl4. Liver inflammation and cholangiocyte activation and proliferation were assessed by qRT-PCR for inflammatory cytokines and by immunohistochemistry with Ki67 (marker of proliferation) and with L3G6 (neutrophil marker). Liver damage and hepatocyte apoptosis were determined by serum liver enzymes and by TUNEL assay. Liver fibrosis was assessed by Sirius Red staining quantitation and by qRT-PCR for fibrotic markers. aSMase activity was inhibited in vivo by anti-IL-6 antibody to WT mice by BDL.

**Results:** Sortilin−/− mice displayed strongly attenuated liver fibrosis following BDL and CCl4 treatment, accompanied by an attenuated in vitro activation phenotype of Sortilin−/− HSC. Reduced Sortilin−/− hepatic aSMase activity was in line with reduced hepatocyte apoptosis following BDL and CCl4 injury and reduced susceptibility of hepatocytes from Sortilin−/− mice to bile acid-induced apoptosis in vitro. The role of aSMase in hepatocyte apoptosis was further demonstrated using in vivo pharmacological inhibition of aSMase activity after BDL. Strikingly, Sortilin−/− mice displayed impaired inflammation and ductular reaction three days after BDL, demonstrated by reduced reactive cholangiocytes, reduced cholangiocyte proliferation and accompanied by reduced serum IL-6. Strikingly, treatment of bile duct-ligated WT mice with a neutralizing antibody to IL-6 attenuated hepatic inflammation and expression of reactive cholangiocyte-derived cytokines and chemokines.

**Conclusion:** Sortilin mediates cholestatic liver damage and fibrosis via its effects on aSMase activity and secretion.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP349 ACTIVATION OF NECROTOPSIS IN HUMAN AND EXPERIMENTAL CHOLESTASIS**


**Introduction:** Targeting necrosis, a programmed necrotic cell death pathway regulated by receptor-interacting protein 3 (RIP3), is being considered as a potential therapeutic approach for the treatment of inflammation-driven diseases. Still, the role on the expression of membrane markers EpCAM and TROP-2 in HPCs. Human liver was dissociated and the cell suspension was analysed and separated by FACs. The sorted cells and the whole liver extracts were evaluated on both protein level (immunohistochemical staining) and RNA level (RNA sequencing). Pathway analysis was performed using KEGG pathways, Ingenuity Pathway Analysis and Gene Set Enrichment Analysis.

**Results:** Immunochemical evaluation of the isolated fractions indicated the enrichment of HPCs in the SP, EpCAM-positive and TROP-2-positive cell fractions. Pathway analysis of the RNA sequencing data from the different isolated HPC fractions shows an enrichment and activation of known HPC pathways like Wnt/β-catenin and Notch pathways, known for their role in proliferation and differentiation of HPCs. In addition we identified several novel pathways activated in human HPC-enriched cells such as the TNF and IL17A pathways. Moreover, comparison of the different isolation methods indicates some slight differences between the different HPC populations, e.g. the ErbB signalling path- way is activated in the TROP-2 positive cells while this is not the case in the EpCAM-positive or SP cell populations.

**Conclusion:** Our results indicate that gene signatures of human HPCs are enriched in pathways already known to be involved in HPC activation in human and in animal models, but we also identify previously unknown pathways like TNF, IL17A and ErbB signalling pathways. Comparison of the 3 isolation methods sheds light on the possible existence of different HPC populations existing in the human liver. The isolated HPC populations will be used to further characterize human HPCs and to understand the molecular mechanisms underlying their activation and differentiation, with the ultimate goal of using HPCs for the treatment of liver diseases.

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of necrosis in the pathogenesis of cholestatic liver injury has been poorly explored. To investigate whether CCRK regulates tumor microenvironment in patients with primary biliary cirrhosis (PBC), a cholestatic chronic liver disease, and in mice after common bile duct ligation (BDL), a classic experimental model of acute cholestasis and secondary biliary cirrhosis, T-cell staining and immunohistochemistry of RIP3 and its target phosphorylation-mixed lineage kinase domain-like protein (p-MLKL) were performed in liver biopsies of patients with PBC and healthy controls. C57BL/6N wild-type (WT) or RIP3-deficient (RIP3-/-) mice were subjected to BDL or sham surgery at 14 days, with subsequent histological and biochemical analysis of hepatic damage. Necrotic markers and the functional crosstalk between RIP3, antioxidant response and iron homeostasis were investigated in vivo and in vitro.

**Aims & Methods:** We aimed to evaluate the role of necroptosis in patients with primary biliary cirrhosis (PBC), a cholestatic chronic liver disease, and in mice after common bile duct ligation (BDL), a classic experimental model of acute cholestasis and secondary biliary cirrhosis. T-cell staining and immunohistochemistry of RIP3 and its target phosphorylation-mixed lineage kinase domain-like protein (p-MLKL) were performed in liver biopsies of patients with PBC and healthy controls. C57BL/6N wild-type (WT) or RIP3-deficient (RIP3-/-) mice were subjected to BDL or sham surgery at 14 days, with subsequent histological and biochemical analysis of hepatic damage. Necrotic markers and the functional crosstalk between RIP3, antioxidant response and iron homeostasis were investigated in vivo and in vitro.

**Result:** In PBC patients, expression of RIP3 and p-MLKL was found increased in hepatocytes surrounded by lymphocytic infiltrates and also in cells morphologically resembling bile duct cells. Moreover, p-MLKL fluorescence co-localized in cells with increased thioflavin T staining, suggesting necrosome assembly and necroptosis activation. BDL in mice resulted in progressive bile duct hyperplasia, multifocal necrosis, fibrosis and inflammation. Concomitantly, necroptosis was activated as evidenced by increased RIP3 expression and activity and sequestration of RIP3 and MLKL in the insoluble protein fraction of the liver. Remarkably, RIP3 deficiency blocked BDL-induced necroinflammation at 3 and 14 days post-BDL. Serum hepatic enzymes, fibrogenic liver gene expression and oxidative stress decreased in RIP3-/- mice at 3 days after BDL. However, at 14 days, cholestasis aggravated and fibrosis was not ameliorated. RIP3 deficiency further associated with increased hepatic expression of heme oxygenase-1 (HO-1) and accumulation of iron in BDL mice. The functional link between HO-1 activity and bile acid toxicity was established in RIP3-deficient primary hepatocyte cultures. The activity of reactive oxygen species (ROS) increased by 14 days after BDL in both WT and RIP3-/- mice, while remaining at basal levels at day 3, indicating that apoptosis is activated at late time-points in the BDL murine model, reflecting the peak of liver fibrosis.

**Conclusion:** In conclusion, necroptosis is triggered in BPD patients and mediates hepatic necroinflammation in BDL-induced cholestasis. Targeting necroptosis may provide an opportunity to develop novel therapeutic strategies to attenuate acute cholestatic liver injury. However, therapeutic strategies to inhibit RIP3-dependent signaling during chronic cholestasis should be undertaken with a complete understanding of the potential duality of this pathway. (Supported by HMP8-ICT/0081/2011, SFRH/BD/91191/2012, SFRH/BD/88212/2012 and SFRH/BD/104160/2014, FCT, Portugal).

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**CHRYSOMALUMIA IN BILE DUCT LIGATED AND CCL4 MICE**

S. Moghadamrad, K. Meyyaz, P. Kellmann, A. De Gottardi

**Introduction:** Chronic liver disease the presence of gut-derived bacterial products and the resultant increase in inflammatory cytokines in the splanchic and systemic circulation may contribute to the progression of fibrosis. However, the composition of the intestinal microbiota and the host-microbe interaction in the development of liver fibrosis remain largely unknown. We hypothesized that fibrosis could be attenuated in a gnotobiotic model of limited intestinal colonization (altered Schaedler flora, ASF) compared to a more complex colonization with specific pathogen free flora (SPF).

**Aims & Methods:** We aimed to investigate the development of fibrosis and portal hypertension in ASF and SPF mice. Liver fibrosis was induced by common bile duct ligation (BDL) for 14 days or intraperitoneal injection of 20% (dilution in olive oil) carbon tetrachloride (CCL4) for 10 weeks in ASF or SPF male, C57BL/6 mice. Hemodynamic measurements were performed after 14 days in BDL or 10 weeks in CCL4 treated mice. Liver histology and collagen deposition were evaluated using Sirius red staining for determination of fibrosis degree. To assess bacterial translocation, mesenteric lymph nodes, spleen and liver were dissected aseptically and then cultured on plates with selective agar and blood agar plates for aerobic and anaerobic culture respectively.

**Result:** There were no differences in portal pressure between sham-operated (controls) ASF or SPF mice. After BDL or CCL4 treatment portal pressure (PP), portosystemic shunts (PSS) and collagen deposition within the liver showed a significant increase in both groups. However, the increase in portal pressure and degree of fibrosis was significantly higher in ASF than SPF mice:

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**Conclusion:** SPF mice presented attenuated fibrosis and portal hypertension compared to ASF mice. Contrary to our hypothesis, these findings suggest that a more complex intestinal bacterial flora may play a hepato-protective role. Our results are in line with studies showing that germ free mice are more susceptible to hepatic injury.

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**MICROBIOTA IN BILE DUCT LIGATED AND CCL4 MICE**

S. Moghadamrad, K. Meyyaz, P. Kellmann, A. De Gottardi

**Introduction:** In chronic liver disease the presence of gut-derived bacterial products and the resultant increase in inflammatory cytokines in the splanchic and systemic circulation may contribute to the progression of fibrosis. However, the composition of the intestinal microbiota and the host-microbe interaction in the development of liver fibrosis remain largely unknown. We hypothesized that fibrosis could be attenuated in a gnotobiotic model of limited intestinal colonization (altered Schaedler flora, ASF) compared to a more complex colonization with specific pathogen free flora (SPF).

**Aims & Methods:** We aimed to investigate the development of fibrosis and portal hypertension in ASF and SPF mice. Liver fibrosis was induced by common bile duct ligation (BDL) for 14 days or intraperitoneal injection of 20% (dilution in olive oil) carbon tetrachloride (CCL4) for 10 weeks in ASF or SPF male, C57BL/6 mice. Hemodynamic measurements were performed after 14 days in BDL or 10 weeks in CCL4 treated mice. Liver histology and collagen deposition were evaluated using Sirius red staining for determination of fibrosis degree. To assess bacterial translocation, mesenteric lymph nodes, spleen and liver were dissected aseptically and then cultured on plates with selective agar and blood agar plates for aerobic and anaerobic culture respectively.

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**Conclusion:** SPF mice presented attenuated fibrosis and portal hypertension compared to ASF mice. Contrary to our hypothesis, these findings suggest that a more complex intestinal bacterial flora may play a hepato-protective role. Our results are in line with studies showing that germ free mice are more susceptible to hepatic injury.
OP345 TOLL LIKE RECEPTOR 2 MODULATES THE INHIBITORY MOTOR RESPONSE INDUCED BY HYDROGEN SULPHIDE IN MOUSE COLON
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Introduction: The recognition of intestinal microbiota is in part carried out by TLR2, a member of the TLR family, which senses lipoprotein and glycolipid moieties present in a variety of pathogens. TLR2 mediates the recognition of bacterial glycolipids including lipoteichoic acid (LTA) and lipooligosaccharides (LOS). However, the role of TLR2 in response to endogenous ligands is not well defined. We previously showed that hydrogen sulfide (H2S) is a potent intestinal neurotransmitter in vivo that inhibits the spontaneous and the stretch-induced motor activity of mouse colon by inducing the expression of the inhibitory neurotransmitter NO and the synthesis of the nitric oxide synthase (NOS)-inhibitor arginine. The aim of this study was to investigate the influence of TLR2 on the motor response induced by H2S. Methods: Male C57/BL10 mice were used for the study. Mice were randomly divided into three groups: a) control mice; b) HOCl-treated mice (H2S donor, 2%); and c) mice treated with an inhibitor of NOS (25 mg/kg L-NMMA). In control and HOCl-treated mice, the motor response induced by H2S was determined in vivo. We also injected into the colon of mice a NO donor (L-NAME) and an NO synthase inhibitor (L-NMMA). In vivo administration of H2S was determined using a spectrophotometric assay of NO. The effects of the NO donor and NO synthase inhibitor were also determined in vitro in the colons of mice. Results: In control mice, the H2S donor induced a dose-dependent inhibition of the spontaneous motor activity of the colon, with a decrease of 50% of the baseline motor activity at 25 mg/kg. This effect was significantly reduced in mice treated with L-NMMA (25 mg/kg), which inhibits NO synthase. The inhibition of NO synthase by L-NMMA prevented the H2S-induced reduction of the motor activity of the colon. Conclusion: Our results indicate that the motor response induced by H2S is mediated by NO and that TLR2 plays a role in this response. Further studies are needed to determine the mechanism by which TLR2 regulates the motor response induced by H2S.

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**Introduction:** Biologics targeting inflammatory cytokines has reveal a new era in inflammatory bowel disease treatment. Direct blockade of HMGB1 can be protective against inflammatory bowel disease. High mobility group protein B1 (HMGB1) acts as an alarmin in early stage and inflammatory cytokine in late stage during inflammation. Direct blockade of HMGB1 can be protective against intestinal inflammation.

**Aims & Methods:** Particular role of anti-HMGB1 neutralizing antibody (HnAb) in inhibiting intestinal inflammation and the underlying mechanism is investigated in DSS-induced mice colitis (DSS-C) models. 200 μg HnAb was administrated intraperitoneally to DSS-C at d0, d3 and d6 in HnAb group, whereas 200 μg anti-lyP-40 (anti-lyP-40/SERPINC1, a natural inhibitor of DPP IV) or saline was used as control. Results: Administration of HnAb ameliorated DSS-C by suppressing inflammatory cytokines and the underlying mechanism is investigated. Moreover, CHR-conditioned AMS expressed significantly more ARG-1 while there is growing awareness of a relationship between Chemokinin (Cg)-A and a susceptibility to inflammatory conditions, the specific interaction between CgA-derived peptides and macrophage plasticity in IBD is unknown. Recently, we have shown a linear correlation between CgA and macrophage markers in vitro, and with active ulcerative colitis, and colitic CgA-deficient mice demonstrated a significant decrease of colitis associated to a modulation of macrophage activation. As CgA is a prohome, herein, we assessed the functional role of a specific CgA-derived peptides (Chromofungin (CHR); Cg-A47-66) in the regulation of acute colitis and the functional plasticity of murine macrophages.

**Conclusion:** CHR proved to be a potent inhibitor of DPP IV in vitro and exhibits substan-tial anti-inflammatory activity in the GI tract in vivo. Results of this study validated the effect of CHR in acute and semi-chronic TNBS-induced colitis in mice in a dose-dependent manner, as indicated by significantly reduced macrophage parameters and MPO activity. Anti-inflammatory effect of EMDB-1 was not blocked by naloxone, thus the opioid receptors were not involved in this mechanism of action.

**Disclosure of Interest:** All authors declared no conflicts of interest.

**Introduction:** Macrophages play a major role in inflammatory bowel disease (IBD) pathogenesis through an inappropriate response to migration, and an impaired transition from a pro-inflammatory (classical activated macrophages (CAMS)) to an anti-inflammatory (alternative activated macrophages (AAMs)) phenotype. We aimed to explore the association between Chromogranin (Cg)-A and a susceptibility to inflammatory conditions, the specific interaction between CgA-derived peptides and macrophage plasticity in IBD is unknown. Recently, we have shown a linear correlation between CgA and macrophage markers in vitro, and with active ulcerative colitis, and colitic CgA-deficient mice demonstrated a significant decrease of colitis associated to a modulation of macrophage activation. As CgA-A is a prohome, herein, we assessed the functional role of a specific CgA-derived peptides (Chromofungin (CHR); Cg-A47-66) in the regulation of acute colitis and the functional plasticity of murine macrophages.

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Introduction: The adaptive immune system plays a crucial role in the pathogenesis of inflammatory bowel diseases (IBD). Interactions in IBD is typically associated with a decrease in local pH. The proton-sensing receptor T-cell death in intestinal inflammation using a murine adoptive transfer colitis model. Aims & Methods: The results of colitis were evaluated by weight change, colonoscopy score, spleen examination of the tumors showed 21 GISTs, 1 schwannoma and 4 early gastric tumors. After marking around a tumor on both the mucosal and serosal surfaces and submucosal injection of sodium hyaluronate, circumferential sero-muscular suturing were made laparoscopically, followed by circumferential mucosal incision endoscopically. The resected specimen was perorally retrieved.

Results: The mean tumor size and resected specimen were 23.3 mm (range, 7–45 mm) and 36.1 mm (range, 20–66 mm), respectively. All lesions were curatively resected in an en-bloc fashion. The mean operation time was 219.0 minutes (range, 188–230), the mean estimated blood loss was 0 g (range, 0–250 g). Patients started oral intake on mean postoperative day 3.1 (range, 2–4), and the mean length of postoperative hospital stay was 8.2 days (range, 6–14). However, there were no severe postoperative complications. Histopathological examination of the tumors showed 21 GISTs, 1 schwannoma and 4 early gastric cancer. No tumor residual or recurrences was confirmed by performing gastroscopy and the mean body weight loss was 2.5 kg (range, –3.2–10.9 kg) during a median follow-up of 11 months (range, 0.37–10.6 years). Conclusion: NEWS is an effective full-thickness resection with minimum possible margin without contamination and tumor dissemination into the peritoneal cavity, considering the quality of life of patients. NEWS could be utilized as a novel treatment option especially for node-negative EGC difficult to resect by ESD, or EGC with possible lymph node metastasis with a combination of sentinel node navigation surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Endoscopic submucosal dissection (ESD) has been widely accepted as an effective treatment for gastrointestinal tumors. However, ESD for early gastric cancer (EGC) with ulcer scarrring is still technically difficult. Non-exposed endoscopic wall-inversion surgery (NEWS) is an advanced method of endoscopic full-thickness resection (EFTR) without transluminal communication, applying ESD technique.

Aims & Methods: The aim of this study is to clarify the short-term outcomes of NEWS for gastric tumors. Between July 2011 and March 2016, 26 patients (9 females, 17 males; mean age 65.9 years, range 49–85 years) underwent NEWS for gastric tumors. After marking around a tumor on both the mucosal and serosal surfaces and submucosal injection of sodium hyaluronate, circumferential sero-muscular suturing were made laparoscopically, followed by circumferential muco-submucosal incision endoscopically. The resected specimen was perorally retrieved.

Results: The mean tumor size and resected specimen were 23.3 mm (range, 7–45 mm) and 36.1 mm (range, 20–66 mm), respectively. All lesions were curatively resected in an en-bloc fashion. The mean operation time was 219.0 minutes (range, 188–230), the mean estimated blood loss was 0 g (range, 0–250 g). Patients started oral intake on mean postoperative day 3.1 (range, 2–4), and the mean length of postoperative hospital stay was 8.2 days (range, 6–14). However, there were no severe postoperative complications. Histopathological examination of the tumors showed 21 GISTs, 1 schwannoma and 4 early gastric cancer. No tumor residual or recurrences was confirmed by performing gastroscopy and the mean body weight loss was 2.5 kg (range, –3.2–10.9 kg) during a median follow-up of 11 months (range, 0.37–10.6 years). Conclusion: NEWS is an effective full-thickness resection with minimum possible margin without contamination and tumor dissemination into the peritoneal cavity, considering the quality of life of patients. NEWS could be utilized as a novel treatment option especially for node-negative EGC difficult to resect by ESD, or EGC with possible lymph node metastasis with a combination of sentinel node navigation surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Somatostatin analogs have been proposed as a rescue therapy in cases of chronic or recurrent obscure gastrointestinal bleeding (GB) or attributable to gastrointestinal angiodyplasias (GIADs). The long-term results with lanreotide are still very scarce.

Aims & Methods: Our aim is to determine the medium and long-term benefit of lanreotide in cases of chronic or recurrent refractory obscure gastrointestinal bleeding or due to gastrointestinal angiodyplasias.

Results: Between Feb 2009 and Sept 2013, 209 patients were randomised to EMR (n = 106) or TEM (n = 103). 4 patients withdrew consent. 1 patient had prostate carcinoma instead of rectal adenoma. The remaining 204 patients (103 EMR, 101 TEM) were treated; 27 (13%) had unexpected cancer and were excluded. One additional patient withdrew consent. Of the remaining 176 (87 EMR, 89 TEM) patients, overall recurrence rates were 15% after EMR and 11% after TEM (relative risk, 0.81; 95% confidence interval 0.54–1.22; p = 0.4). EMR was statistically not non-inferior to TEM. The number of recurrence-free days alive and out of hospital, analysed by intention to treat. The trial was designed to demonstrate non-inferiority of EMR with regards to recurrence rate with an upper limit of 10%. Secondary outcomes were quality of life, anorectal function and costs. This trial is registered in the Dutch Trial Registry (NTR1422).

Conclusion: Due to unexpected high recurrence rates after both TEM and EMR, non-inferiority of EMR could not be demonstrated. Taking into account the high rate of unexpected malignancies, a trend towards more severe complications after TEM and the cost-effectiveness of EMR, EMR is the recommended technique in case of similar expertise of TEM and EMR.

Disclosure of Interest: All authors have declared no conflicts of interest.
iron doses, and non-diagnostic endoscopies. Differences from data between one year before and each one of the three years after starting lanreotide were evaluated using Wilcoxon test, with significance level of p < 0.05.

Results: Twenty-two patients (median age 76.1 years, range 56–90; 50% male sex) were included. Before starting treatment 19 were ASA III, 22.7% consumed antplatelet and 31.8% anticoagulants. At the end of follow-up only one patient had stopped the anticoagulant. The bleeding was attributed to GIAD in 77.3% and 22.7% was obscure. The bleeding was overt in 68.2% and occult in 31.8%. Before starting lanreotide 4 patients had received endoscopic treatment using argon plasma coagulation (APC), 2 hormonal therapy and 1 thalidomide. Two patients received APC concomitant to lanreotide, and 1 hormonal therapy after stopping this one without reaching bleeding cessation. The average duration of treatment with lanreotide was 28.4 months (range 6–36). Mean follow-up was 32.4 months (range 9–36), with the results shown in the table. Five patients did not complete the follow-up for not related to GIB deaths. No side effects forced to suspend lanreotide.

Conclusion: The use of lanreotide for at least 6 months in patients with chronic or recurrent obscure gastrointestinal bleeding or from gastrointestinal angiodysplasias, refractory to or not candidates for other therapies, is safe and is associated with a decrease in consumption of medical resources within the three years following its indication.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP362 SOMATOSTATIN ANALOGUES ARE LESS EFFECTIVE IN FOLLOWING ITS INDICATION.

K. Grooteman

OP363 ESOPHAGEAL VARICES POST BANDING ULcer BLEEDING - DETERMINANTS AND IMPACT IN MORTALITY

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Introduction: Endoscopic band ligation (EBL) is the choice for both prophylaxis and treatment of esophageal varices hemorrhage. Post-EBL ulcer bleeding is a deemed complication for which risk factors and impact in mortality are not clearly understood.

Aims & Methods: We aimed at identifying risk factors for variceal post-EBL ulcer bleeding and determine its impact in short and long-term mortality. We conducted a case control study. Cases: all admissions for post-EBL ulcer bleeding, in a tertiary gastroenterological service, from January 2003 to December 2015. Controls: EBL treated patients without post-therapeutic ulcer bleeding. Matching was made for Child-Pugh-Turcotte (CPT) score and indication (bleeding vs elective) in a 1 case for 2 controls ratio. Patient’s demographics, comorbidities and endoscopic findings were reviewed from medical records. Endpoints were re-bleeding from post therapeutic ulcer and mortality assessed at 28, 90 and 360 days post-therapeutic.

Results: A total of 50 post-EBL ulcer bleeding cases and 100 controls were included. Mean age (57.1 ± 12.0); male:female ratio (4:1.1). Cirrhosis etiologies: alcoholic (30.7%), HCV (29.3%) and HBV (15.7%). CPT distribution: A (17.3%) B (46%) and C (36.7%); mean MELD was 14.5 ± 6.1. All patients underwent EBL and 7.3% also received a sclerosing agent. Mean time to rebleed: 12.6 ± 5.4 days. A higher number of rubber bands (5.8 ± 1.7 vs 5 ± 2.1; p = 0.003), lower baseline hemoglobin (10.7 ± 1.5 vs 11.5 ± 2.1 g/dL; p = 0.007), hemodynamic instability (OR:2.0 p = 0.048) portal vein thrombosis (OR:2.8, p = 0.022), HBV cirrhosis (OR:6.2, p = 0.007), and endoscopic stigmata of active or recent bleeding (OR:5.0 p < 0.001) correlated with rebleeding. In multivariate logistic regression analysis HBV cirrhosis, multiple concomitant aetiologies of cirrhosis and endoscopic stigmata of recent bleeding were independently associated with rebleeding. Post-EBL ulcer bleeding did not significantly impacted overall short and long term mortality. However CPT class B patients with post-EBL ulcer bleeding showed a trend for lower survival which was significant at 180 days (16% vs 6% log rank p = 0.04).

Conclusion: We identified both patient’s and endoscopic features correlating with post-EBL ulcer bleeding, namely HBV infection related cirrhosis, higher number of concomitant aetiologies/aggressors, and endoscopic stigmata of recent/active bleeding. Though overall patient’s short and long-term mortality was not affected by post-EBL ulcer bleeding, CPT class B patients showed a trend for

### Table (OP361)

<table>
<thead>
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<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>p value</th>
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<td>Admission days - Prior 3y</td>
<td>33.4</td>
<td>9.0</td>
<td>10.8 8.5</td>
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<td></td>
<td>24.3</td>
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<td>7.1</td>
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<td></td>
<td>Iron iv doses - Prior 3y</td>
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<td>2.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.1</td>
<td>5.9</td>
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lower survival. Thus, we hypothesize that CPT class B patients may be a cluster of patients with low hepatic reserve, to whom post-EBL bleeding may impose an additional risk for disease progression, that can significantly impact on survival.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP364 INTERNATIONAL PROSPECTIVE STUDY OF UPPER GI HAEMORRHAGE: DOES WEEKEND ADMISSION AFFECT OUTCOME?

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Introduction: Weekend admissions have been associated with higher mortality. For upper gastrointestinal haemorrhage (UGIH) some studies show significantly increased mortality1 and delayed endoscopy while the UK UGHI audit reported no difference2. We studied whether out of hours (OOH) admissions had more morbidity, were less stable and/or had higher mortality.

Aims & Methods: Prospective study over 12 months (from March 2014) from 2 UK and 2 international centres. Admission time, demographics, pulse, BP, lab results, endoscopy findings, further procedures and 30d mortality were recorded. 3 pre-endoscopy scores (Glasgow Blatchford (GBS), AIMS65 and admission Rockall scores) and 2 post-endoscopy scores (PNED and full Rockall scores) were determined. Chi-squared, Fisher’s exact and Kruskal-Wallis tests were used as appropriate.

Disclosure of Interest: All authors have declared no conflicts of interest.

Results: 2181 consecutive patients, 60% male, median age 66 years were seen. There were no significant differences in mortality, need for endoscopic therapy, surgery/embolisation or rebleeding between 24hr and 00:00am admission or between weekday and weekend admissions. There were four differences in co-morbidity, mean ASA 2.3, pulse or BP when evaluated the hemostatic success. In the multivariate analysis, large ulcer size (>20 mm), Forrest classification of the PUD in the second endoscopic therapy, gastric or duodenal location, were not statistically significant different between groups when evaluated the hemostatic success. The number of red blood cells (RBC) transfused (OR 0.66, p =0.019) and larger ulcer (>20 mm) were independent risk factors for hemostasis failure. Early surgery or angiography should be considered in this group of patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP366 A HISTORY OF ISCHEMIC HEART DISEASE, HIGH BLOOD UREA NITROGEN AND C-REACTIVE PROTEIN LEVELS, AND LOW HEMOGLOBIN LEVELS: AS PREDICTIVE CLINICAL FINDINGS FOR EARLY DEATH AFTER PERCUTANEOUS ENDOSCOPY GASTROSTOMY

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Introduction: Percutaneous endoscopic gastrostomy (PEG) is accepted as the method that enables enteral feeding in patients with swallowing difficulties. However, complications and early death are considerably prevalent after PEG. To decrease the incidence of early mortality after PEG, it is very important to identify risk factors of this procedure.

Aims & Methods: The aim of our study was to determine factors that could predict early death within 30 days following PEG. A retrospective analysis of the records of all patients who underwent PEG at Kure Medical Center and Chugoku Cancer Center from April 2008 to March 2014 was performed. We examined clinical and preparative laboratory data and extracted predictive factors of early death after PEG by using univariate and multivariate analyses.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
heart disease (P < 0.01), high blood urea nitrogen (P = 0.02) and C-reactive protein levels (P < 0.01), and anemia (P = 0.0001).

### Odds ratio (95% CI) p-Value

- History of ischemic heart disease: 2.32 (1.2–4.3) < 0.01
- Blood urea nitrogen level ≥ 30 mg/dl: 3.14 (1.8–5.5) < 0.0001
- C-reactive protein level ≥ 2.6 mg/dl: 4.04 (2.2–7.3) < 0.0001
- Albumin level ≤ 2.7 mg/dl: 4.2 (2.1–8.2) < 0.0001
- Hemoglobin level ≤ 11.2 g/dl: 4.0 (2.0–8.0) < 0.0001

### Conclusion

A history of ischemic heart disease and laboratory data, such as high blood urea nitrogen and C-reactive protein levels and low hemoglobin levels may be useful predictive clinical factors for early death after PEG. If patients have a history of ischemic heart disease, high blood urea nitrogen, high C-reactive protein, or anemia, PEG should be considered carefully.

### Disclosure of Interest

All authors have declared no conflicts of interest.

**WEDNESDAY, OCTOBER 19, 2016 10:30-12:00**

### IMMUNOTHERAPY IN CANCER – ROOM 1.61/1.62

#### OP360 GLUTAMINOLYSIS INHIBITION AS A THERAPEUTIC STRATEGY IN GLUTAMINE-ADDICTED KRAS MUTANT COLORECTAL CANCER

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**Introduction**

Colorectal cancer (CRC) with KRAS mutations represents an unmet clinical need due to the lack of effective therapies. A defining characteristic of oncogenic KRAS-driven cancers is an altered cellular metabolism, in which glucose and glutamine metabolism are extensively rewired to satisfy their anabolic needs. In this study, we investigated the metabolic dependencies of KRAS-mutant CRC, established the role of glutaminolysis in KRAS-mutant CRC growth and evaluated the synergism between glutaminolysis inhibition and chemotherapy.

**Aims & Methods**

Metabolic dependencies of KRAS mutant CRC cell lines were assessed by colony formation and apoptosis assays. Glutamine metabolism in KRAS mutant CRC cell lines were traced using stable U-13C-glutamine labeling and Ultra-High Performance Liquid Chromatography-Mass Spectrometry (UPLC-MS). Role of glutaminase (GLSI) and the mitochondrial glutamate transporter (SLC25A22) in mediating glutaminolysis was evaluated. Finally, the functional effect of glutaminolysis inhibition (via GLSI or SLC25A22 blockade) on tumor growth in chemotherapy resistant models were tested.

**Results**

Deprivation of glucose, glutamine or their combination in six KRAS mutant CRC (DLD1, HCT116, LOVO, SW480, SW620 and SW1116) and four KRAS wild type cell lines (CACO-2, HT29 and SW480) revealed that KRAS mutant CRC cells were profoundly sensitive to glutamine deprivation as compared with KRAS wild type CRC cells, whilst exhibiting resistance to glucose deprivation. This indicates the supply of glutamine is obligatory for KRAS mutant CRC survival. U-13C-glutamine labeling in DLD1 cells and UPLC-MS revealed that a majority of glutamine was metabolized into glutamate, aspartate and the intermediates of the tricarboxylic acid (TCA) cycle, indicating that glutamine-derived carbohydrates were channeled to the mitochondria for the replenishment of TCA cycle (a process known as glutaminolysis). We further revealed that glutamine was first converted to glutamate by GLSI at the outer side of inner mitochondrial membrane, which is coupled to SLC25A22 for the import of glutamate into the mitochondrial matrix. Consistent with this model, the silencing of GLSI or SLC25A22 significantly suppressed cell proliferation in KRAS mutant CRC cells, indicating that their coupled action is indispensable for cell growth. U-13C-glutamine tracing in DLD1 cells with SLC25A22 knockdown showed an attenuated entry of glutamine-derived carboxylate into the TCA cycle, confirming its involvement in glutaminolysis. Inhibition of SLC25A22-dependent glutaminolysis triggered metabolic stress, suppressed ATP production and promoted oxidative stress. Moreover, a combinatorial approach utilizing SLC25A22-shRNA plus 5-Fluorouracil synergistically inhibited growth of KRAS mutant CRC in vitro and in subcutaneous xenograft models.

**Conclusion**

KRAS mutant CRC cells are addicted to glutamine and the blockade of glutaminolysis enzymes GLSI and SLC25A22 suppressed cell survival. SLC25A22 knockdown endowed therapeutic resistance to CRC and its synergistic effect with chemotherapy warrants further investigation.

**Disclosure of Interest**

All authors have declared no conflicts of interest.

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**Disclosure of Interest**

All authors have declared no conflicts of interest.
Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP370 SPONTANEOUS BACTERIAL PERITONITIS – DOES THE INFECTION ACQUISITION SITE MATTER?
A.G. Antunes1, C. Teixeira1, P. Costa1, B.M. Santos Peixe2, A. Alves2, S. Gomes2, C. Teixeira1, P. Oliveira1, F. Thursby-Pelham2, B. Haysom-Newport4, L. Gadeke1, F. Thursby-Pelham2, R. Ellis1, P. Goggin1, G. Longcroft-Wheaton5, P. Bhandari2
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3Dept. Of Gastroenterology, Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal

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Introduction: Spontaneous bacterial peritonitis (SBP) develops in up to 25% of patients with cirrhosis and its associated significant short and long-term morbidity and mortality. With the amelioration of medical care, the use of antibiotics for primary and secondary prophylaxis of SBP, there is some controversy concerning whether the acquisition site of the infection has an effect on the prognosis of SBP and if the international guidelines for antibiotic therapy (mainly based on the acquisition site) are still considered to be the best practice.

Aims & Methods: A retrospective analysis of clinical, laboratory and microbiological data from patients with SBP between 2010 and 2014. Medical records and laboratory data were reviewed. For defining the acquisition site of the infection, we followed the criteria described by European Center for Disease Prevention and Control (ECDC). Healthcare-associated infections and Nosocomial infections were analysed. Multiresistant bacteria (MDR) were more frequently by gram positive bacteria (p<0.001).

Results: We identified 222 episodes of SBP, from which 110 were considered as community-acquired (C); hospital-acquired in 56.9% (n=64) and 1-year mortality was 56.9%. In 85 episodes we evaluated microbiological isolation (MDR = 28%); with a predominance of gram negative (53.6%). Community-acquired SBP were more frequently caused by gram negative bacteria and Nosocomial-acquired SBP were mainly caused by gram positive bacteria (p=0.033). SBP secondary to MDR-bacteria were more frequent in Nosocomial-acquired group (19.64 vs 6.36%; p=0.003).

Conclusion: Nosocomial-acquired SBP were associated with longer hospitalizations (17.8 vs 11.7 days; p=0.007). No statistically significant differences were noticed between centers when analysed microbiological isolation rate, gram staining of MDR isolations. There were no statistically significant differences between Community-acquired SBP and Nosocomial-acquired SBP for the variables age, gender, Child-Pugh, MELD, Hb, leukocytes, platelets, CRP, Na, INR, bilirubin, albumin, ascites fluid characteristics, gastrointestinal bleeding, acute kidney injury, infection or hemodynamic instability (p>0.05). Nosocomial-acquired SBPs were associated with longer hospitalizations (17.8 vs 11.7 days; p=0.007).

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016
10:30-12:00
IMPROVING QUALITY OF SCREENING COLONOSCOPY – ROOM N2

OP371 SEVEN YEARS OF QUALITY ASSURANCE IN SCREENING COLONOSCOPY IN AUSTRIA
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3Main Association of the Austrian Social Insurance Institutions, Vienna/Austria
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Introduction: Screening colonoscopy only effectively prevents from colorectal cancer if performed with high quality.

Aims & Methods: Austria implemented a quality assurance program in screening colonoscopy in 2007. This study provides a report on 8 years of quality assured screening colonoscopy.

Results: In the investigated time period, 301 endoscopic units provided data of 159,246 screening colonoscopies. 49.1% were female. Colonoscopy adherence was 84.2% over 8 years. Significant increases over time were found for ADRs, which rose from a mean of 51.6% (SD 10.7%) in 2008 to 24.2% (11.6%) in 2013-2014, corresponding to an average increase of +1.5% per two-year-period (95% confidence interval [95%CI] +0.9%, +2.2%, p<0.001). Likewise, proximal lesion detection rates rose from 15.8% (SD 9.8%) to 21.7% (SD 13.3%, +2.5% per two-year-period, 95%CI +1.9%, 3.1%, p<0.001). Adverse events occurred in 0.3%, 63% thereof were associated with polypectomy. There was a decline in complication rates of ~7.3 per 10,000 endoscopies per two-year-period (95%CI -13.1, -1.5 per 10,000 endoscopies per two-year-period, p=0.013). Sedation induced pain probability of 0.1% (95%CI 0.1% in sedated and 0.16% in unsedated patients, p=0.025).

Conclusion: This study showed a strong improvement in quality of screening colonoscopy performed within a quality assurance program in Austria between 2007 and 2014. Both overall adenoma detection rate and detection rate of proximal lesions increased strongly in the investigated study period. Interestingly, the detection rate of advanced adenomas decreased.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP372 ENDORINGS™ INCREASES ADR EVEN IN HIGH-RISK SCREENING COLONOSCOPY: RESULTS OF A SINGLE CENTRE PILOT STUDY
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2Gastroenterology, King’s College Hospital, London/United Kingdom

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Introduction: Colonoscopy remains the gold standard procedure for screening and polyp detection, with adenoma detection rate (ADR) being a widely accepted key performance indicator (KPI). It has long been recognised that even experienced endoscopists incur an appreciable ‘miss-rate’ and a number of novel devices have been marketed to assist this aspect of practice. The Endorings™ device is a simple soft silicone, single-use device consisting of a series of rings arranged around a central tubular core. As the colonoscope is inserted the rings fold back to allow inflation and flare on withdrawal to flatten colonic folds and aid inspection.

Aims & Methods: This was a single-centre pilot study to determine the effect of Endorings used in a high-risk cancer screening population (national), when used by experienced operators with an established ADR already in place, on ADR and key performance indicators (KPIs).

Results: The ADR without Endorings (n=85) was 49.4% with a per-procedure detection rate (ppr) of 0.97. With the device (n=66), ADR was 66.7% (p=0.0006) with ppr of 1.625. This represents a 35% increase in ADR and a 68% increase in the number of polyps detected at any given procedure.

Conclusion: Use of the Endorings™ device was associated with a significant increase in ADR. Qualitatively, the three-ring design was felt to interfere with normal intubation such that insertion technique had to be modified. An updated double insertion with two rings in slightly different positions along the central tube, has been produced and appears to offer a significant advantage in this regard. Furthermore, the central tube can be pushed further along the distal end of the colonoscope to allow the terminal ileum to be intubated with the device in place. The Endorings™ may offer an advantage in screening colonoscopy and, in this cohort, further prospective investigation is warranted.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP373 THE FIRST RANDOMISED CONTROLLED TRIAL OF ENDOCUFF VISION®-ASSISTED COLONOSCOPY VERSUS STANDARD COLONOSCOPY FOR POLYP DETECTION IN BOWEL CANCER SCREENING PATIENTS (E-CAP STUDY)
R. Bhattacharrya1, F.J.Q. Chedgy2, K. Kandiah3, C. Fogg4, B. Higgins5, B. Haywood-Newport6, L. Gadeke1, P. Jeyes-Pelham2, R. Ellis1, P. Goggin3, G. Longcroft-Wheaton5, P. Bhandari2
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Introduction: Up to 25% of colonic polyps are missed during colonoscopy. The Endocuff Vision® is a cap with soft flexible arms which extends to the end of a colonoscope and improves views during withdrawal. We have performed the first randomised controlled trial to identify the role of Endocuff Vision® in improving polyp detection.

Aims & Methods: Our aim was to investigate the impact of Endocuff Vision®-assisted colonoscopy on polyp detection, as compared to standard colonoscopy, in the UK Bowel Cancer Screening Programme (BCSP). This was a single-centre, parallel group, randomised controlled trial. Ethics approval was obtained (ref: WEDNESDAY, OCTOBER 19, 2016 10:30–12:00: UNITED EUROPEAN GASTROENTEROLOGY JOURNAL 4(5S)
14/SC/0207). Patients attending for BCSP colonoscopy were stratified based on whether they were attending for index screening colonoscopy or for polyp surveill ance. Within each stratum participants were randomised to either Standard or Endocuff assisted colonoscopy. All procedures were performed by experi enced, nationally accredited BSCP endoscopists, who had carried out >5000 colonoscopies and had ec.europa.eu/healthtopics/cancer/cancer-prevention/colonoscopy. The Baseline parameters and indication for colonoscopy were similar in both groups. The ADR, adenoma per patient, number of adenomas by size and advanced adenomas for each group are presented in Table 1. G-EYE colonoscopy improved ADR by 45.6% when compared to SC. More specifically, the G-EYE colonoscopy increased the number of advanced adenomas and large-size adenomas by 96.9% and 96.2%, respectively. Procedural times were similar in both groups.

Table 1: Results Summary

<table>
<thead>
<tr>
<th></th>
<th>SC</th>
<th>G-EYE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR (per patient)</td>
<td>33.8%</td>
<td>49.2%</td>
</tr>
<tr>
<td>Adenoma per patient</td>
<td>0.57</td>
<td>0.93</td>
</tr>
<tr>
<td>Large adenomas (≥10mm)</td>
<td>26</td>
<td>51</td>
</tr>
<tr>
<td>Advanced adenomas</td>
<td>32</td>
<td>63</td>
</tr>
</tbody>
</table>

Conclusion: Our study shows that the G-EYE endoscope can substantially improve ADR when compared to SC. In addition to diminutive and small adeno mas, the G-EYE endoscope detects a larger number of advanced and large-size adenomas. Consequently, we conclude that the G-EYE endoscope can significantly enhance the quality of CRC screening and thus reduce colonic miss rates and interval cancer incidents.

Disclosure of Interest: H. Jacob: Board of directors
All other authors have declared no conflicts of interest.

OP375 EFFICACY AND SAFETY OF THE NOVEL II. PEG AND ASCORBATE BOWEL PREPARATION NER1006 VERSUS TRISULFATE SOLUTION IN ONSHORE OVERNIGHT SPLIT-DOSING ADMINISTRATION: RESULTS FROM THE PHASE 3 STUDY NOCT

Introduction: Successful colon cleansing enables effective colonoscopy. PEG based split dosing preparations are traditionally seen as the gold standard in cleaning, but many still require a high preparation volume intake. NER1006 is an ultra-low volume PEG3350 split bowel preparation (1l) developed in Europe and currently at Phase 3 clinical development. The low volume of NER1006 is achieved through the use of ascorbate in the second dose only.

Aims & Methods: This phase 3, randomised, multicentre, colonoscopy-blinded, non-inferiority study assessed the efficacy, safety and tolerability of a 2-day overnight split-dosing regimen of either NER1006 (N2D) or trisulfate solution (TS) in patients undergoing colonoscopy. Two alternative primary endpoints were evaluated: overall bowel cleansing success and ‘Excellent plus Good’ cleansing rate in the colon ascenders using the Harefield Cleansing Scale (HCS). Secondary endpoints included hierarchical evaluation of lesion detection rates (key), and cleansing assessment using the Boston Bowel Preparation Scale (BBPS, supportive). Patient tolerability, acceptability and compliance were assessed using questionnaires. Safety was monitored through adverse events and clinical laboratory evaluation. The threshold for statistical significance in this study was P < 0.025. The confidence interval (CI) for the difference between the groups used a 10% margin to demonstrate non-inferiority vs. TS.

Results: Patients were randomised to receive either N2D (n = 310) or TS (n = 311). For N2D and TS, respectively, the mean age (SD) was 57.7 (10.36) and 57.3 (10.56) years. The distribution of males vs. females was 158 (51.6%) vs. 152 (48.4%) for N2D and 169 (54.3%) vs. 142 (45.7%) for TS. High successful overall bowel cleansing efficacy was achieved in both treatment groups (Table 1). N2D demonstrated non-inferiority (lower CI limit > -10%) to TS for both alternative primary endpoints. Numerically, more patients on N2D achieved an ‘Excellent plus Good’ cleansing rate in the colon ascenders compared with TS. Non-inferiority for N2D in adenoma detection rate in the colon ascenders was not demonstrated; other key secondary endpoints were not formally tested. Tolerability and acceptability as assessed by the Bowel Cleaning Impact Questionnaire (BCIQ) were comparable for N2D and TS (Table 1). Compliance rates were high in both treatment groups. There were no deaths. NER1006 was not associated with any serious treatment-emergent adverse events (TEAEs). The most frequently reported related TEAEs in both treatment groups were nausea and vomiting.

Conclusion: When administered as a 2-day split dosing regimen, and compared to trisulfate solution, NER1006 was non-inferior in overall bowel cleansing success and in achieving an ‘Excellent plus Good’ cleansing rate in the colon ascenders. Both treatments were well tolerated; most TEAEs were mild or moderate in severity and reflected the expected safety profile of respective therapies. The
Table 1 (OP375): Efficacy and safety endpoints

<table>
<thead>
<tr>
<th>Abstract legend</th>
<th>NER1006 2-day split-dosing</th>
<th>Comparator: trisulfate solution</th>
<th>CI for the difference [P value]</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFFICACY</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary endpoint: Patients with successful overall bowel cleansing efficacy (HCS) [n]</td>
<td>235 (85.1%)</td>
<td>238 (85.0%)</td>
<td>−8.15%* [0.528]</td>
</tr>
<tr>
<td>Supportive secondary endpoint: Patients with successful overall bowel cleansing efficacy (BBPS) [n]</td>
<td>228 (82.6%)</td>
<td>227 (81.1%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>Primary endpoint: Excellent plus Good cleansing rate in colon ascendens [n]</td>
<td>99 (35.9%)</td>
<td>82 (29.3%)</td>
<td>−1.69%* [0.059]</td>
</tr>
<tr>
<td>Key secondary endpoint: Adenoma detection rate, colon ascendens</td>
<td>14.1%</td>
<td>17.1%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Adenoma detection rate, overall colon</td>
<td>33.7%</td>
<td>35.0%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Polypl detection rate, colon ascendens</td>
<td>18.5%</td>
<td>23.9%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Polypl detection rate, overall colon</td>
<td>45.7%</td>
<td>48.6%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Compliance rate (min 75% of both doses taken) [n]</td>
<td>255 (92.4%)</td>
<td>255 (91.1%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>BOCLR score [mean (SD)]</td>
<td>39.9 (17.70)</td>
<td>39.6 (17.51)</td>
<td>n.a.</td>
</tr>
<tr>
<td>SAFETY Safety set, n = 262</td>
<td>Safety set, n = 265</td>
<td></td>
<td>n.a.</td>
</tr>
<tr>
<td>All treatment-emergent adverse events [n]</td>
<td>118</td>
<td>67</td>
<td>n.a.</td>
</tr>
<tr>
<td>Patients with any related treatment-emergent adverse event [n]</td>
<td>39 (14.9%)</td>
<td>25 (9.4%)</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

* = 97.5% 1-sided CI; ** = 95% 2-sided CI; n.a. = not applicable

1L NER1006 showed high efficacy and safety in overnight split-dosing administration.

Disclosure of Interest: M. DeMicco: Contractor for Norgine through Anaheim Clinical Trials LLC; Principal Investigator for the NOCT study.

L.B. Clayton: Employee of Norgine
R. Ng Kiai Shing: Employee of Norgine
M.S. Epstein: Contractor for Norgine through Investigative Clinical Research. Investigator for the NOCT study.

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Introduktion: Split-dose cleansing regimen for colonoscopy is recommended over day-before preparation by practice guidelines and it has been shown to increase the adenoma detection rate. Nevertheless, the compliance with split-dose prescription for early-morning colonoscopy (8-10 am) is poor [1].

Aims & Methods: Present randomized study was aimed at evaluating weather the addition of oral instructions to a self-explanatory booklet for bowel preparation increases compliance with split-dose. We prospectively enrolled consecutive 50-70yr-old inpatients undergoing screening colonoscopy from 8:00 to 10:00 am. Exclusion criteria were inability to provide consent and contraindications to the preparation adopted in the study. All patients received a low-volume preparation and written explanation by healthcare professionals. Conclusion: Present data show an excellent compliance with split-dose prescription for early morning colonoscopy in both written only and oral and written instruction groups, leading to very satisfactory levels of colon cleansing. This finding underlines that the adoption of a self-explanatory booklet clearly describing the benefits of split-dose marginalizes the need of additional oral instructions. This result is relevant in an open-access system, where routine oral education is not applicable, and does not support ESGE indications, which recommend both oral and written explanation by healthcare professionals.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

WEDNESDAY, OCTOBER 19, 2016 10:30–12:00

BURDEN OF LIVER DISEASE – ROOM L7

OP377 THE BURDEN OF OVERT AND OCCULT LIVER CIRRHOSIS IN PATIENTS WITH METABOLIC SYNDROME: ANALYSIS FROM A LARGE GENERAL PRACTITIONERS DATABASE
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2Dept of Medicine, Internal Medicine and Hepatology, University of Padova, Padova, Italy, Padova/Italy
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Introduction: Liver cirrhosis represents the end stage of chronic liver disease, characterized by high mortality and morbidity (1,2) with relevant health and social costs (3). Metabolic syndrome represents one of the major risk factors of liver disease in western countries (4). The real prevalence of this condition is difficult to assess, since liver disease is silent until clinical decompensation of cirrhosis occurs.

Aims & Methods: The aim of this study was to estimate the prevalence of occult liver disease in the Veneto region and to compare the results with the burden of cirrhosis occurs.

Results: During the study period (January–April 2016), 286 patients were enrolled (mean age 59.8±7, males 53.7%), 143 in group A and 143 in group B; of them 266 have undergone colonoscopy (group A: 130, group B: 136). The two groups were well balanced as concerns age, gender, education, employment and marriage status. Split-dose was adopted by 106/130 and by 118/136 patients in group A and B, respectively (81.5% vs 86.8%, p = 0.317). Among patients who complied with split-dose the quality of bowel cleansing was adequate (BBPS ≥ 4 in each segment of the colon) in 215/224 (96.0%). No significant differences between group A and B were observed with regards to adherence to preparation scheme, which were both optimal, (98.1% vs 97.5%, p = 0.693) and to the adequacy of bowel prep (BBPS > 2 in each segment) (97.2% vs 94.9%, p = 0.785).

No variable was significantly associated with split-dose uptake at logistic regression analysis.

Disclosure of Interest: All authors have declared no conflicts of interest.
was recorded. Sex distribution of these patients was similar to that of the patients with cirrhosis with a mean age (SD) of 61.15 ± 13.9 years old, while age was higher in patients with elevated transaminases (mean age (SD) = 55.5 vs 48.9, p < 0.0001). Patients with overt diagnosis of cirrhosis were 0.3% of the overall population, while thrombocytopenia, as indication of occult cirrhosis, was detected in 13% of the remaining patients. The epidemiological profile of these two groups was similar [M:F = 1.59; mean age (SD) = 65.6 ± M:1.67; mean age (SD) = 65, p = ns], but significantly different (p < 0.0001) compared to the normal population and to subjects with only liver enzyme alterations.

Patients with occult and overt cirrhosis presented a similar prevalence of metabolic syndrome profile (49% and 56% respectively), while these figures were lower in patients without signs of liver disease (33%, p < 0.0001).

**Conclusion:** In conclusion, a large proportion of patients with biochemical signs of chronic hepatitis and cirrhosis are still undiagnosed. Metabolic syndrome seems to be the major risk factor that characterizes patients with more severe liver disease.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**Table 1 (OP379): All-cause resource use pre- and post-RFX initiation**

<table>
<thead>
<tr>
<th>6 months (n = 114)</th>
<th>12 months (n = 102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>n*</td>
<td>n*</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Hospitalsisations with overnight stay per patient</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>101</td>
</tr>
<tr>
<td>Total bed days</td>
<td>2.2 (1.9)</td>
</tr>
<tr>
<td></td>
<td>1.0 (1.3)</td>
</tr>
<tr>
<td></td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>1.7 (2.0)</td>
</tr>
<tr>
<td>Total bed days per inpatient</td>
<td>59.99</td>
</tr>
<tr>
<td></td>
<td>28.6 (31.4)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>31.7 (35.9)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Critical care bed days per inpatient</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>7.9 (10.1)</td>
</tr>
<tr>
<td></td>
<td>0.046</td>
</tr>
<tr>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>Emergency room visits per patient</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td>1.9 (2.3)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>2.4 (3.4)</td>
</tr>
<tr>
<td></td>
<td>0.009</td>
</tr>
</tbody>
</table>

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**OP378 THE NATIONAL BURDEN IN FRANCE OF HOSPITAL CARE FOR PATIENTS WITH HEPATIC ENCEPHALOPATHY: DATA FROM THE FRENCH NATIONAL HOSPITAL DATABASE (PMSI)**

A. Abergel1, H. Hagege2, R. Benamouzig3, C. Bureau4, C. Blein5, C. Amaz3, E. Ribot-Mariotte3, M. Hudson6, H. Hagege, C. Bureau, C. Blein, C. Amaz, and E. Ribot-Mariotte were contracted by HEVA, who were commissioned by the French Ministry of Health to conduct this study and Alfa Wassermann to participate in this study.

**Aims & Methods:** A retrospective observational study in 11 specialist National Health Service (NHS) centres of 145 patients prescribed RFX for HE between July 2008 and May 2014. Local clinical staff reviewed patients' medical records for demographics, RFX prescribing and adverse drug reactions (ADRs) to RFX. Details of inpatient hospitalisations and hospital visits in the 12 months pre- and post-RFX initiation were extracted from NHS Trust electronic databases. Ethics reference 14/WS/1017.

**Results:** Of the 145 patients evaluated, 89 (61%) were male. At RFX initiation, mean age was 61 years (standard deviation [SD] = 11), 119 patients (82%) were on lactulose. Child-Pugh score was recorded for 67 (44%) patients (10% Class A, 54% B, 36% C). Resource use in the 612 months pre- and post-RFX initiation is shown in Table 1; to avoid nonsurvivor confounding this analysis includes the 114 patients (78%) who were alive at 6 months and 102 (70%) alive at 12 months post-RFX initiation. 3 patients (2%) had ADRs and 4 (3%) developed C difficile infection.

**Conclusion:** In UK clinical practice, treatment with RFX for HE is well-tolerated and associated with significant reductions in hospitalisation frequency, bed occupancy (including critical care) and emergency room visits; reductions are observed within 6 months of treatment initiation and sustained at 12 months. This is the first study to demonstrate a reduction in critical care bed occupancy with RFX.

**Disclosure of Interest:** R. Aspinall: Consultant and UK advisory board member for Norgine R. Radwan: Employee of Norgine G. Shaya: Employee of Norgine H. Sodatonou: Employee of Norgine C. Cipelli: Consultant for Norgine, Employee of pH Associates which was commissioned by Norgine Pharmaceuticals to provide support with study design and management, data analysis and scientific editorial services M. Hudson: Consultant for Norgine, Attended advisory board and has given sponsored lectures (national or international) on behalf of Norgine.

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**Disclosure of Interest:** All authors have declared no conflicts of interest.
OP382 PREGNANCY OUTCOME IN MORE THAN 5000 BIRTHS TO WOMEN WITH VIRAL HEPATITIS IN A POPULATION-BASED COHORT STUDY IN SWEDEN

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2Division Of Epidemiology And Public Health, University of Nottingham, Nottingham/Sweden
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Introduction: Previous studies have shown inconsistent results with respect to hepatitis B (HBV), Hepatitis C (HCV) and pregnancy outcome.

Aims & Methods: The aim of this study was to investigate pregnancy outcome in women with HBV or HCV. In a nationwide cohort of pregnancies between 1997 and 2011 we investigated the risks of adverse pregnancy outcomes in 3,077 women to HBV and 2,150 births to women with HCV using data from Swedish healthcare registries. Births to women without HBV (n=1,428,338) and births without HCV (n=1,429,165) served as population controls. Crude and adjusted relative risks (RR) were calculated using Poisson regression analysis.

Results: Women with HCV were more likely to smoke (47.62% vs. 8.65%) and to have alcohol dependence (18.79% vs. 1.07%) compared with population controls. Most women were born in non-Nordic countries. HCV was associated with a decreased risk of pre eclampsia (aRR: 0.42, 95% CI: 0.25-0.65), an increased risk of late neonatal death (7-27 days: aRR: 4.47, 95% CI: 1.01-12.44) and an increased risk of preterm birth (aRR: 1.31, 95% CI: 1.08-1.59). HBV was associated with an increased risk for preterm birth (aRR: 1.21, 95% CI: 1.01-1.44).

Conclusion: Both HBV and HCV are risk factors for preterm births, while HCV seems to be associated with a protective effect against pre eclampsia. Future studies should corroborate these findings.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016
10:30-12:00
TRANSLATIONAL ASPECTS OF IBD – ROOM L8

OP383 ALTERATION OF THE RENIN-ANGIOTENSIN SYSTEM IN THE CIRCULATION, TERMINAL ILEUM AND COLON IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A POTENTIAL NOVEL THERAPEUTIC TARGET

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Introduction: The renin-angiotensin system (RAS) has well-recognised roles in cardiovascular and renal homeostasis, but may also regulate inflammation, fibrosis or angiogenesis in multiple other organs, including the gastrointestinal tract. The newly recognised alternative RAS axis comprising angiotensin converting enzyme 2 (ACE2) and its receptor, mediate anti-inflammatory and anti-fibrotic effects as opposed to the classical RAS axis are upregulated in patients with IBD. However, mucosal Ang (1–7) is reduced, suggesting dysregulation and a potential role of the RAS in pathogenesis of inflammation, or perpetuation of inflammation in IBD. Novel therapies that increase mucosal Ang (1–7) may have a role in IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP384 BLOCKADE OF AE7/INTEGRIN CONTROLLS TRAFFICKING OF CD8+ AND TH9 LYMPHOCYTES FROM IBD PATIENTS TO THE INFLAMED GUT IN VIVO

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Introduction: The anti-CD8+ antibody vedolizumab (VDZ), which inhibits homing of lymphocytes via interaction of α4β7 with MAdCAM-1, has greatly increased therapeutic options in patients with IBD. However, lymphocyte homing may also occur via other homing molecules like the α4β1 integrin and a considerable portion of patients does not respond to VDZ therapy. The anti-CD8+ antibody etrolizumab (ETZ) is currently tested in phase III trials and with the binding of αEβ7 to E-Cadherin, which is believed to mediate epithelial retention of homed lymphocytes.

Aims & Methods: We aimed to compare lymphocyte trafficking upon blockage of αEβ7 vs. α4β7 integrin. Hence, αEβ7 and α4β7 expression was determined on peripheral blood and lamina propria lymphocytes subsets in IBD and CD patients and healthy donors by flow cytometry or immunofluorescence staining, respectively. The regulation of αEβ7 expression upon lymphocyte stimulation and incubation with cytokines was studied. In vitro adhesion assays the adhesive capacity of lymphocytes to MAdCAM-1 and E-Cadherin was measured. The potential of VDZ and the ETZ surrogate antibody FIB504 (ETZs) were tested. Finally, lymphocytes from UC patients were treated with either of the compounds, fluorescence labelled and injected into the ileocoeal region of immunosuppressed mice. Gut homing was assessed by in vivo confocal microscopy and flow cytometry of lamina propria cells.

Results: AE7 expression was significantly higher on CD8+ lymphocytes both in the peripheral blood and the gut. Among both subsets αEβ7 expression was correlated with IL-9 secretion, while CD4+IL9+ cells expressed less αAβ7 than other CD4+ subsets. At the same time, CD8+ cells exhibited a notably greater potential to increase αEβ7 expression upon T cell stimulation and TGF-β production, while less increased expression of αEβ7 was observed on CD8+ cells. ETZs markedly inhibited binding of CD4+ and CD8+ lymphocytes to rhE-Cadherin and blocked the adhesion of CD4+ and CD8+ lymphocytes to hMAdCAM-1 to a degree comparable with VDZ. Fewer lymphocytes bound to a mix of both ligands upon treatment with ETZs compared with VDZ. In our humanized mouse model the portion of human CD8+ cells in the murine gut was significantly reduced three hours after injection when cells were treated with ETZs vs. VDZ. Among CD4+ cells, the fraction of T11+ cells was decreased, while the expression of αEβ7 on CD8+ cells from IBD patients treated with VDZ was higher in the maintenance than in the induction phase of treatment.

Conclusion: VDZ may not equally cover all pathogenetically relevant lymphocyte subsets. It is striking to insufficient therapeutic response in pre-treated patients. ETZ seems to offer superior reduction of intestinal lymphocyte infiltration especially concerning CD8+ and TH9 cells.

Disclosure of Interest: S. Zundler: The etrolizumab Surrogate antibody was produced by Sanofi, CA, USA. p<0.001 was neither involved in conception and design of the study nor in analysis and interpretation of the results. SZ received funding from Takeda.
References

OPT385 VITAMIN D REGULATES DENDRITIC CELL ACTIVITY AND TRAFFICKING IN CROHN’S DISEASE

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2Antigen Presentation Research Group, Imperial College, London/United Kingdom
3Gastroenterology Unit, Hospital U. La Princesa, IP, and CIBEREhdu, Madrid/Spain
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Introduction: Dendritic cells (DC) can determine whether the mucosal immune system mounts an inflammatory or regulatory response to antigen and likely contributes to the pathogenesis of Crohn’s disease. Vitamin D down-regulates DC inflammatory responses and could prove beneficial as a treatment adjunct in Crohn’s. Vitamin D also modulates DC homing marker expression. This study assessed the effect of high dose parenteral vitamin D treatment on circulating DC phenotype and function in patients with active luminal Crohn’s disease receiving anti-TNFα therapy.

Aims & Methods: Peripheral blood mononuclear cells were isolated from 14 patients with active luminal Crohn’s disease and suboptimal vitamin D levels (<75 nmol/L) prior to and 6 weeks after starting anti-TNFα (infliximab) therapy. Patients with low vitamin D (<50 nmol/L) were also given a single high dose of parenteral vitamin D (300,000 international units 1,25(OH)2 vitamin D3). Flow cytometry was used to identify total DC, (HLA-DR+), myeloid (CD11c+CD123-) and plasmacytoid DC (pDC, CD11c-CD123+) subsets. Expression of phenotype markers (including maturation status, homing markers and pattern recognition receptors) and on-going intracellular DC cytokine production during 4 hours’ culture were assessed.

Results: Production of TNFα by myeloid DC was significantly reduced (p = 0.016) in those patients who received vitamin D alongside anti-TNFα therapy, beyond that of those who received anti-TNFα therapy alone (mean treatment TNFα production 24.9% ± 39.1% respectively). There was a significant correlation between increase in vitamin D level and decrease in TNFα production by myeloid DC (p = 0.025, R2 = 0.76). An increase of serum 25(OH) vitamin D greater than 20 nmol/L was associated with a decrease in myeloid DC TNFα production. Anti-TNFα therapy alone induced a significant upregulation of the skin homing marker cutaneous lymphocyte antigen (CLA) on myeloid DC (p = 0.0055), an effect which was not seen in patients receiving adjunctive vitamin D.

Conclusion: High dose parenteral vitamin D, given as an adjunct to anti-TNFα therapy in Crohn’s, promotes down-regulation of circulating myeloid DC production of TNFα. This may influence the subsequent interaction of DC and T cells. TNFα promotes a TH-17 response characteristic of Crohn’s inflammation; thus the ability of vitamin D to further block TNFα production may promote a more regulatory T cell response and improve outcomes when used as an adjunct to anti-TNFα therapy. The upregulation of the skin homing marker CLA following anti-TNFα therapy may explain the high rates of cutaneous side effects to this drug class. The down-regulation of CLA by vitamin D in this setting may be particularly useful in those patients suffering cutaneous sequelae of anti-TNFα therapy.

Disclosure of Interest: P. Hendy: Advisory board: Dr Falk; AbbVie. All other authors have declared no conflicts of interest.

OPT387 A PROTEOMIC APPROACH TO EXPLORE THE PROTECTIVE ROLE OF INULIN IN PREVENTING LPS-INDUCED HUMAN COLONIC SMOOTH MUSCLE IMPAIRMENT

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Introduction: Fructans, such as inulin, are dietary fibers which stimulate gastrointestinal motility and the host response, reducing the radical-mediated oxidative stress induced by LPS (APEX1, CCT7). Moreover the anti-inflammatory properties of inulin are well demonstrated by the increased expression of some detoxification enzymes (MT2A, GSTK1, and UGT2B4) and to reduce the upregulation of inflammatory cytokines was up-regulated in Crohn’s, with myeloid DC producing higher levels of IL-6 than controls (p = 0.0042 and p = 0.013 respectively). Expression of maturation marker CD80 was increased on myeloid DC in Crohn’s but not on plasmacytoid DC (p = 0.027 and p = 0.13 respectively). Expression of IFNα, II-1β, II-12, CD40, CD80, TL12 and TL1R4 on DC did not differ between Crohn’s and controls for either DC subset.

Conclusion: The increased myeloid DC expression of gut homing phenotype may contribute to the pathogenesis of Crohn’s disease compared with controls. Our data suggest that the exposure of colonic mucosa to inulin is able to inhibit LPS-induced inflammation whilst plasmacytoid DC might be involved in cutaneous Crohn’s disease and the skin sequelae of anti-TNFα therapy.

Disclosure of Interest: P. Hendy: Advisory board: Dr Falk; AbbVie. All other authors have declared no conflicts of interest.

OPT386 CIRCULATING DENDRITIC CELL SUBSETS IN CROHN’S DISEASE SHOW ALTERATIONS IN TISSUE HOMING AND CYTOKINE PRODUCTION

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Introduction: Crohn’s disease is characterised by an exaggerated immune response to mucosal antigen. Dendritic cells (DC) have also capable of identifying homing markers on T cells which direct T cell migration to sites including the skin, gut and lymphoid tissue. We characterised homing marker profile and ongoing cytokine production of circulating DC subsets from patients with Crohn’s disease and from healthy controls.

Aims & Methods: DC within peripheral blood mononuclear cells from adults with active luminal Crohn’s disease or from healthy controls were characterised using flow cytometry. DC were identified as HLA-DR+ and negative for markers of other cell lineages (CD3, CD14, CD16, CD19, CD34). Myeloid DC (mDC, CD11c+CD123) and plasmacytoid DC (pDC, CD11c+CD123+) were assessed for phenotype (maturation status, homing markers and pattern recognition receptors) and on-going cytokine production by surface and intracellular staining techniques.

Results: In patients with Crohn’s disease (n = 20), a greater proportion of myeloid DC expressed a gut-homing profile (CLA+β7, p = 0.0013) compared to healthy controls (n = 13) where most myeloid DC were not tissue-specific (CD11c+CLA-CD123) (p = 0.0016). In controls, gut-homing DC (CLA+β7, p = 0.0013) were the majority compared with myeloid DC expressing anti-TNFα therapy. This may influence the subsequent interaction of DC and T cells in Crohn’s, with myeloid DC being central to gut inflammation whilst plasmacytoid DC might be involved in cutaneous Crohn’s disease and the skin sequelae of anti-TNFα therapy.
Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

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Introduction: SRGAP1 (Slit-Robo GTPase-activating protein 1) functions as a GAP for Rho-family GTPases and downstream-activated protein 1 signaling. Here we aim to investigate the biological functions of SRGAP1 and comprehensively reveal its regulation by deregulated miRNAs in gastric cancer.

Aims & Methods: We aim to investigate the biological functions of SRGAP1 and comprehensively reveal its regulation by deregulated miRNAs in gastric cancer.

Results: We aimed to investigate the biological functions of SRGAP1 and comprehensively reveal its regulation by deregulated miRNAs in gastric cancer.

Conclusion: SRGAP1 is over-expressed in GC and plays an oncogenic role in GC through activating Wnt/beta-catenin pathway. Apart from gene amplification and mutation, the activation of SRGAP1 in GC is partly due to the downregulation of miR-340 and miR-124.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016
10:30-12:00
GASTRIC AND JUNCTURAL CANCERS – ROOM 1.86

OP388 TLR4 IS STILL ACTIVE IN GP96-DEFICIENT MACROPHAGES
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Introduction: GP96 is an endoplasmic reticulum chaperone for multiple protein substrates which plays an important role in innate and adaptive immunity. Lack of this protein in intestinal macrophages (iMACS) of Crohn’s Disease (CD) patients is correlated with a loss of tolerance against the host gut flora, triggering a chronic and persistent inflammation. iMACS are crucial for pathogen recognition at the mucosal surface of the gastrointestinal tract and Toll-like receptors (TLR), one of the best investigated family of pattern recognition receptors, lead to the phosphorylation of NF-κB after their activation. Previous studies of our group revealed a strong expression of TLR2 and 4 on macrophages isolated from both, wild-type (WT) and KO mice, and treated with LPS (100 ng/ml) for 2 hours. Transduced MM6 cells and peritoneal macrophages, TLR2 and TLR4 expression was analyzed by flow cytometry and the expression of NF-κB, IL-8, IL-6 and TNF-α was determined by Western blot, PCR and ELISA. Results are expressed as percentage or fold induction ± SEM. All experiments were performed with an n ≥ 3.

Results: After checking that the efficiency of lentiviral knockdown was more than 90% with flow cytometry experiments we observed that the expression of TLR4 and TLR2+gp96 shRNA transduced cells were slightly decreased, 81% and 77% respectively, compared with mock-transduced MM6 cells, 92% and 97% respectively. In line with this, the analysis of the expression of TLR4 and TLR2 receptors in peritoneal macrophages showed a similar slight decrease in KO mice (74.4% and 77.0% respectively) compared with WT mice (78.2% and 90.5% respectively). The functionality of TLR4 receptor was also analyzed and treatment with LPS induced a significant increase in the ratio p-IκB-α/IκB-α in gp96−/− macrophages (1.6 fold induction) and in KO peritoneal macrophages (5.1±1.5) and in protein expression of p NF-κB in both gp96 shRNA (1.7) and in KO peritoneal macrophages (1.5±0.6) compared with non-treated mock-transduced cells and WT peritoneal macrophages. Furthermore, LPS induced a significant increase in the mRNA expression of IL-6 (11.7±2.6), IL-12 (12.3±3.9) and TNF-α (7.9±1.9) in KO peritoneal macrophages compared with non-treated macrophages. Conclusion: TLR4 receptor is still active and functional even in the absence of gp96.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP391 SRGAP1, A CO-TARGET OF MIR-340 AND MIR-124, FUNCTIONS AS A POTENTIAL ONCOGENE THROUGH AMPLIFICATION AND RECURRENT MUTATION IN GASTRIC TUMORIGENESIS
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Introduction: SRGAP1 (Slit-Robo GTPase-activating protein 1) functions as a GAP for Rho-family GTPases and downstream-activated protein 1 signaling. Here we aim to investigate the biological functions of SRGAP1 and comprehensively reveal its regulation by deregulated miRNAs in gastric cancer.

Aims & Methods: We aim to investigate the biological functions of SRGAP1 and comprehensively reveal its regulation by deregulated miRNAs in gastric cancer.

Results: We aimed to investigate the biological functions of SRGAP1 and comprehensively reveal its regulation by deregulated miRNAs in gastric cancer.

Conclusion: SRGAP1 is over-expressed in GC and plays an oncogenic role in GC through activating Wnt/beta-catenin pathway. Apart from gene amplification and mutation, the activation of SRGAP1 in GC is partly due to the downregulation of miR-340 and miR-124.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP389 A NEW, BIOLOGICALLY RELEVANT CLASSIFICATION FOR ADENOCARCINOMA AT THE GASTRO-OESOPHAGEAL JUNCTION

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Introduction: Adenocarcinomas at the gastro-esophageal junction (GOJ) are currently stratified according to the Swietert classification by location of the main tumour mass (GOJ1: 1-5 cm proximal to the junction, GOJ2: 1 cm proximal to 2 cm distal to the junction, GOJ3: 2-5 cm distal to the junction). Though this system is currently the standard for this group of tumours, it is unclear whether this also reflects the molecular phenotype and hence how this stratification might influence therapy and prognosis in an era of personalised medicine.

Aims & Methods: The aim of this study was to determine the molecular phenotypes of GOJ tumours and to relate this to the Swietert classification. The gene expression profile of 107 treatment-naive gastro-oesophageal adenocarcinomas at the gastro-oesophageal junction (GOJ) was assessed by the Illumina HTv4.0 beadchip array (GOJ1: 35, GOJ2: 31, GOJ3: 18, true gastric comparators: gastric fundus/proximal body: 6, distal body: 9, antrum: 8). Only tumours of intestinal Lauren type were included. Gene expression data was analysed using limma in R, unbiased sub-group assignment was performed applying a model-based algorithm using MCLUST in R. Gene-set enrichment based pathway analysis was done using GAGE in R based on KEGG and Gene Ontology terms. Whole genome sequencing was performed for a subset of 30 GOJ tumours (5 for GOJ1, 10 for GOJ2, and 15 for matched germline) to assess mutational burden, recurrently mutated genes, copy number aberrations, and mutational signatures in the identified subgroups.

Results: The Swietert classification did not reveal differential gene expression between the distinct groups of the molecular classification. Pathway analysis of the respective groups revealed significant differences in biological pathways and survival and may thus have implications for prognosis and targeted therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
clinical implications that targeting SRGAP1 might have therapeutic potential for GC.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP392 HOXB7 PROMOTES EPITHELIAL-MESENCHYMAL TRANSITION AND METASTASIS IN GASTRIC CANCER

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Introduction: In the previous study we observed that HOXB7 is highly expressed in gastric cancer and promote migration or invasion, and inhibit apoptosis in gastric cancer cells.

Aims & Methods: We aimed in this study to demonstrate the roles of HOXB7 in development of epithelial-mesenchymal transition (EMT) and metastasis in gastric cancer using in vitro and in vivo model. We established HOXB7-expression stable cell lines (MKN45-B7) and mock cells (MKN45-mock). Western blot was performed to validate EMT markers and phospho-Akt/PTEN activity. By injection of stable cell lines, xenograft tumors were produced on the 8-week old male Balb/C nude mice (nu/nu). 4 weeks after injection, we extracted xenograft tumors, and implanted fragment of tumors on the stomach of another 8-week old nude mice. 6 weeks after implantation, mice were sacrificed and their peritoneal metastasis, perigastric lymph node and volume of gastric tumor were compared between both groups.

Results: MKN45-B7 cells frequently showed fibroblast-like mesenchymal phenotype, whereas most of MKN45-mock cells showed epithelial phenotype. Mesenchymal markers (snail, vimentin) were upregulated and epithelial marker (E-cadherin) was downregulated in MNK45-B7 cells, as well as phospho-Akt level was increased and PTEN expression was decreased compared by MKN45-mock cells. The volume of xenograft tumor was significantly increased in MKN45-B7 cell-injected mice than MKN-mock cell injected mice. Mean number of peritoneal metastasis/perigastric lymph node and volume of gastric tumor were also significantly increased in MKN45-B7 tumor-implanted mice. When we transiently transfected siAkt on MKN45-B7 cells, snail and vimentin expression were down-regulated, whereas E-cadherin expression was up-regulated, compared by siControl-transfected MKN45-B7 cells.

Conclusion: Our findings suggest that HOXB7 may play crucial role in inducing EMT and promoting metastasis in gastric cancer via modulating Akt/PTEN axis.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP393 SIGNIFICANCE OF COLONOSCOPY IN PATIENTS WITH GASTRIC HIGH GRADE DYSPLASIA OR EARLY GASTRIC CARCINOMA

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Introduction: Relationship of gastric cancer and colon cancer, it is not yet clearly identified. But usually there is high risk of colorectal cancer known as gastric cancer patients.

Aims & Methods: The purpose of this study was to discuss the development risk of colorectal neoplasms in patients with gastric cancer (high-grade dysplasia, HGD and early gastric cancer, EGC) who underwent endoscopic submucosal dissection (ESD) compared to healthy controls. We also investigated the associated risk factors for colorectal neoplasm and colon cancer. The study group included a total of 209 patients with gastric cancer (4 cases: high-grade dysplasia, HGD and early gastric cancer, EGC) who underwent endoscopic submucosal dissection (ESD) compared to healthy controls. All of the patients underwent concurrent screening colonoscopy between January 2009 and May 2014. High risk colorectal neoplasm was defined as >1 cm, adenoma with villous component, adenoma with HGD, or more polyph of adenocarcinoma.

Results: High-risk colorectal neoplasm was found in 50/209 patients (23.9%) in patient group and 47/610 (7.7%) in controls (P < 0.05). Colon cancer was diagnosed in 16/209 patients (7.6%) in patient group and 18/610 (2.9%) in controls (P < 0.03). The risk of high-risk colorectal neoplasm was associated with age, DM, colon cancer family history, and presence of gastric cancer category 4. The risk factors of colon cancer were associated age, and colon cancer family history, and presence of gastric cancer category 4.

Conclusion: Colonoscopy is important for high-risk colorectal neoplasms and colon cancer in patient group who underwent gastric ESD was higher than that in the control group. Therefore, patients undergoing ESD with category 4 lesions may need screening colonoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP394 PALLIATIVE CHEMOTHERAPY AND TARGETED THERAPIES FOR ESOPHAGEAL AND GASTRO-ESOPHAGEAL JUNCTION CANCER

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Introduction: More than 50% of patients with esophageal (EC) or gastro-oesophageal junction cancer (GEJC) have metastatic disease at the time of diagnosis. Chemotherapy and targeted therapies are increasingly used for palliative treatment with the intent to control tumor growth, improve quality of life, and prolong survival. To date, scientific proof is lacking.

Aims & Methods: Therefore, the aim of this study was to systematically review and compare the effectiveness of chemotherapy and targeted therapy to best supportive care (BSC) and, to compare the addition of a cytostatic or targeted therapeutic to a control arm in patients with EC/GEJC. This abstract is based on a pre-peer review of a formal Cochrane Review. Upon completion and approval, the final version is expected to be published in the Cochrane Database of Systematic Reviews. We searched the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE, and searched reference lists of studies.

Results: The search was not restricted to English language publications only. Randomized controlled trials were included. The primary outcome was overall survival (OS) and included a significant benefit of OS in favor of the arm with the additional cytostatic or targeted therapeutic with a HR of 0.77 (95% CI 0.70 to 0.85). The median increased survival time was limited, one month for adding an additional cytostatic or targeted therapeutic to the control arm. Subanalysis with second line therapies showed a similar benefit as first line therapies. Rumurcunab was the only agent, investigated more than once, that significantly improved both OS and PFS. Palliative chemotherapy and/or targeted therapy increased the frequency of treatment related toxicity of at least grade 3. However, treatment related deaths did not occur more frequently. Quality of life studies, that reported this outcome, often improved in the arm with an additional agent.

Conclusion: Palliative chemotherapy and/or targeted therapy significantly increased OS compared to BSC in patients with esophageal or gastrooesophageal junction carcinoma. Addition of chemotherapy, or targeted therapy agents have an increased OS, PFS and improvement of quality of life, on the expense of treatment-associated toxicity of at least grade 3. Based on the meta-analysis, palliative chemotherapy and/or targeted therapy should be considered standard care for esophageal and gastrooesophageal junction carcinoma.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016

10:30-12:00
ABSTRACTS ON FIRE: NEW APPROACHES TO COLORECTAL DISEASE – HOTSPOT 2

OP395 ECONOMIC EVALUATION OF ANTIBIOTIC THERAPY VS APPENDICITIS FOR TREATMENT OF UNCOMPLICATED ACUTE APPENDECTOMY: RESULTS OF THE APPAC RANDOMIZED CLINICAL TRIAL

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**Introduction:** Appendectomy has been the standard treatment for acute appendicitis for more than 30 years. Appendectomies are performed annually in the United States1. Although appendectomy is generally well tolerated, it is a major surgical intervention and can be associated with postoperative morbidity. Our APPAC trial2 comparing antibiotic therapy with appendectomy for uncomplicated acute appendicitis in our Appendicitis Acuta (APPAC) randomized clinical trial. The Appendix Acuita trial multicenter, open-label, non-inferiority randomized clinical trial was conducted in Finland from November 2009 until June 2012. A total of 530 adult patients aged 18 to 60 years with CT-scan confirmed uncomplicated acute appendicitis were enrolled in six Finnish hospitals. Patients were randomly assigned to resection or conservative treatment. The main outcome measure was the time to discharge. We used an open-label, parallel-group, multicenter, randomized clinical trial between May 2010 and September 2012. The primary endpoint was the quality of life measured by the colorectal quality of life index (GIQLI) questionnaire. The secondary endpoint was the time to discharge. Between July 1, 2010 and April 1, 2014, 109 patients were randomly assigned to either conservative treatment, according to current day practice, or possible recurrent appendicitis during the one-year follow-up period.

**Results:** In the operative group, the overall societal costs were 16 times higher than in the antibiotic group. In both groups productivity losses represented a slightly higher proportion of overall societal costs than all treatment costs together, with diagnostic and medicines having a minor role. Patients in the operative group were prescribed significantly more sick leave days (16.96, SD 22.7) vs (114.4 (SD 22.3) vs 10.0, p = 0.001). When the age and sex of the patient as well as the hospital of care were controlled simultaneously, the operative treatment option generated significantly more costs in all models.

**Conclusion:** To our knowledge, this is the first randomized study comparing antibiotic therapy and appendectomy in uncomplicated adult acute appendicitis to resection for analysis. Avoiding an apparently unnecessary surgery in our study resulted in major cost savings. Although 27% of the antibiotic group patients underwent surgery, the differences in costs both to the service providers and to the society overall strongly support evaluating antibiotic therapy as the first alternative for uncomplicated adult appendicitis. Further studies evaluating the optimal treatment of uncomplicated appendicitis are strongly encouraged also from an economic standpoint.

**Disclosure of Interest:** P. Salminen: Research grant / a government research grant (EVO) awarded to Turku University hospital. All other authors have declared no conflicts of interest.

**References**

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**Introduction:** Sessile Serrated Adenomas/Polyps (SSA/P) are responsible for nearly 10% of colorectal cancer (CRC). Despite the utility of novel imaging-enhancing techniques including narrow band imaging it is difficult to differentiate hyperplastic (HP) polyps from SSA/Ps. Vast proportion of endoscopists leave the diminutive and possibly small HP polyps in situ in the recto sigmoid area (diagnose and disregard approach). Hence there is a possibility of leaving SSA/P in the recto sigmoid region which could potentially lead to CRC later in life.

**Aims & Methods:** We aim to estimate the prevalence of SSA/P in recto sigmoid colon at screening colonoscopy and flexible sigmoidoscopy (FS). Patients aged >55 years underwent a screening colonoscopy (n = 500) or a flexible sigmoidoscopy (n = 500) at our institution between August 2014 and April 2015 were included. Data collected from 500 consecutive patients who underwent a colonoscopy or a FS. Demographic, procedural and polyp data were retrieved from our endoscopy database.

**Results:** 99.6% of (498/500) colonoscopy and 97.6% of flexible sigmoidoscopy procedures were completed. Screening colonoscopy detected 1006 polyps and FS detected 987 polyps. Polyp size ranged between 1–80 mm (colonoscopy mean size 6 mm, SD 7.2 mm; FS mean 3.4 mm; SD 3.9 mm). While colonoscopy detected 43 SSA/Ps (4.3%), FS detected only 6 SSA/Ps (2.4%) which equates to an overall prevalence of 3.9% (49/1255). Table 1 summarises the SSA/P prevalence data from our cohort. In rectum there were 8 SSA/Ps detected and resected which equals to a 3.6% of all rectal polyps. All SSA/Ps detected in rectum were less than 10 mm in size (range 2–9 mm). Prevalence of SSA/Ps in proximal colon was 4.5%.

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**Introduction:** Appendectomy has been the standard treatment for acute appendicitis for more than 30 years. Appendectomies are performed annually in the United States. Although appendectomy is generally well tolerated, it is a major surgical intervention and can be associated with postoperative morbidity. Our APPAC trial comparing antibiotic therapy with appendectomy for uncomplicated acute appendicitis in our Appendicitis Acuta (APPAC) randomized clinical trial. The Appendix Acuita trial multicenter, open-label, non-inferiority randomized clinical trial was conducted in Finland from November 2009 until June 2012. A total of 530 adult patients aged 18 to 60 years with CT-scan confirmed uncomplicated acute appendicitis were enrolled in six Finnish hospitals. Patients were randomly assigned to resection or conservative treatment. The main outcome measure was the time to discharge. We used an open-label, parallel-group, multicenter, randomized clinical trial between May 2010 and September 2012. The primary endpoint was the quality of life measured by the colorectal quality of life index (GIQLI) questionnaire. The secondary endpoint was the time to discharge. Between July 1, 2010 and April 1, 2014, 109 patients were randomly assigned to either conservative treatment, according to current day practice, or possible recurrent appendicitis during the one-year follow-up period.

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**Disclosure of Interest:** P. Salminen: Research grant / a government research grant (EVO) awarded to Turku University hospital. All other authors have declared no conflicts of interest.

**References**
OP398 SERRATED POLYPOSIS SYNDROME: A SURGICAL PERSPECTIVE
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Introduction: Serrated Polyp Syndrome (SPS) is associated with an increased risk of colorectal cancer (CRC). Some patients may require colonic surgery but the literature regarding indication, procedure performed, outcomes and surgical decision making is sparse. We aimed to address these issues.

Aims & Methods: 434 patients with SPS were retrospectively enrolled from 7 centers in the Netherlands and 2 in the UK. Data were retrieved from medical charts, pathology and endoscopy reports and collected in a centralized database. Data relating to surgical resection and surveillance outcomes were assessed.

Results: A total of 164 (38%) patients underwent colorectal surgery; 114 (70%) for CRC, 31 (19%) for high polyp burden and 14 (9%) for unresolvable polyps. Surgery for SPS Cancer Twenty seven (25%) SPS cancers were managed with total colectomy and ileorectal anastomosis (IRA), with the remaining 87 (75%) patients having a more limited resection. 90% of those undergoing IRA had a formal diagnosis of SPS at the time of their surgery compared with only 39% of those undergoing more conservative resections. Fifty eight (90%) patients had a resection for cancer before a diagnosis of SPS was made. Total polyp burden (median 40 v 22.5, p < 0.01) and proximal polyp numbers (median 20 v 12, p < 0.019) were significantly higher in those having more extensive surgery. In the limited resection group eight (9%) patients had a history of colorectal cancer due to polyp removal (0.31%) and 194 in individuals without adenomas (0.15%). The strongest predictors for colorectal cancer risk were adenoma size ≥20 mm in diameter (HR 8.70, 95% CI 5.43–13.95, P < 0.001), high-grade dysplasia (HR 4.15; 95% CI 2.05–8.43, P < 0.001) and ≥12 adenomas (HR 3.13; 95% CI 1.60–6.12; P = 0.001). In a novel risk classification system using only these three predictors the number of individuals in the high-risk group was reduced by 56% with no increase in risk of overlooked cancer (absolute risk difference per 10,000 individuals 2.2–95% CI –11.9–16.3).

Conclusion: Limiting surveillance recommendations to patients with adenomas ≥20 mm in diameter or high-grade dysplasia or ≥3 adenomas significantly reduces the need of surveillance colonoscopies without increasing the risk for overlooked cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP399 IMPROVED RISK CLASSIFICATION FOLLOWING COLORECTAL ADENOMA REMOVAL
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Introduction: Current colonoscopy surveillance recommendations after polyp removal are arbitrary and resource demanding. We developed a novel risk classification system for colorectal cancer following adenoma removal.

Methods: We included individuals without adenomas and derived a novel risk classification system.

Results: Among 159,928 individuals (median age 56 years; 37.8% males) with a median follow-up of 7.1 years we identified 82 colorectal cancers after adenoma removal (0.31%) and 194 in individuals without adenomas (0.15%). The strongest predictors for colorectal cancer risk were adenoma size ≥20 mm in diameter (HR 8.70; 95% CI 5.43–13.95, P < 0.001), high-grade dysplasia (HR 4.15; 95% CI 2.05–8.43, P < 0.001) and ≥12 adenomas (HR 3.13; 95% CI 1.60–6.12; P = 0.001). In a novel risk classification system using only these three predictors the number of individuals in the high-risk group was reduced by 56% with no increased risk of overlooked cancer (absolute risk difference per 10,000 individuals 2.2–95% CI –11.9–16.3).

Conclusion: Limiting surveillance recommendations to patients with adenomas ≥20 mm in diameter or high-grade dysplasia or ≥3 adenomas significantly reduces the need of surveillance colonoscopies without increasing the risk for overlooked cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP400 COST-EFFECTIVENESS ANALYSIS OF POST-POLYPECTOMY COLONOSCOPY SURVEILLANCE USING JAPANESE DATA: RISK-STRATIFIED SURVEILLANCE BASED ON POLYP RESULTS IS MORE COST-EFFECTIVE
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Introduction: To maximize the usefulness of total colonoscopy (CS) in reducing deaths from colorectal cancer (CRC), it is essential that cost-effective post-polypectomy CS surveillance programs are implemented. However, this has not been well examined. European Union and United States guidelines for post-polypectomy surveillance recommend risk-stratified programs based on initial CS results.日本のガイドラインにおいて、術後結腸鏡検査予防を実施する際のリスクを考慮に入れた分類を行うことが推奨されている。しかし、これについては十分に研究がなされていません。Europe and United States guidelines for post-polypectomy surveillance recommend risk-stratified programs based on initial CS results.1,2 Japanese guidelines, however, recommend that post-polypectomy surveillance CS should be performed within 3 years of polypectomy, regardless of the results of resected polyps.3 Given that different surveillance programs are recommended in different settings, it is important to determine the most cost-effective surveillance program.

Aims & Methods: The aim of this study was to determine the most cost-effective post-polypectomy CS surveillance program by performing a Markov model analysis using Japanese data. The model was developed by simulating the clinical course of CRC as a transition from normal epithelium, low-risk adenomatous polyps sized 1-4 mm and 5-9 mm, high-risk adenomatous polyps, CRC, and finally to death from CRC.4 High-risk polyps included intramuscular cancers and adenomas with a diameter ≥10 mm, with high-grade dysplasia, or with villous histology (≥25%). The initial population comprised 100,000 average-risk individuals aged 40 years. Parameters of transition probabilities, costs, and test accuracies were derived from prospective randomized controlled trials and based on Japanese data.5 Four surveillance
strategies were evaluated for costs, gained quality-adjusted life-years (QALYS), and the required number of CS procedures. In strategy 1, post-polypectomy surveillance CSs were performed 1 year after polypectomy regardless of the polyp results. In strategy 2, the interval between surveillance CSs and polypectomy was 3 years regardless of the polyp results. Strategy 3 was a risk-stratified one, where surveillance CSs were performed 3 years after the resection of high-risk polyps and 5 years after that of low-risk polyps. In strategies 1, 2, and 3, surveillance CSs were performed 10 years after normal CSs. Strategy 4 was also a risk-stratified one with more intense use of CS than strategy 3; the interval between surveillance CSs and resection of high-risk polyps, low-risk polyps, and no polyps were 1, 3, and 5 years, respectively. In all strategies, a fecal immunochromat-ical test-based CRC screening program was provided before surveillance, and uptake rates were set at 60% in the base-case analysis. A probabilistic sensitivity analysis (PSA) was also performed for all model parameters.

Results: QALYs and costs per person in strategy 1 were as follows: strategy 1, 23,004 QALYs and US$1,024.88; strategy 2, 23,000 QALYs and $1,009.02; strategy 3, 23,015 QALYs and $977.40; strategy 4, 23,046 QALYs and $970.31. The required numbers of CS procedures per person in strategy 1, 2, 3, and 4 were 2.143, 1.664, 1.617, and 2.548, respectively. Risk-stratified strategies (strategies 3 and 4) yielded higher QALYs with lower costs than strategies 1 and 2. Comparing strategy 3 with strategy 4, yielded QALYs were higher and required cost was lower in strategy 4. Strategy 4 was most-cost-effective, showing simple dominance over the other strategies, followed by strategy 3; however, strategy 4 required the most CS procedures. The PSA showed that the probability of strategy 4 being chosen as the most cost-effective at the willingness-to-pay value of $50,000 was 67.8%.

Conclusion: After polypectomy, risk-stratified CS surveillance programs based on the polyp results should be recommended owing to higher expected effectiveness and cost-effectiveness. Furthermore, more intense use of CS procedures in risk-stratified surveillance can heighten the effectiveness and cost-effectiveness in the Japanese setting. However, it does require a larger number of CS procedures; thus, it would be preferable to determine the most appropriate use of CS procedures in risk-stratified surveillance programs depending on the nationwide availability of CS resources.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

**Table (OP401)**

<table>
<thead>
<tr>
<th>JNET</th>
<th>Type 1</th>
<th>Type 2A</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vessel pattern</strong></td>
<td>Invisible</td>
<td>Regular caliber</td>
<td>Variable caliber</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regular distribution</td>
<td>Irregular distribution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(meshed/spiral pattern)</td>
<td></td>
</tr>
<tr>
<td><strong>Surface pattern</strong></td>
<td>Regular dark or white spots</td>
<td>Regular (tubular/branched/papillary)</td>
<td>Irregular or obscure</td>
</tr>
<tr>
<td></td>
<td>Similar to surrounding normal mucosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Most likely histology</strong></td>
<td>Hyperplastic polypl/Sessile serrated poly</td>
<td>Low grade intramucosal neoplasia</td>
<td>High grade intramucosal neoplasia/Shallow submucosal invasive cancer</td>
</tr>
</tbody>
</table>

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Introduction: There have been many narrow-band imaging (NBI) magnifying endoscopic classifications advocated (Nano, Hiroshima, Showa, and Jikei classifications) so far in Japan. NBI magnifying endoscopy for qualitative and quantita-tive diagnosis for colorectal lesions is useful, however, some discussion in Japan has raised issues such as i) the presence of multiple terms for the same or similar findings, ii) the necessity of including surface patterns in magnifying endoscopic classifications, and iii) differences in the NBI findings between poly-poid and superficial lesions. To resolve these issues and unify the classifications, the Japan NBI Expert Team (JNET) was set up in 2011. The aim of this study is to scientifically evaluate the NBI scale and determine the NBI findings and diagnostic criteria used in the unified classification (The JNET classification).

Aims & Methods: The JNET classification, which is a modification of NICE classification, consists of 4 categories (Types 1, 2A, 2B, and 3) based on vessel and surface patterns without color. We made a hypothesis that each of them are correlated with the histopathological findings of hyperplastic polypl/sessile ser-rated polypl (SSP), low grade intramucosal neoplasia, high grade intramucosal neoplasia/shallow submucosal invasive cancer, and deep submucosal invasive cancer, respectively. A web image interpretation study using the modified Delphi (UMIN000010292: Multicenter study for developing universal NBI magnifying endoscopic classification of colorectal tumors in Japan) was conducted. 25 specialists in magnification evaluated NBI magnifying findings and histology with 100 NBI still images on the web.

Results: Univariate and multivariate analyses and analysis on diagnosability from 5 candidate NBI magnifying findings such as 1) loose vessel areas, 2) interruption of thick vessels, 3) scattered vessels, 4) thick, linearized/meandering atypical vessels in the tumor, and 5) amorphous areas of surface patterns for Type 3, and i) variable caliber of vessels, ii) thick vessels iii) irregular distribution of vessels, iv) vessel meandering, and v) irregular or obscure surface pattern for Type 2B. Among the five candidate NBI findings, three findings such as 1) loose vessel areas, 2) interruption of thick vessels, and 5) amorphous areas of surface patterns were identified as the diagnosis of type 3. In addition, three findings such as i) variable caliber of vessels, III) irregular distribution of vessels, and V) irregular or obscure surface pattern were selected for the diagnosis of type 2B.

Conclusion: Subclassification of NICE Type 2 (2A & 2B) could be performed scientifically with NBI magnifying findings without color using web image interpretation study, which could conduct differential diagnosis between low grade intramucosal neoplasia and high grade intramucosal neoplasia/shallow submu-coal invasive cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP402 CLASSES OF TYPE-II PIT PATTERN REVEAL ALTERNATIVE TUMORIGENIC PATHWAYS OF COLORECTAL SERRATED LESIONS


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Introduction: Colorectal serrated lesions (SLs) include hyperplastic polyp (HP), traditional serrated adenoma (TSA) and sessile serrated adenoma/polypl (SSA/P). Emerging evidences suggest that SSA/Ps are precursor lesions of colorectal cancers (CRCs) with BRAF mutation and the CpG island methylator phenotype (CIMP). We have previously reported that Type II-Open (Type II-O) pit patterns, which is highly specific to SSA/P. However, clinicopathological and molecular features of SLs without Type II-O pits remain unclear.

Aims & Methods: We aimed to identify clinicopathological and molecular features of SLs without Type II-O pits. We analyzed the methylation of CIMP markers (MINT1, 2, 3, p16 and MLH1) and BRAF and KRAS mutations in 448 premalignant and malignant colorectal tumors. By using magnifying endoscopy, surface microstructures of colorectal lesions were classified into Type II pit or tumor pit (Type III, IV or V pit) according to the Kudo’s pit pattern classification system. Type II pit was subclassified into classical Type-II pit, Type II-O pit, Type II-Long (Type II-L) pit. CIMP status (CIMP-high, -low and -negative) was determined by using the five methylation markers.

Results: Endoscopic findings were classified as 41 Type II pit, 8 Type II-L pit, 92 Type II-O pit, 21 Type II plus tumor pit, 22 Type II-L plus tumor pit, 50 Type II-O plus tumor pit and 214 tumor pit. We identified Type II-L plus tumor pit, which was specific to TSA with KRAS mutation and CIMP-low (sensitivity, 60%; specificity, 96%). As compared to lesions with only Type II-O pits, KRAS mutation and CIMP-low were more frequent in lesions with Type II-L plus tumor pit. Progression of Type II-L pit lesions to TSA was associated with KRAS mutation and accumulation of moderate DNA methylation. In contrast, BRAF mutation was frequently observed in colorectal cancers with Type II plus tumor pit. These results suggest that lesions with Type II-O pit and those with Type II-L plus tumor pit appear to develop through distinct tumorigenic pathways, though the majority of lesions with Type II or Type II-O pit were the same HP.

Conclusion: Our data suggest that Type II-L plus tumor pit is a useful hallmark of the premalignant stage of CRCs with KRAS mutation and CIMP-low.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP403 ARTIFICIAL INTELLIGENCE (AI) IN ENDOSCOPY–DEEP LEARNING FOR OPTICAL BIOPSY OF COLORECTAL POLYPS IN REAL-TIME ON UNALTERED ENDOSCOPIC VIDEOS


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Introduction: ASGE-PIVI guidelines support a “resect and discard” strategy for diminutive colon polyps, provided that the predictive value of technology allowing for “optical biopsy” depicts at least 90% agreement in assignment of post-polypectomy surveillance intervals using pathology as standard. In addition, in order for a technology to be used to guide the decision to leave suspected diminutive rectosigmoid hyperplastic polyps in place (without resection), the technology should provide 90% negative predictive value for adenomatous histology. Such standards with optical biopsy might be achievable with experts (although even that is unclear) but do not cross over into general clinical practice. Several groups have looked at supporting the process of optical biopsy decision making on endoscopic assessment of the histology of diminutive colorectal polyps using traditional machine learning, but to date there are significant limitations in terms of (1) using still images only, and non-realtime computer support, both of which are not clinically efficient or effective, and (2) often involving magnification endoscopy that is not yet a widespread clinical practice. Deep learning is a branch of artificial intelligence which is a significant advance on traditional machine learning, and with huge computational power, machines can now recognize objects in real time. We sought to apply novel deep learning techniques to optical biopsy for colon polyps.

Aims & Methods: We aimed to evaluate deep learning applied to the classification of colorectal polyps into NICE types 1 and 2, in real-time on unaltered endoscopic videos, for the support of clinically efficient optical biopsy. We used 92 videos of small colorectal polyps (<10 mm) under white light (WL) and narrow-band imaging (NBI) (38 NICE type 1, 52 NICE type 2), using Olympus 190 series colonoscopes. “Optical biopsy” was done on all polyps by an expert with >95% accuracy (using pathology as the reference standard) prior to removal and histological confirmation. We investigated a Deep Learning Artificial Intelligence model with a proprietary deep convolutional neural network (DCNN) for the computer-assisted NICE type 1&2 differentiation. We designed a 5-class model representing Types 1, 2, and unsuitable (frames without statistically representative information–blur, bubbles, liquid). The model operated at the individual frame level, without prior segmentation. For model training purposes, each frame was manually tagged. The final dataset was split into training and validation sets, without overlap. Finally, the analysis was performed separately for NBI and WL frames, allowing for reporting of frame processing time and classification performance.

Results: A total of 33,954 training frames were used, split equally across NBI & WL, and type 1, type 2, & unsuitable classes. We performed a 5-fold cross-validation on the tagged frames for quality control. The trained DCNN model was then used to evaluate the unaltered videos in real-time, with an accuracy for polyp classification of 90% for NBI, and 83% for WL. The confusion matrix on whole-video classification of colorectal polyps gives a sensitivity of 93% and specificity of 85% for NBI. Finally, the processing time of our DCNN model ran at between 25 and 30 frames per second (fps) using a decent gamer-grade GPU (NVIDIA Titan-X) on an unaltered video feed of 60 fps, delivering near-realtime computer support.
**Conclusion:** To our knowledge, this is the first application of deep learning to the optical biopsy challenge for polyp differentiation into NICE types 1&2 using non-magnification colonoscopy and NBI, specifically in a clinically representative workflow where computer support is provided in realtime on unaltered endoscopic video streams. Although the present investigation was carried on a limited datasets of 92 videos, our deep learning model has shown clinically efficient and relevant performance for optical biopsy, well aligned with PIVI guidelines and the performance of experts. Ongoing work will determine if such a computer support solution could aid in the widespread adoption of a “resect and discard” strategy, and reduce the economic burden of pathological evaluation of benign diminutive colon polyps.

**Disclosure of Interest:** M.F. Byrne: Chairman of Satis Operations Inc
D.K. Rex: Olympus consulting and research support
N. Chapados: Imagia has commercial interests in artificial intelligence
F. Soudan: Imagia has commercial interests in artificial intelligence
C. Oertel: Imagia has commercial interests in artificial intelligence
M. Linares Perez: research support from Satis Operations Inc
R. Kelly: research support from Satis Operations Inc
F. Chandelier: Shareholder in Cadens Medical Imaging

All other authors have declared no conflicts of interest.

<table>
<thead>
<tr>
<th>Age, mean (SD), y</th>
<th>48 (7)</th>
<th>48 (7)</th>
<th>50 (17)</th>
<th>52 (14)</th>
</tr>
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<tbody>
<tr>
<td>Women, n (%)</td>
<td>5 (63)</td>
<td>5 (46)</td>
<td>19 (54)</td>
<td>17 (53)</td>
</tr>
<tr>
<td>Body mass index, mean (SD), kg/m²</td>
<td>22.6 (3.6)</td>
<td>23.3 (4.1)</td>
<td>22.2 (3.1)</td>
<td>22.2 (2.8)*</td>
</tr>
<tr>
<td>Stoma present, n (%)</td>
<td>7 (88)</td>
<td>11 (100)</td>
<td>10 (29)</td>
<td>10 (32)*</td>
</tr>
<tr>
<td>Colon-in-continuity, n (%)</td>
<td>1 (13)</td>
<td>1 (9)</td>
<td>22 (63)</td>
<td>24 (77)*</td>
</tr>
<tr>
<td>Estimated small bowel length, mean (SD), cm</td>
<td>128 (98)</td>
<td>129 (77)*</td>
<td>54 (43)*</td>
<td>73 (56)*</td>
</tr>
<tr>
<td>Baseline PS, mean (SD), L/wk</td>
<td>21.6 (8.1)</td>
<td>15.9 (10.4)</td>
<td>11.5 (5.9)</td>
<td>11.2 (6.4)*</td>
</tr>
<tr>
<td>Baseline PS duration, mean (SD), y</td>
<td>7.2 (7.4)</td>
<td>8.1 (8.0)</td>
<td>5.6 (5.3)</td>
<td>6.1 (5.7)*</td>
</tr>
</tbody>
</table>

* n = 31, 1 n = 9, 2 n = 32, 3 n = 30.

**Disclosure of Interest:** U. Pape: Has received grant/research support and served as an advisory board member or speaker’s bureau for NPS Pharmaceuticals, Inc., Shire plc, and Fresenius Kabi GmbH; served as a study investigator for NPS Pharmaceuticals, Inc.
P.B. Jeppesen: Has received grant/research support and served as a consultant, advisory board member, and study investigator for NPS Pharmaceuticals, Inc.
H. Lee: Employee and stockholder of Shire plc.
A.A. Grimm: Employee of Shire plc.
S.J. O’Keefe: Has received research funding support from NPS Pharmaceuticals, Inc.

This clinical trial was funded by NPS Pharmaceuticals, Inc., Bedminster, NJ. NPS Pharmaceuticals, Inc., is a wholly owned indirect subsidiary of Shire plc.

This analysis research was funded by Shire plc.