Aims & Methods: The objective of this study was to compare infliximab with laparoscopic ileocecal 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 ileocecal resection. Patients with a prior ileocecal resection, a diseased length >4 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 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 infliximab versus 17.8% in the resection group). All authors have declared no conflicts of interest.
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 interventional study (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 diversity level. A dysbiosis index (DI) was calculated for each patient based on a weighted principle component analysis of multidimensional and predictive abilities (R^2Ycum 0.652, Q^2 cum 0.541), showing that bacterial profiles could be determined in order to identify patients whom are likely to respond favourably.


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 6 patients 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, not all traditional diet group responders (n=10) had more severe dysbiosis than responders (n=12) (3 (3–4–4) DI; 2 (2–3–3) 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 FODMAPs, and had significant reduction in potentially beneficial Bifidobacterium after the intervention (33 (25.4–122.4) PSI) compared to before (152 (45.7–70) PSI, p=0.005) which was even more prominent in non-responders. An OPLS-DA model of before the low-FODMAP intervention demonstrated satisfactory model fitting, and randomization to each group was validated. A similar 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 predictability (R^2Ycum 0.742, Q^2 cum 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 need to be determined in order to identify patients whom are likely to respond favourably.

Disclosure of Interest: L. Öhman: Unrestricted research grants from AstraZeneca; C. M. Renner: Unrestricted research grants from AstraZeneca; J. van der Meulen: Unrestricted research grants from Genzyme.

All authors have declared no conflicts of interest.

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

Disclosure of Interest: All authors have declared no conflicts of interest.
Vedolizumab (VDZ) specifically targets the gut lymphocytes and has been approved for the treatment of patients with moderate to severe Crohn’s disease (CD) and ulcerative colitis (UC). 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). Clinical response (clinical symptoms and physical global assessment) was correlated to VDZ TC. All patients with UC received sigmoidoscopy at trough during induction (w2 and w6) and early maintenance (w10, w14 and w22).

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Introduction: Vedolizumab (VDZ) specifically targets the alpha-4 delta-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). 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). Clinical response (clinical symptoms and physical global assessment) was correlated to VDZ TC. All patients with UC received sigmoidoscopy at trough during induction (w2 and w6) and early maintenance (w10, w14 and w22).

Vedolizumab trough concentrations, in μg/mL, median [IQR] (n), during induction (w2 and w6) and early maintenance (w10, w14 and w22), treatment correlated with biological remission (CRP ≤ 5 mg/L) were assessed at w6 and w22 in patients with CD. An ELISA for measuring vedolizumab TC was developed in house. TC are shown as median [IQR].

Table 1: Vedolizumab trough concentrations, in μg/mL, median [IQR] (n), during induction (w2 and w6) and early maintenance (w10, w14 and w22) treatment correlated with biological remission (CRP ≤ 5 mg/L) at w22 in patients with CD.

<table>
<thead>
<tr>
<th></th>
<th>Biological remission at w22</th>
<th>No biological remission at w22</th>
</tr>
</thead>
<tbody>
<tr>
<td>w2*</td>
<td>31.8 [23.9–38.9] (23)</td>
<td>23.6 [18.4–31.9] (17)</td>
</tr>
<tr>
<td>w10***</td>
<td>37.9 [24.4–45.1] (15)</td>
<td>12.8 [7.5–19.3] (10)</td>
</tr>
<tr>
<td>w14**</td>
<td>25.8 [16.1–39.4] (22)</td>
<td>14.0 [9.7–18.6] (17)</td>
</tr>
<tr>
<td>w22***</td>
<td>16.1 [9.5–25.2] (23)</td>
<td>6.3 [2.8–11.2] (17)</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01; ***p < 0.001 Endoscopic healing was achieved in 65% (13/20) of patients with UC. Patients with endoscopic healing had significantly higher VDZ TC at w6 (30.5 ± 38.0), compared to patients who did not achieve endoscopic healing (16.6 ± 11.0; p = 0.02). Clinical response was achieved in 69% (47/68) of the patients. Only in patients with UC, clinical response was associated with higher VDZ TC at w2 (27.8 ± 22.3; n = 16) and w6 (22.0 ± 17.8; n = 16) compared to absence of clinical response (21.6 ± 16.5; 10.0–25.2) and 16.6 ± 11.0 [10.0–20.6]; resp., n = 7) (p = 0.03 and p = 0.02).

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.


J. Johanns: Employee of Janssen Research & Development, LLC

G. Van Assche: Employee of Janssen Research & Development, LLC

S. Vermeire: Grant/research support Takeda, MSD, Abbvie Consultancy/speakers' fees from Abbvie, MSD, Takeda, Pfizer, Galapagos, Genentech/Roche, Mundipharma, Celgene, Hospira, Second Genome

All other authors have declared no conflicts of interest.

OP0907 EARLY VEDOLIZUMAB DRUG LEVELS AND INDUCTION SUCCESS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab is an anti-a4β7 monclonal antibody effective in active 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 Siemens-based assay was developed for measurement of vedolizumab (Zeria, Mitsubishi Tansha, MSD, and Abbvie Consultancy: Abbvie, Ferring, Boehringer-Ingelheim and Takeda.

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J. Johanns: Employee of Janssen Research & Development, LLC

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All other authors have declared no conflicts of interest.

*"u2013" means w22***

"w22*** means w22

"w22" means w22

"w22" means w22

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R. Elakim: Prof. Elakim has received consulting and lecture fees from Takeda, Abbvie and Pfizer. Research support from Takeda, 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.

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OP008 PREDICTORS OF NON-RESPONSE OR LOSS OF RESPONSE TO TUMOUR NECROSIS FACTOR ANTAGONIST THERAPIES IN INFLAMMATORY BOWEL DISEASE

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8Safety Statistics & Observational Research Analytics, Takeda Development Centre Europe Ltd. to conduct the study
9Investigacio´n Sanitaria Princesa (IP) and Centro, Madrid/Spain
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11Global Outcomes Research, Takeda Development Centre Europe Ltd, London/United Kingdom

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Introduction: Tumour necrosis factor antagonists (anti-TNFs) are effective at inducing and maintenance 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.

Aims & Methods: The 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 or golimumab) during June 2009 to June 2011 (CD) or June 2009 to June 2013 (UC). 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 required 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 (SD = 13.7); 51%: male. Most patients had a Charlon comorbidity index (CCI) score of 0–1 (83%), 16% were current smokers, mean BMI was 24.8 (SD = 5.1). Mean duration therapy: 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</th>
<th>(95% Confidence Interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with Ulcerative Colitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal Bleeding (Reference: None)</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Passing blood alone</td>
<td>0.24 (0.06–0.97)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Passing blood with stool ≥50% of time</td>
<td>0.35 (0.10–1.19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Passing blood with stool &lt;50% of time</td>
<td>0.17 (0.05–0.62)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endoscopic Findings (Reference: Inactive; Mild)</td>
<td></td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>- Moderate</td>
<td>3.19 (1.14–8.97)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Severe</td>
<td>4.86 (1.61–14.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with Crohn’s Disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Liquid or Soft Stools per Day&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1.12 (1.00–1.24)</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>C-reactive Protein (CRP)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1.02 (1.00–1.03)</td>
<td></td>
<td>0.03</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. 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 requirements for patients.


References:
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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 efficient 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 comotherapy 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 comotherapy in 69.1%, 24.8% and 6.1% of CD patients and 78.2%, 17.7% and 4.1% of UC patients, respectively. Subsequently, 36.8% and 20% of CD patients were exposed to anti-TNFs monotherapy and comotherapy, 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 patients and 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, with 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, or speaker fees for Hospira. All other authors have declared no conflicts of interest.
OP101 CHARACTERISTICS OF CHILDREN WITH CROHN’S DISEASE FAILING SUSTAINED REMISSION DESPITE ANTI-TNF EXPOSURE

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10UZ Antwerpen, Antwerpen/Belgium
11CHC Liege, Liege/Belgium
12St Lucas, Gent/Belgium
13Imelda ziekenhuis, Bonheiden/Belgium
14UCL Mont Godinne, Namur/Belgium
15UCL Luc, Brussels/Belgium
16ULB Erasme, Brussels/Belgium
17CHU Liege, Liege/Belgium
18St Pierre, Ottignies/Belgium
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Introduction: The identification of children at risk for failure to reach sustained remission despite exposure to anti-TNF remains challenging in Crohn’s disease (CD).

Aims & Methods: Data from BELCRO (Belgian observational prospective cohort of pediatric CD) were analysed after 5 yrs follow-up. Disease severity was scored at diagnosis and yearly thereafter as inactive, mild and moderate-to-severe on a 3-point scale based on PDAI/PGA scores. Sustained remission was defined as inactive disease for ≥ 2 yrs follow-up. Univariate analyses were performed between anti-TNF exposed patients with or without sustained remission and correlations assessed between variables and the outcomes average disease activity and sustained remission.

Results: Of 66 anti-TNF exposed patients (median (IQR) age 13.1 (11.5–15.2) yrs, 50% male), 17% failed to reach sustained remission. Disease location was similar in both groups and mild disease at diagnosis (45% vs. 16%; p = 0.03) more frequent in the group failing to reach sustained remission. There were no differences between gender, BWC 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 = 55)</th>
<th>Sustained remission (n = 15)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediatric follow-up and infliximab</td>
<td>23 (42)</td>
<td>12 (80)</td>
<td>0.01</td>
</tr>
<tr>
<td>Paediatric follow-up and adalimumab</td>
<td>1 (9)</td>
<td>8 (53)</td>
<td>0.63</td>
</tr>
<tr>
<td>Adult clinic follow-up and infliximab</td>
<td>6 (55)</td>
<td>14 (25)</td>
<td>0.05</td>
</tr>
<tr>
<td>Adult clinic follow-up and adalimumab</td>
<td>2 (18)</td>
<td>4 (7)</td>
<td>0.25</td>
</tr>
<tr>
<td>Paediatric follow-up and adjustments</td>
<td>1 (9)</td>
<td>8 (53)</td>
<td>0.63</td>
</tr>
<tr>
<td>Adult follow-up and adjustments</td>
<td>1 (9)</td>
<td>3 (11)</td>
<td>0.65</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 (0–3) vs. 0 (0–3); p < .01) and MINE (median 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 = 0.04) 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 sustained remission despite exposure to anti-TNF. Further investigation 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: F. Smets: None communicated
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S. Van Biervliet: None communicated
E. Van de Vijver: None communicated
H. Poets: None communicated
P. Bosuyt: Advisory board: Mundipharma, Dr Falk Benelex, MSD, Janssen-Cilag. Lecturing fee: Abbvie, Takeda, Vifor Pharma

T. Moreels: None communicated
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D. Franchimont: None communicated
V. Muls: None communicated
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All other authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
10:30–12:00

IS MASS ERADICATION OF H. PYLORI RATIONAL? – ROOM C

OP101 IS HELICOBACTER PYLORI ERADICATION ABLE TO IMPROVE THE SCORES OF ATROPHIC GASTRITIS AND INTESTINAL METAPLASIA? – LONG-TERM FOLLOW-UP STUDY IN HIGH RISK POPULATION OF GASTRIC CANCER
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Introduction: Helicobacter pylori (H. pylori) is a risk factor of atrophic gastritis (AG) and intestinal metaplasia (IM) which can undergo to gastric cancer. However, the reversibility of AG and IM by H. pylori eradication is controversial, so far.

Aims & Methods: This study was performed to evaluate the reversibility of AG and IM by anti-H. pylori therapy in large number of patients for a long period in South Korea. A total of 810 patients with follow-up at least 1 year were enrolled from January, 2006 to September, 2014. On the basis of H. pylori infection status and eradication, the subjects were divided into three groups, as follows: Group A (n = 214) included those patients who were H. pylori negative. Group B (n = 580) had successful eradication result for H. pylori. Group C (n = 116) had not received eradication therapy or showed eradication failure. The histological features of the AG and IM in the antrum and body were measured, respectively, using Sydney system scores. All of three groups were followed at 1, 2, 4 and more years.

Results: In patients with successful eradication (Group B), grades of AG and IM in both antrum and body significantly decreased at 1, 2, 4 and more years (p < 0.0011 (Table). In contrast, in the H. pylori negative group (Group A), no significant change was documented for grades of AG and IM in either antrum or body except for grades of IM in body at 2 years and AG in body at 4 years (Table). Similarly, in Group C, no significant change was documented for grades of AG and IM in either antrum or body except for scores of AG in body at 5 or more years (Table).

Table: Histological changes in atrophic gastritis and intestinal metaplasia at 1, 2, 4 and 5 or more years after eradication therapy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at eradication (years)</td>
<td>45.3 ± 13.0</td>
<td>47.0 ± 10.7</td>
<td>47.8 ± 11.0</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 78 (81.2%) Female 16 (18.8%)</td>
<td>Male 268 (92.8%) Female 24 (7.2%)</td>
<td>Male 47 (40.2%) Female 29 (59.8%)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: No disclosure.
OP012 THE EFFECT OF CURRENT HELICOBACTER PYLORI INFECTION ON GASTRIC CANCER IN A LARGE POPULATION
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Introduction: The association between risk of gastric cancer and Helicobacter pylori (H. pylori) infection has been well documented in the past decades. However, the role of current infection of H. pylori on the development of gastric cancer is not clear.
Aims & Methods: The Korean National Health and Nutrition Examination Survey (KNHANES) provided information about current infection of H. pylori in a large general population.
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 1.04–1.08), first-degree relatives with gastric cancer (OR 2.08, 95% CI 1.30–3.32), and high HDL (≥60 mg/dL) reduced the risk of gastric cancer (OR 0.49, 95% CI 0.22–0.94). In sub-analysis by 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 paired non-tumor and hepatocellular carcinoma (HCC) tissues compared to adjacent normal liver specimens by transcriptome sequencing. APLN is an endogenous ligand for the G-protein-coupled APJ 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 examined using transgenic mice, cancer cell cycle, apoptosis and murine xenograft assays. Downstream effectors and pathways were identified by promoter luciferase reporter assay and western blot. Clinical implication of APLN expression was examined in human HCC tissues.
Results: Liver cancer was induced in genetically obese mice (db/db, deficient in leptin receptor) and wild-type mice with diethylnitrosamine. APLN was expressed in 18 paired hepatocellular carcinoma (HCC) tumor tissues compared to adjacent normal tissue samples. APLN was also overexpressed in human HCC tissues as compared to adjacent normal tissues at mRNA level (28 pairs of non-tumor and HCC tissue pairs). APLN was expressed in 9 pairs of HCC tumors compared to adjacent non-tumor tissues. APLN was also overexpressed in human HCC tissues as compared to adjacent normal tissues at mRNA level (28 pairs of non-alcoholic steatohepatitis (NASH)-HCC and 26 pairs of HBV-HCC patients). APLN was ubiquitously expressed in eight HCC cell lines (7404, HepG2, Huh6, Huh7, PLC5, SKHep1 and two NASH-HCC cell lines HCK2-1 and HCK1-10), 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, MIA, HCK2-1 and HCK1-10) was found to promote cell proliferation, accelerate G1/S phase progression by increasing cyclin D1 (E2F1) expression, and induced cells more resistant to MG132 or staurosporine induced apoptosis. Silencing of APLN by shAPLN transfection (HepG2 and SK-Hep1) had the opposite effects in vitro and significantly inhibited cell growth in vivo. Promoter luciferase reporter assay revealed that APLN promoted the PI3K–AKT pathway. Ectopic expression of APLN or exogenous addition of APLN peptide induced the phosphorylation of AKT and glycogen synthase kinase β. Conversely, silencing of APLN or administration of ML221, an antagonist of APLN receptor, inactivated PI3K-AKT signaling. APLN expression was significantly higher in late stage HCC (IIb/IV) than early stage HCC (I) (P < 0.05 for our cohort, and P < 0.01 for TCGA cohort). Kaplan-Meier curves showed that higher APLN expression was significantly associated with shortened survival in patients with HCC (N = 43 for our cohort, and N = 328 for TCGA cohort; both P < 0.05).
Conclusion: APLN plays an important oncogenic role in promoting liver tumor growth via activation of PI3K–AKT pathway. Higher expression of APLN is correlated with a more advanced clinical stage and worse prognosis in HCC patients.
Disclosure of Interest: All authors have declared no conflicts of interest.

OP014 TUMORS SKEW THE CCR2-DEPENDENT ANTI-TUMOR RESPONSE INITIATED BY IMMUNE ENGINEERING AND SENESCENCE TOWARDS TUMOR GROWTH PROMOTION
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Introduction: Oncogene-induced senescence induces the immune-mediated clearance of these precancerous senescent hepatocytes, preventing malignant transformation and tumor initiation; a process termed ‘senescence surveillance’ (1). However, senescent hepatocytes can give rise to hepatocellular carcinoma (HCC), if the senescence program is abrogated and/or senescent cells are not cleared (1). We set out to identify the mechanism of recruitment of senescent cell-clearing macrophages. Furthermore, we studied the effect of senescence-associated immune responses on liver cancer growth in patients with chronic liver disease, in which full-blown tumor cells in the liver.
Aims & Methods: To induce senescence in mouse livers, either oncogenic Nras (NrasG12V) or an effector loop mutant (NrasG12V/D38A), which is incapable of downstream signaling and senescence induction, were hydrodynamically delivered into C57BL/6, CCR2 KO and p19 KO mice. To achieve tumor development in senescent livers, luciferase-expressing hepatocellular carcinoma cells were intrasplenically injected into mice after hydrodynamic gene delivery. Tumor growth was assessed using weight and bioluminescence measurements as well as quantification of macroscopic tumors. Senescent livers with or without tumors were analyzed using flow cytometry and immunohistochemistry.
Results: In tumor-free livers, senescent hepatocytes induced CCR2+ immature myeloid cell (iMC) accumulation, followed by iMC maturation into macrophages, which clear senescent hepatocytes. In CCR2 KO mice, iMC recruitment and macrophage accumulation was impaired, causing persistence of oncogenic Nras-expressing hepatocytes and ultimately HCC development. In contrast, however, tumor cells in senescent livers blocked the maturation of CCR2+ iMC into macrophages, which lead to an accumulation of iMC. These iMC inhibited NK cell cytotoxicity against tumor cells, as demonstrated by reduced NK cell degranulation in hepatocellular carcinoma through senescence-induced iMC to accelerate tumor growth. Accordingly, in CCR2 KO mice or C57BL/6 wild type mice depleted of iMC, senescence-induced tumor growth promotion was abrogated. Finally, gene expression and immunohistochemistry analyses in peritumoral tissue of patients with hepatocellular carcinoma confirmed the association of senescence-induced CCL2 expression, myeloid cell accumulation, NK cell inhibition and poor prognosis.
Conclusion: Senescent hepatocytes may reduce senescence-augmented immunosuppression induced by liver tumors. Distant metastasis is associated with immune context dependent functions in preventing HCC initiation, but also promoting progression of established HCC. These findings hold important translational significance for clinical practice. 1. CCR2 antagonists may fuel liver cancer growth in patients with chronic liver disease, in which senescent hepatocytes accumulate. 2. In patients with HCC, CCR2 antagonists may reduce senescence-augmented immunosuppression induced by liver tumors.
Disclosure of Interest: All authors have declared no conflicts of interest.

References
Abstract No: OP015

Table I: 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 – ileocecal 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>18 (54.5)</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>.030</td>
<td>23 (46.0)</td>
<td>.017</td>
<td>209 (33.9)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>4 (12.5)</td>
<td>.001</td>
<td>5 (10.0)</td>
<td>.081</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>.064</td>
<td>11 (23.9)</td>
<td>.98</td>
<td>95 (15.2)</td>
</tr>
<tr>
<td>Transverse</td>
<td>5 (15.6)</td>
<td>.001</td>
<td>14 (30.4)</td>
<td>.132</td>
<td>132 (20.5)</td>
</tr>
<tr>
<td>Ascending and caecum (+ICV)</td>
<td>10 (31.3)</td>
<td>.001</td>
<td>15 (32.6)</td>
<td>.924</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>&lt;.030</td>
<td>56 (8.7)</td>
</tr>
<tr>
<td>Previous biopsy (%)</td>
<td>na</td>
<td>.001</td>
<td>16 (32.0)</td>
<td>.90</td>
<td>90 (13.8)</td>
</tr>
<tr>
<td>SPOT mark within 10 mm of lesion (%)</td>
<td>na</td>
<td>.001</td>
<td>13 (26)</td>
<td>25 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Histopathology (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional adenoma</td>
<td>25 (79.6)</td>
<td>.004</td>
<td>44 (90.0)</td>
<td>.147</td>
<td>482 (77.5)</td>
</tr>
<tr>
<td>Serrated adenoma</td>
<td>2 (6.4)</td>
<td>.001</td>
<td>4 (10.0)</td>
<td>.135</td>
<td>21 (3.7)</td>
</tr>
<tr>
<td>Cancer</td>
<td>0 (0)</td>
<td>.001</td>
<td>0 (0)</td>
<td>.04</td>
<td>4 (0.6)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0)</td>
<td>.001</td>
<td>0 (0)</td>
<td>1 (0.2)</td>
<td></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>
Aims & Methods: We aimed to assess the feasibility, safety and efficacy of KAR for RPDLs. This is a prospective observational study of patients who underwent KAR for RPDLs over the study period. The polyp characteristics and histology are described in Table 1. The curative resection after a single KAR was achieved for 98% and a negative predictive value of 100% for correctly identifying recurrence. The median procedure time among the self-completion cases was 27 min (range 12–56 min). No adverse events were observed in any group. Conclusion: KAR for RPDLs is safe and effective with a high curative resection rate. No adverse events were observed. This is the largest reported series of KAR for RPDLs. Our data demonstrate 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, it will play an increasingly significant role in the management of RPDLs.

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

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 (%) LST – G, nodular mixed LST – G, homogenous LST – NG Is</td>
<td>29 (72.5) 2 (5) 2 (5) 7 (17.5) 13 (32.5) 30 (75) 6 (15) 3 (7.5) 1 (2.5)</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 TARR, it will play an increasingly significant role in the management of RPDLs.

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

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

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Introduction: Endoscopic mucosal resection (EMR) of large sessile and lateral spreading colorectal lesions ≥20 mm is safe and effective. The main limitation is adenoma recurrence, which occurs in up to 20% at first surveillance colonoscopy (SC1), mandating a structured surveillance program. Surveillance procedures create compliance burdens, additional costs and potential patient morbidity. Endoscopically invisible microadenoma present at the margin of the resected LSL may account for adenoma recurrence. Adjacent thermal ablation of the EMR defect margin may reduce adenoma recurrence rates.

Aims & Methods: A prospective multi-center randomized control study was performed (NCT01789749). The primary endpoint was histological recurrence at SC1. Standard inject and resect EMR technique was used for all lesions. Exclusion criteria included attempted previous lesions, incomplete snare excision or involvement of the ileocecal valve. After successful completion of the EMR, a self-completion rate was significantly higher (62.8% vs. 39%, P = 0.03). The median procedure time among the self-completion cases did not differ significantly between the two groups (58.5 vs. 50.5 min, P = 0.14). No severe adverse events were observed in either group.

Conclusion: SB Jr supported Flushknife significantly improved residents’ self-completion rate for colorectal ESD compared with the Flushknife alone, with no increase in procedure time or adverse events. (University hospital Medical Information Network Clinical Trials Registry number UMIN000009497).

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

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

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Introduction: Endoscopic polypectomy using snare is a frontline treatment for colorectal adenomatous polyps. The technique is an important tool for the management of colorectal neoplasms and the prevention of colorectal cancer. However, the technique has limitations, including peduncularity and the small size of the polyp. The aim of the study was to assess the feasibility, safety and efficacy of KAR for RPDLs over the study period. The polyp characteristics and histology are described in Table 1. The curative resection after a single KAR was achieved for 98% and a negative predictive value of 100% for correctly identifying recurrence. The median procedure time among the self-completion cases was 27 min (range 12–56 min). No adverse events were observed in any group. Conclusion: KAR for RPDLs is safe and effective with a high curative resection rate. No adverse events were observed. This is the largest reported series of KAR for RPDLs. Our data demonstrate 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, it will play an increasingly significant role in the management of RPDLs.

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

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

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

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Introduction: Rectal polyps extending to the dentate line (RPDL) pose a technical challenge to endoscopic resection due to the narrow lumen, rich venous/hemorrhoidal plexus and proximity to the skin. Conventional snare EMR is challenging due to the restricted space and lack of precision with the snare. This has led to the challenge to endoscopic resection due to the narrow lumen, rich venous/hemorrhoidal plexus and proximity to the skin. Conventional snare EMR is challenging due to the restricted space and lack of precision with the snare. This has led to the development of a new technique in the treatment of RPDLs. As KAR is a viable alternative to full ESD, this study aimed to assess the feasibility, safety and efficacy of KAR for RPDLs. This is a prospective observational study of patients who underwent KAR for RPDLs over the study period. The polyp characteristics and histology are described in Table 1. The curative resection after a single KAR was achieved for 98% and a negative predictive value of 100% for correctly identifying recurrence. The median procedure time among the self-completion cases was 27 min (range 12–56 min). No adverse events were observed in any group. Conclusion: KAR for RPDLs is safe and effective with a high curative resection rate. No adverse events were observed. This is the largest reported series of KAR for RPDLs. Our data demonstrate 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, it will play an increasingly significant role in the management of RPDLs.

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Disclosure of Interest: All authors have declared no conflicts of interest.
OP019 EVALUATION OF THE LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION PERFORMED WITH A SEGMENTAL HEMOClip FOR EARLY COLONIC NEOPLASMS
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Introduction: Endoscopic submucosal dissection (ESD) is one of the most useful methods for treating early colonic neoplasms. It is considered a minimally invasive treatment in addition to a biopsy. In addition, ESD can be used to perform immunohistochemistry. The ESD group in this study was the SB Jr group.

Results: In the hemoclip group (n = 20), among the 1.5, 2.0, 2.5, and 3.0 cm defects, the mean number of clips (3.8 ± 0.8, 4.8 ± 0.8, 6.0 ± 1.6, and 8.4 ± 2.1, respectively, p = 0.001) and closure time (5.3 ± 1.8, 7.6 ± 0.5, 9.9 ± 3.3, and 13.9 ± 4.1 min, respectively, p = 0.001) differed significantly. In the twin-grasper group (n = 15), among the 2.0, 2.5, and 3.0 cm defects, the mean number of clips (4.0 ± 1.0, 5.0 ± 0.7, and 5.4 ± 1.1, respectively, p = 0.101) and closure time (7.7 ± 3.1, 8.1 ± 2.7, and 7.9 ± 2.7 min, respectively, p = 0.586) did not differ significantly. In 3 cm defects, the number of mean hemoclips used per case and total closure time were significantly lower in the twin-grasper group than 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

MORNING, OCTOBER 17, 2016 7:30–12:00 TOPICS FROM LATIN AMERICA – ROOM M
OP021 ENDOSCOPIC TREATMENT OF COMPLEX BILIARY STONES: SPYGlass + ELECTROHYDRAULIC LITHOTRIPSY X BALLOON DILATION OF THE MAJOR PAPILLA – PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL
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Introduction: Endoscopic technique is the first choice for the treatment of bile duct stones, with success rates, ranging from 85% to 95%, and relatively low complication rate. However, some stones can become a great challenge for endoscopists. Complementary methods are available as mechanical lithotripsy and papillary balloon dilation after sphincterotomy. Single operator cholangioplasty combined with electrohydraulic lithotripsy (EHL) is emergent in this scenario.

Aims & Methods: We compare the success between two methods in the endoscopic removal of difficult bile duct stones: Spyglass associated with EHL. X Balloon dilation of the major duodenal papilla. 100 patients were randomized into two groups. Group one was Spyglass + EHL and group 2 balloon dilation. From April of 2014 to present date (March 2016) we have enrolled 82 patients. Include criteria were: Over 18 years, difficult biliary stones, signed term of consent. All patients receive antibiotic prophylaxis with 400 mg of Ciprofloxacin IV. Failures in both groups were submitted to plastic stenting. To compare the methods we use the student t-test and Mann-Whitney Rank Sum test. Complications were analyzed by the Fisher test and Q squared.

Results: The average age was 55.1 /+ /– 16.9 years. Women corresponded to 76.54% of the patients. Success rate reached 77.7% in group 1 and 72.2% in group 2 (P = 0.568). Median procedure time was 71.08 minutes (17–150) in group 1 and 49.81 (17–180) in group 2 (P = 0.021). X-ray time was 10.89 minutes in group 1 and 10.16 in group 2 (P = 0.052). Median number of stones per patient in group 1 and 2 respectively were 2.21 (1–8) in group 1 and 2.22 (1–15) in group 2 (P = 0.065). Size of the stones in group 1 was 1.88 (1–3.5) and 2.09 (1–3.5) in group 2 (P = 0.015). Minor adverse event occurred in one patient of each group. There was one death not related to procedure (cardiologic cause).

Conclusion: To our knowledge this is the largest randomized controlled trial comparing this two techniques. We found so far an overall success rate of 77.7% in Spyglass + EHL procedure and 72.2% in balloon dilation group.

The results between hemoclip group and twin-grasper group

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number of endoclips</th>
<th>Procedure time(min)</th>
<th>Complete closure in water leak</th>
<th>Endoscopic fail</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0 cm hemoclip</td>
<td>4.8 ± 0.8</td>
<td>7.6 ± 0.5</td>
<td>60%</td>
<td>0%</td>
</tr>
<tr>
<td>2.0 cm twin-grasper</td>
<td>4.0 ± 1.0</td>
<td>7.7 ± 0.6</td>
<td>80%</td>
<td>0%</td>
</tr>
<tr>
<td>p-value</td>
<td>0.207</td>
<td>0.776</td>
<td>0.545</td>
<td></td>
</tr>
<tr>
<td>2.5 cm hemoclip</td>
<td>6.0 ± 1.6</td>
<td>9.9 ± 3.3</td>
<td>60%</td>
<td>0%</td>
</tr>
<tr>
<td>2.5 cm twin-grasper</td>
<td>5.0 ± 0.7</td>
<td>8.3 ± 1.9</td>
<td>60%</td>
<td>0%</td>
</tr>
<tr>
<td>p-value</td>
<td>0.202</td>
<td>0.996</td>
<td>0.384</td>
<td></td>
</tr>
<tr>
<td>3.0 cm hemoclip</td>
<td>8.4 ± 2.1</td>
<td>13.9 ± 4.1</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>3.0 cm twin-grasper</td>
<td>5.4 ± 1.1</td>
<td>9.1 ± 2.7</td>
<td>60%</td>
<td>0%</td>
</tr>
<tr>
<td>p-value</td>
<td>0.022</td>
<td>0.06</td>
<td>0.58</td>
<td></td>
</tr>
</tbody>
</table>
It is important to highlight that only one session of SpgGlass + EHL was performed in each patient of our protocol. Better success rates can be achieved with two or more sessions and increase up to 90%. Cross-over of the failure cases in both groups is bringing us a very interesting result and suggests that in some cases the methods can be complementary. There was no statistical difference between the groups, although spgGlass group had numerically a little higher success rate. The study provides us an evidence-based algorithm of difficult stones endoscopic treatments. In addition, we observed potential advantages when we associate the methods, providing one step more before declaring endoscopic failure in treating a difficult biliary stone. 

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

**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 and comparative (before and after) pilot study that includes symptomatic patients with GAVE (endoscopic and histologic diagnosis). Naïve or refractory patients (defined as more than 5 previous APC or 3 BL without endoscopic, clinical and laboratorial response) between 18 and 90 years old were included. We excluded patients with GAVE without clinical manifestations or anemia of other GI source. After a creation of a “safety cushion” with the use of APC, this could have the advantage of a deeper and safer treatment compared with other endoscopic modalities.

**Characteristics of procedures, patients and outcome**

<table>
<thead>
<tr>
<th>PATIENT</th>
<th>AGE/GENDER</th>
<th>CLINICAL PICTURE</th>
<th>CLINICAL HISTORY</th>
<th>NUMBER OF PACKED RBC TRANSFUSED</th>
<th>NUMBER OF HYBRID APC TREATMENTS</th>
<th>TIME</th>
<th>GAVE TYPE</th>
<th>COMPLICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58/F</td>
<td>Anemia</td>
<td>Naive</td>
<td>2</td>
<td>1</td>
<td></td>
<td>Watermelon</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>60/F</td>
<td>Melena</td>
<td>Refractory</td>
<td>10</td>
<td></td>
<td></td>
<td>Watermelon</td>
<td>Mild abdominal pain</td>
</tr>
<tr>
<td>3</td>
<td>61/F</td>
<td>Melena</td>
<td>Refractory</td>
<td>15</td>
<td>1</td>
<td></td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>79/F</td>
<td>Melena</td>
<td>Refractory</td>
<td>9</td>
<td>1</td>
<td></td>
<td>Watermelon</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>67/F</td>
<td>Anemia</td>
<td>Refractory</td>
<td>12</td>
<td>2</td>
<td></td>
<td>Watermelon</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>55/F</td>
<td>Anemia</td>
<td>Naive</td>
<td>2</td>
<td>1</td>
<td></td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>67/F</td>
<td>Anemia</td>
<td>Naive</td>
<td>8</td>
<td>1</td>
<td></td>
<td>Watermelon</td>
<td>Mild abdominal pain</td>
</tr>
<tr>
<td>8</td>
<td>48/M</td>
<td>Melena</td>
<td>Naive</td>
<td>6</td>
<td>1</td>
<td></td>
<td>Watermelon</td>
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</tr>
<tr>
<td>9</td>
<td>89/F</td>
<td>Melena</td>
<td>Refractory</td>
<td>14</td>
<td>1</td>
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<td>None</td>
<td>None</td>
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**Mean**

<table>
<thead>
<tr>
<th>NAIVE VS REFRACTORY</th>
<th>NAIVE</th>
<th>REFRACTORY</th>
<th>Median 9</th>
<th>1 Treatment</th>
<th>2 Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>88.8%</td>
<td></td>
<td></td>
<td></td>
<td>21.2%</td>
<td></td>
</tr>
<tr>
<td>66.6%</td>
<td></td>
<td></td>
<td></td>
<td>33.4%</td>
<td></td>
</tr>
<tr>
<td>77.8%</td>
<td></td>
<td></td>
<td></td>
<td>22.2%</td>
<td></td>
</tr>
</tbody>
</table>

**Total**

<table>
<thead>
<tr>
<th>AGE/GENDER</th>
<th>NAIVE</th>
<th>REFRACTORY</th>
<th>Median 9</th>
<th>1 Treatment</th>
<th>2 Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>55.6%</td>
<td></td>
<td></td>
<td></td>
<td>21.2%</td>
<td></td>
</tr>
<tr>
<td>77.8%</td>
<td></td>
<td></td>
<td></td>
<td>33.4%</td>
<td></td>
</tr>
<tr>
<td>55.6%</td>
<td></td>
<td></td>
<td></td>
<td>22.2%</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Based on these preliminary results, Hybrid-APC is safe and effective for the treatment of GAVE (naive or refractory) with the advantage of needing only 1 or maximum 2 applications and with excellent results at medium term. 

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

**References**


**MONDAY, OCTOBER 17, 2016**

**PREVENTION OF GI CANCERS: NUTRITION AND CHEMOPREVENTION – ROOM 1.61/1.62**

**OP023 CD24 INDUCES THE ACTIVATION OF β-CATENIN IN INTESTINAL TUMORIGENESIS**

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**Introduction:** CD24 is a GPI-linked protein that functions as an adhesion molecule and is overexpressed at an early stage of CRC. The Wnt/β-catenin signaling pathway plays an important role in CRC carcinogenesis process. We had shown that CD24 could affect the tumorigenesis process in Apc Min mice. 

**Aims & Methods:** Aim to study the cellular interactions between CD24 and β-catenin, and their effects on intestinal tumorigenesis Methods CD24-inducible 293T-Res cells previously developed in our lab and SW480 CRC cells stably transduced with CD24 were used to study this interaction in vitro. Apc Min and CD24 knockout (KO) mice, both on a C57BL/6j genetic background, were crossed to generate double KO transgenic mice. Genotypes were routinely verified by analysis of DNA extracted from tail biopsies. Small and large bowel polyps were counted macroscopically following methylene blue staining and histology was verified microscopically. Colonic polyps were measured and counted previous treatments in refractory patients were 4 (3–9). All patients reached normal Hb levels after 6 months. The mean difference between prehybrid-APC (5.98 ± 1.49 g/dl) and 6 (post hybrid-APC (13.7 ± 0.76 g/dl) was 7.74 g/dl (p < 0.0001 CI 95% 6.84–8.64) student T-test. 8 patients received 1 session and 1 required 2. No major complications were observed (Table 1).
Disclosure of Interest: This indicates an important, previously under-estimated macrophage-
Conclusion: pro-IL-1β form upon cytosolic presence of danger molecules and induce the cleavage of
Results: expression induction Depletion of CD24 alleles in Apc Min mice led to a sig-
nificance reached in the number of polyps in the intestine: C37BL/10 mice carrying the
Regulation of this event is essential for the clearance of injured cells and for initiate the
In this study, we aimed to address whether loss of PTPN2 in macrophages affects inflammasome activation and whether this affects colitis severity in PTPN2-LysMCre mice did not differ from that observed in WT animals. Further, inhibition of IL-1β in PTPN2-LysMCre mice but there was no overt effect on colitis severity. Of interest, however, and in contrast to their WT littermates, PTPN2-LysMCre mice did not develop any
contrast to their WT mice. Of interest, however, and in contrast to their WT littermates, PTPN2-LysMCre mice did not develop any

All other authors have declared no conflicts of interest.

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Introduction: Variants in the gene locus encoding protein tyrosine phosphatase non-receptor type 2 (PTPN2) are associated with Crohn’s disease (CD) and ulcerative colitis (UC). We have previously shown that loss of PTPN2 in T cells results in enhanced colitis and signs of autoimmunity. Inflammasomes form upon cytosolic presence of danger molecules and induce the cleavage of pro-IL-1β and pro-IL-18 into their active forms. Secretion of IL-1β is an impor-
tant activator of stem cell and adaptive immune functions, while IL-18 is involved in epithelial cell protection.

Aims & Methods: In this study, we addressed whether loss of PTPN2 in macrophages results in inflammasome activation and, subsequently, in 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, mild acute pancreatitis, one perforation that required surgery and one duo-
majors of clinical presentation of acute pancreatitis, one major and one minor. Of interest, there was no significant difference between the two groups in terms of age, sex, and body mass index (BMI).

The results of the study showed that the addition of PTPN2 significantly reduced the severity of acute pancreatitis, as measured by the reduction in the number of infected cells and the decrease in the inflammatory response. The study also demonstrated that PTPN2 expression was upregulated in infected cells, indicating a role for PTPN2 in the regulation of the inflammatory response to infection.

Conclusion: PTPN2 is an important regulator of inflammatory response and stress response, and its downregulation in infected cells is associated with an increased inflammatory response. These findings suggest that PTPN2 may serve as a potential therapeutic target for the treatment of acute pancreatitis.
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</td>
<td>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>
</tr>
<tr>
<td>Specimen bloodiness: n (%)</td>
<td>Median (IQR)</td>
<td>1 (1-2)</td>
<td>2 (1-3)</td>
<td>1 (1-1)</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td>Moderate</td>
<td>52 (59.1)</td>
<td>32 (36.4)</td>
<td>55 (64.7)</td>
<td>43 (51.6)</td>
<td>0.008</td>
</tr>
<tr>
<td>Severe</td>
<td>16 (18.2)</td>
<td>22 (25.0)</td>
<td>10 (11.8)</td>
<td>18 (19.8)</td>
<td></td>
</tr>
<tr>
<td>ROSE-Diagnostic performance: % (95% CI)</td>
<td>Accuracy</td>
<td>98.9 (93.8–100)</td>
<td>92.6 (83.7–97.6)</td>
<td>97.1 (89.6–99.6)</td>
<td>98.8 (93.2–100)</td>
</tr>
<tr>
<td>EUS-FNA-Diagnostic performance: % (95% CI)</td>
<td>Accuracy</td>
<td>98.9 (93.8–100)</td>
<td>93.2 (85.7–97.6)</td>
<td>97.6 (91.8–99.7)</td>
<td>97.8 (92.3–99.7)</td>
</tr>
</tbody>
</table>

Adverse events: n (%) | 4 (4.5) | 3 (3.4) | 7 (8.2) | 10 (11.0) | 0.179 |

Technical failure: n (%) | 0 | 5 (5.7) | 1 (1.2) | 7 (7.7) | 0.179 |

Diagnostic cell block: n (%) | 71 (80.7) | 63 (71.6) | 56 (65.9) | 76 (73.6) | 0.177 |

EUS-FNA-Diagnostic performance: % (95% CI) | Accuracy | 98.9 (93.8–100) | 93.2 (85.7–97.6) | 97.1 (89.6–99.6) | 98.8 (93.2–100) |

References

All other authors have declared no conflicts of interest.

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

Disclosure of Interest:

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

All other authors have declared no conflicts of interest.

Abstract No: OP026

TECHNIQUES FOR EUS-GUIDED FNA OF PANCREATIC MASSES

J.Y. Bang1, S. Hebert-Magee, M. Hasan, U. Navaneethan, R. Hawes, S. Varadarajulu

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Introduction: Prior studies comparing the 22 and 25G needles and utility of suction EUS-FNA on diagnostic adequacy, particularly with the 19-gauge EUS-FNA needle.

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 passes were performed for cell block (offsite) evaluation, an experienced pathologist rendered rapid on-site assessment.

Results: 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 15% difference in diagnostic accuracy and cell block yield between the type of needle 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.

Diagnostic cell block: n (%) | 71 (80.7) | 63 (71.6) | 56 (65.9) | 76 (73.6) | 0.177 |

EUS-FNA-Diagnostic performance: % (95% CI) | Accuracy | 98.9 (93.8–100) | 93.2 (85.7–97.6) | 97.1 (89.6–99.6) | 98.8 (93.2–100) |

Technical failure: n (%) | 0 | 5 (5.7) | 1 (1.2) | 7 (7.7) | 0.179 |

Adverse events: n (%) | 4 (4.5) | 3 (3.4) | 7 (8.2) | 10 (11.0) | 0.179 |

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

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

Disclosure of Interest: L. Palazzo: Laurent 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


OP027 RANDOMIZED PHASE II STUDY

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Introduction: For 10 years, EUS-guided biliary drainage has been an option as EUS guided choledocho-duodenostomy or hepatico-gastrostomy. Two small randomized studies showed no difference between EUS guided biliary drainage (EBD) and ERCP drainage. The aim of this work was to evaluate in a multicenter randomized study the puncture 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 as gastrostomy or Whipple resection.

Aims & Methods: Inclusion criteria were: benign or malignant obstructive jaundice with failure of ERCP. Exclusion criteria were: ascites, blood coagulation disorders, and the presence of duodenal stenosis of the patient heterogeneity and small sample size. Also, the optimal tissue acquisition technique for onsite and offsite specimen assessment is unclear.

Aims & 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 passes were performed for cell block (offsite) evaluation, an experienced pathologist rendered rapid onsite evaluation (ROSE) for specimen adequacy. Cross-over to alternate arms was permitted if ROSE was indeterminate at 8 passes. 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 adequacy and accuracy 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 15% difference in diagnostic accuracy and cell block yield between the type of needle 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.

Diagnostic cell block: n (%) | 71 (80.7) | 63 (71.6) | 56 (65.9) | 76 (73.6) | 0.177 |

EUS-FNA-Diagnostic performance: % (95% CI) | Accuracy | 98.9 (93.8–100) | 93.2 (85.7–97.6) | 97.1 (89.6–99.6) | 98.8 (93.2–100) |

Technical failure: n (%) | 0 | 5 (5.7) | 1 (1.2) | 7 (7.7) | 0.179 |

Adverse events: n (%) | 4 (4.5) | 3 (3.4) | 7 (8.2) | 10 (11.0) | 0.179 |

Disclosure of Interest: R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc.
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 sustained patency without tumor ingrowth/overgrowth.\(^1\)

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 defined by absence of tumor ingrowth/overgrowth), 3) clinical success (oral intake without vomiting), and 4) 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 2010. Results: A total of 82 patients (mean age 66 years ± 13.5 and 40.2% female) were identified: 30 in EUS-GE and 52 in ES. Technical and clinical success were not significantly different (86.7% EUS-GE vs. 94.2% ES) \(p = 0.2\), and 83.3% EUS-GE 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 \(p = 0.004\). Rates and severity of AEs (as per the ASGE lexicon) were also similar occurring in 16.7% EUS-GE vs. 11.5% ES \(p = 0.5\). Multivariable analysis revealed that 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.

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

Y. Chen,1 T. Ito,1 T.H. Baron,1 J. Nieto,2 Y. Hatao-Chavez,1 J.S. Grimm2, S. Ngamruengphong3, M. Bekhrad1, G. Hajiyeva1, A. Ismail1, A. Alawad1, V. Kumbhar1, M. Khashab1

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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 sustained patency without tumor ingrowth/overgrowth. Results: A total of 205 patients (mean age 34.8 ± 12.5 years, 181 males) underwent both EUS-GE and ES. Technical success was achieved in 203 patients (99%). Per-procedure adverse events occurred in 8 (3.9%) patients (bleeding in 6 and perforation in 2). WON resolved with BFMS in 158 (77%). Endoscopic re-intervention was required in 49 (23.9%) patients, for persistent or new onset symptoms, was approached in step-up manner. At first, de-clogging of BFMS alone succeeded in 10 out of 21. Second step of n sky-cystic catheter placement through BFMS followed by irrigation with saline and hydrogen peroxide improved 16 out of 9. 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 percutaneous 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 survival dependent on when chemotherapy can be re-started. However, little information is known about clinical 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. Descriptive, biochemical, and outcome data were registered. We used Kaplan-Meyer 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 restared 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 [1.39–6.56], \(p = 0.005\)). Conclusion: This 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.
**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 (1:2 female to male ratio). Concomitant commination of the common bile duct sample was aspirated using balloon catheter and immersed immediately in liquid nitrogen (−196°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 carotenoids 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 carotinoid correlated significantly with carotinoids in BC, with S-CA19-9, S-ALP and S-AST levels and significantly with S-IgG. Patients with dysplasia or CCA had markedly elevated bilirubin, S-IgA, CA19–9, ALP, AST and IgG levels and significantly with neutrophils in BC, with S-CA19–9, S-ALP and S-AST levels and significantly with S-IgG. Patients with dysplasia or CCA had markedly elevated 26 kU/l (OR 7.4 [95% 2.0–27.6], P = 0.003) and S-CA19–9 > 26 kU/l vs < 26 kU/l (OR 7.4 [95% 2.0–27.6], P = 0.003).

**Conclusion:** S-ALP, AST and IgG seem to be good surrogate markers for bile duct inflammation compared to biliary carotenoids. Risk of dysplasia is associated with bile duct inflammation assessed by brush cytology neutrophils, B-carotinoid and S-CA19–9 levels > 26 kU/l. These variables seem be useful for individual risk stratification for PSC patients for disease progression and dysplasia.

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

**References**


**Aims & Methods:** To determine the prevalence and prognostic potential of novel target-specific PAbs regarding long-term disease course in a cohort of a primary sclerosing cholangitis [PSC] patients. Aims & Methods: Sera of 69 PSC patients (median age [range] 32–79 years, cumulative concomitant IBD 76% and cirrhosis 20%) were tested by indirect immunofluorescence test (IIFT) system with GP2 and CUZD1 expressing transfected HEK 293 cells [anti-rPAg2 and rPAg1 IgA/IgG]. Classical serologic markers of IBD were also assessed (pANCA and pANCA by ELISA). A previously reported inflammatory bowel disease [IBD] patient cohort (CD:264 and UC:179) were the controls. Poor disease outcome was defined as orthotopic liver transplantation [OLTx] and/or liver-related death during the follow-up (median: 94 months).

**Results:** A total of 43.5% of PSC patients were positive for either of the two target-specific anti-PABs, with a significant difference compared to patients with CD (26.8%, p < 0.01) 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 positivity was associated with shorter time to OLTx and/or liver-related death [pLogRank < 0.01], and remained an independent predictor after adjusting for the presence of cirrhosis in Cox-regression analysis (HR: 4.31 [1.05–17.61]). Conclusion: Our small-scale study has shown that occurrence of target-specific PAbs is common in PSC. Association of IgA type anti-GP2 antibody with faster disease progression serves as an additional hint towards the significance of gut-liver interaction in the disease course of PSC.

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

**References**


**Disclosure of Interest:** All authors have declared no conflicts of interest.
**OP035 GUT BARRIER FAILURE BIOMARKERS ARE ASSOCIATED WITH POOR DISEASE OUTCOME IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS**


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

**Introduction:** Gut-liver interaction is a pathognomonic 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 mediators of gut barrier dysfunction were assessor in a cohort of patients with PSC. Association of these markers with disease specific characteristics and the long-term disease course was evaluated.

**Aim:** Aims of this study were 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 ursodeoxycolic (UDCA) acid scaffolds were incubated with HepG2 cells in the presence of different agonists. In particular, derivatives with a higher FXR expression is significantly decreased in livers of non-alcoholic fatty liver disease (NAFLD) patients and genetic ablation leads to hepatic steatosis and hyperlipidaemia. The FXR gene expression further enhanced their predictive potential (HRF95\%CI: 11.30(2.84–44.93) for \(p = 0.001\)).

**Conclusion:** The results suggest a potential role of FXR agonists in the treatment of NAFLD.

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

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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. FXR expression is significantly decreased in livers of non-alcoholic fatty liver disease (NAFLD) patients and genetic ablation leads to hepatic steatosis and hyperlipidaemia. The FXR gene expression further enhanced their predictive potential (HRF95\%CI: 11.30(2.84–44.93) for \(p = 0.001\)).

**Aims & 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 (CA), deoxycholic (DCA), chenodeoxycholic (CDCA) and ursodeoxycholic (UDCA) acid scaffolds were incubated in HepG2 cells with different agonists. In particular, derivatives with a higher FXR

**Conclusion:** The results suggest a potential role of FXR agonists in the treatment of NAFLD.

**References:**
1. Nakazawa T, Naitoh I and Hayashi K. Usefulness of Intraductal Ultrasonography in the Diagnosis of Cholangiocarcinoma and IgG4-related Sclerosing Cholangitis. *Clinical Endoscopy* 2012; 45: 331-9
PNPLA3 rs738409 in PSC

<table>
<thead>
<tr>
<th>Variable, mean(SD)</th>
<th>CC, n = 334</th>
<th>CG, n = 197</th>
<th>GG, n = 32</th>
<th>p for linearity</th>
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<tr>
<td>Males, n (%)</td>
<td>195(38)</td>
<td>124(63)</td>
<td>17(53)</td>
<td>0.75</td>
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<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>
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<tr>
<td>Weight, kg, males</td>
<td>82(14)</td>
<td>80(15)</td>
<td>81(14)</td>
<td>0.37</td>
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<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(75)</td>
<td>153(77)</td>
<td>21(65)</td>
<td>0.49</td>
</tr>
<tr>
<td>Age at diagnosis of IBD, 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>5.4(3.3)</td>
<td>5.7(3.7)</td>
<td>0.88</td>
</tr>
<tr>
<td>Dominant strictures, n (%)</td>
<td>128(36)</td>
<td>61(36)</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>8.1</td>
<td>15.2</td>
<td>12.5</td>
<td>0.25</td>
</tr>
<tr>
<td>S-ALP, U/l &lt; 100</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-ALT, U/l &lt; 50</td>
<td>74(125)</td>
<td>78(96)</td>
<td>61(50)</td>
<td>0.35</td>
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<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). 49 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
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 inhibition of calcineurin as applied in human immunosuppression is associated with increased incidence of CRC. However, calcineurin and NFAT are also associated with reduced intestinal tumor formation and growth in the Apcfl/wt and ApcMin/+lines as well as samples of more than 700 CRC patients were studied. For mechanistic studies, organoid cultures, immortalized IECs and CRC cell lines were generated. 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 promoted tumor development in a cell-intrinsic manner.

Technical University of Munich (TUMOR DEVELOPMENT) and the University of Heidelberg (Aims & Methods)

Comparison of Colon Cancer Exosomes

Introduction: Colon cancer (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 ALG2-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, cytokertatin (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 detected 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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Introduction: Na+/H+ exchanger regulatory factor (NHERF) family of proteins is involved in the regulation of epidermal growth factor receptor and cellular proteins. 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 cell lines (HCT116, SW480, and HT-29). We validated tumor growth and lysis confirmed the reduction of cell proliferation by Ki67 immunostaining. In particular these findings indicate that E2 seems to modulate the myeloid response and to profoundly affect the inflammatory microenvironment associated with CRC.

Results: We found that NHERF2 expression is elevated in advanced-stage CRC. Knockdown of NHERF2 decreased cancer cell proliferation and invasion in vitro, and tumor growth in a mouse xenograft tumor model. Histologic analysis confirmed the reduction of cell proliferation by Ki67 immunostaining. In addition, deletion of NHERF2 in ApMin/+ (ApMin+/+;Nherf2/-/-) mice resulted in decreased tumor growth in ApMin/+ mice and increased lifespan. Blocking NHERF2 interaction with a small peptide designed to bind the second PDZ domain of NHERF2 attenuated cancer cell proliferation. Although NHERF2 is known to facilitate the effects of lysophosphatidic acid receptor 2 (LPAR2) on cell migration and invasion, the role of LPAR2 in NHERF2 regulation and tissue remodeling has not been investigated.

Conclusion: This study demonstrated NHERF2 stimulates colon cancer growth by intersecting at multiple signaling nodes. NHERF2 potentiates the oncogenic effects in part by regulation of Stat3 and Erk, which is consistent with the role of LPAR2 in cancer progression. NHERF2 blocks the Stat3 phosphorylation followed by the increase in CD24.

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

References:

OP041 THE EXTRACELLULAR MATRIX PROTEIN EMILIN2 AS A NEW POTENTIAL REGULATOR OF THE MYELOID RESPONSE AND THE INFLAMMATION-INDUCED COLON CARCINOGENESIS

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Introduction: EMILIN2 is an extracellular matrix molecule belonging to the EMIN Domain ENadowed (EDEN) protein family that exerts pleiotropic effects in the tumor microenvironment. EMILIN2 functions as a tumor suppressor molecule in colorectal cancer (4). Our preliminary results highlight a possible new function for E2 in the control of CRC incidence. In particular these findings indicate that E2 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 subjecting the mice 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 unidifferentiated and at an advanced stage compared to the tumors from control mice. Surprisingly, 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 cyc1 D1 and c-Myc were not altered in the tumors and in the normal mucosa of the two mouse models. Histopathologically and IHC analyses 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.

Conclusion: Our results led us to suggest that EMILIN2 may affect colon carcinogenesis 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:


**OP042 THE ROLE OF miRNA-145 IN COLON CANCER STEM CELL (CCSC) DIFFERENTIATION**

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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 differ- entiation potential. miRNAs have recently emerged as promising candidates to initiation, metastasis and relapse through their unlimited self-renewal and differ-

**Conclusion:** miR-145 appears to be involved in colon sphere formation, reducing the number of colon spheres. Similar results were observed with the second and third generation of cell line-derived colon spheres.

**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).**

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

**Disclosure of Interest:** A.G. McNicholl: Speaker for allergan

M. Castro: Teaching activities for Allergan

J.P. Gisbert: Scientific Advisory for Casen Recordati Teaching activities for Allergan and Zambon


All other authors have declared no conflicts of interest.

**Contact Email Address:** J.P.Gisbert@gmail.com

**Introduction:** 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 2013 to March 2016. At baseline, demo-

**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-

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

**Disclosure of Interest:** A.G. McNicholl: Speaker for allergan

M. Castro: Teaching activities for Allergan

J.P. Gisbert: Scientific Advisory for Casen Recordati Teaching activities for Allergan and Zambon


All other authors have declared no conflicts of interest.
treatment, there were no significant differences between the eradication rates from EPZ and VPR regimes.

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

References

OP045 STROMAL MYOFIBROBLASTS ORCHESTRATE GASTRIC EPITHELIAL WNT-SIGNALING AND STEM CELL KINETICS IN H. PYLORI INFECTED GASTROESENTERAL MUCOSA

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1Gastroenterology and Hepatology, Charité University Medicine Berlin, Berlin, Germany
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3Department Of Molecular Biology, Max Planck Institute for Infection Biology, Berlin/Germany

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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 and 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-signalizing reporter mice and the murine and as well as human 3D-organoid 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 and whether stem cells in the stomach 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 increased the expression of R-spondin 3, which also induces the expansion of Axin2-positive cells and results in gland hyperplasia. By increasing gland turnover following infection, R-spondin counterbalances bacterial glandular 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, production kinetics and modulation by 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

OP046 THE ANTI-APOPTOTIC FACTOR CLUSTERIN IS INVOLVED IN INTRAGASTRIC ACIDITY WHICH IS MOST MARKED CLOSE TO THE GASTROESOPHAGEAL JUNCTION

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Introduction: A negative association exists between H. pylori infection and both gastroesophageal reflux disease1 and oesophageal adenocarcinoma2 and this may be due to the infection reducing 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 antrum and the fundus of the stomach.

Aims & Methods: We studied 31 H. pylori-positive and 28 H. pylori-negative volunteers, matched for age, gender and BMI. Jumbo biopsies were taken at eleven pre-determined locations from the gastroesophageal junction and stomach. 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 relative to the probes. The biopsy specimens were scored quantitatively for inflammation and stained with monoclonal antibody to H/K+-ATPase and sucrase I for calculating parietal cell and chief cell densities respectively.

Results: The mean age of the H. pylori-positive group was 55 years (38–78y) compared to 56 years (24–74y) for the H. pylori-negative group. Under fasting conditions, the H. pylori-positive group had less intragastric acidity compared to the H. pylori-negative group. At the 2.2, 3.3 and 4.4 cm distal to the peak LOS pressure (all p < 0.05), but there was no significant difference in the sensors 5.5 and 6.0 cm distal to peak LOS pressure (Table 1). The postprandial acid pocket was thus attenuated in H. pylori positives 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 determination of reduction was similar for the two cell types. The cardiac 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.

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

<table>
<thead>
<tr>
<th>Sensor location</th>
<th>H. pylori negative Median pH (IQR)</th>
<th>H. pylori positive Median pH (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1cm proximal</td>
<td>7.06 (1.42)</td>
<td>7.00 (0.75)</td>
</tr>
<tr>
<td>1.1cm distal</td>
<td>5.25 (4.19)</td>
<td>6.40 (1.72)</td>
</tr>
<tr>
<td>2.2cm distal</td>
<td>5.18 (2.83)</td>
<td>3.21 (4.64)</td>
</tr>
<tr>
<td>3.3cm distal</td>
<td>4.59 (2.29)</td>
<td>2.07 (2.29)</td>
</tr>
<tr>
<td>4.4cm distal</td>
<td>1.81 (2.09)</td>
<td>2.93 (3.25)</td>
</tr>
<tr>
<td>5.5 cm distal</td>
<td>2.13 (2.02)</td>
<td>3.48 (2.89)</td>
</tr>
<tr>
<td>6.6cm distal</td>
<td>3.39 (2.19)</td>
<td>4.10 (2.23)</td>
</tr>
</tbody>
</table>
Conclusion: The majority of H. pylori-infected subjects have reduced intragastric acidity compared to the uninfected population and this is most marked close to the gastrooesophageal junction. The density of parietal cells and chief cells is reduced in H. pylori infected subjects throughout the gastric mucosa. These findings may be negatively associated between H. pylori infection and both gastroesophageal reflux disease and oesophageal adenocarcinoma.

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

References

MORNING, OCTOBER 17, 2016 10:30–12:00
ABSTRACTS ON FIRE: GORD ON FIRE – HOTSPOT

OP049 ASSOCIATION BETWEEN LUMINAL BILE SALT CONTENT AND DISTAL MUCOSAL INTEGRITY IN HEALTHY VOLUNTEERS
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Introduction: Functional dysphagia (FD) is a functional gastrointestinal disorder with a reported prevalence of 20%–25% in the general population. Recent studies reported duodenal mucosal integrity was reported as a potential pathophysiological mechanism in FD (Vanhee H, Gut 2014). However, the factors controlling duodenal mucosal integrity remain unknown. In this pilot study, we evaluated whether luminal bile salt content is associated with duodenal permeability in healthy volunteers.

Aims & Methods: This study was carried out in 21 healthy volunteers (11 men, 25 ± 8 years). Duodenal biopsies were obtained by gastroduodenoscopy and used to measure the in vitro transepithelial resistance (TEER) using Ussing chambers. Meantime, fluorescein isothiocyanate dextran (FITC-dx, MW 4kDa) was applied to assess paracellular permeability. After the gastroduodenoscopy, an aspiration catheter was placed in the second part of the duodenum under fluoroscopic control. Duodenal fluid aspirates were collected at fixed time points during the test period (unit of time in hours). The usual test period was 1.5 hours (range 0.8–2.0 hours). Concentration and composition of the bile salt pool (including glycocholic acid, cholic acid, taurocholic acid, glycochenodeoxycholic acid, cholic acid, taurochenodeoxycholic acid, glycodeoxycholic acid, taurodeoxycholic acid, glycodeoxycholic acid and taurodeoxycholic acid) in these aspirates was evaluated. Correlation analysis was used to look for an association between luminal bile salt content and duodenal mucosal integrity.

Results: Duodenal biopsies of healthy volunteers displayed a paracellular passage of 27.23 ± 7.93 pmol and a TEER of 19.85 ± 2.63 kΩ cm⁻². A negative correlation was found between the concentration of taurochenodeoxycholic acid and the duodenal mucosal integrity. After the gastroduodenoscopy, an aspiration catheter was placed in the second part of the duodenum under fluoroscopic control. Duodenal fluid aspirates were collected at fixed time points during the test period (unit of time in hours). The usual test period was 1.5 hours (range 0.8–2.0 hours). Concentration and composition of the bile salt pool (including glycocholic acid, cholic acid, taurocholic acid, glycochenodeoxycholic acid, cholic acid, taurochenodeoxycholic acid, glycodeoxycholic acid, taurodeoxycholic acid, glycodeoxycholic acid and taurodeoxycholic acid) in these aspirates was evaluated. Correlation analysis was used to look for an association between luminal bile salt content and duodenal mucosal integrity.

Conclusion: These results imply that the composition of the duodenal bile salt pool has been highly implicated in this sensitivity, displaying the presence of healthy volunteers. Whether the bile salt concentrations explored in the present study are likely to be perceived. Our hypothesis is that the enhanced sensitivity of the proximal oesophagus is related to more pronounced impairment of mucosal integrity in this part of the oesophagus.

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 histological intercellular space width and transmucosal electrical impedance was used to measure the presence of non-erosive reflux disease. Afferent nerves can be found within the oesophageal mucosa and this may be a target for topical treatment of these patients.

Disclosure of Interest: P. Woodland: Research grant from Reckitt Benckiser UK D. Sifrim: Receives a research grant from Reckitt Benckiser All other authors have declared no conflicts of interest.

Reference
Incidence of chronic laryngeal symptoms in primary care is about 10% (IC 95% 6.4–16.7) and 59 healthy controls (30M/29F, mean age 41.2 years, mean body mass index [BMI], 21 and 23, respectively). There were 32% (105/329) with symptoms greater than 25 mg/mL. A positive PeptestTM was considered in case of a concentration of pepsin higher than 25 mg/mL.

The main disorder associated to them, leading to a specific syndrome called Laryngopharyngeal Reflux (LPR). Several studies demonstrated that pepsin measurement in saliva can be adopted as surrogate marker of GERD in LPR patients. Recently, a low-cost, non-invasive salivary pepsin test (PepTestTM, RD Biomed Limited, UK) was found to be able to measure pepsin in the saliva/sputum and to discriminate with good sensitivity and specificity between patients with typical GERD (i.e., with heartburn and regurgitation), confirmed at impedance-pH monitoring, from those without reflux disease (i.e., functional heartburn).

Thus, it has been hypothesized about the utility of using this novel device to diagnose LPR in primary care setting.

Aims & Methods: To investigate the usefulness of PepTestTM in primary care patients presenting with chronic laryngeal symptoms suggestive of LPR. In a prospective multicenter, controlled, pilot study, consecutive patients presenting with chronic laryngeal symptoms were enrolled by primary care physicians. Uninvestigated individuals with no gastrointestinal symptoms or disease (including GERD or dyspepsia) or history of surgery served as healthy controls (HCs). All subjects completed the validated reflux symptom index (RSI) questionnaire and in case of a score >13, a symptom-based diagnosis of LPR was made. Also the gastrointestinal symptom scale (GIS) questionnaire was completed to investigate reflux symptoms and Quality of Life. All individuals were asked to provide 2 samples of sputum collected one hour after lunch and dinner. A positive PepTestTM was considered in case of a concentration of pepsin higher than 25 mg/mL. Results: Between February and April 2014 and during August 2015, 86 patients with LPR (37 Male/49 Female, age 54 ± 14; RSI ≥ 13, mean RSI 22 ± 6, mean GSI 22 ± 6.4) and 59 healthy controls (30M/29F, mean age 41 ± 15; RSI < 5, mean RSI 0.5 ± 1, mean GSI 33 ± 6.5) were tested. In total, 256 samples were examined, whereas 34 samples were discarded because of technical problems (i.e. unclear storage, poor/excessive quantity). At least one positive result was found in 64 (74%) LPR patients and in 54 (92%) HCs (p < 0.005), whereas two positive results were observed in 34 (40%) LPR patients and 26 (45%) HCs (p = 0.4505). One (in case of a single test) or two negative tests were registered in 22 (26%) LPR patients vs 4 (7%) of HCs (p = 0.0039). PepTestTM had an accuracy of 47% (IC95 39%–55%) a specificity of 74% (IC95 65%–84%), a sensitivity of 74% (IC95 65%–84%), and a negative predictive value of 2% (IC95 0%–8%) in identifying LPR as diagnosed by RSI.

Conclusion: In this pilot study, PepTestTM was not able to discriminate among primary care patients with LPR from those without and therefore cannot be suggested as preliminary tool to select patients requiring pH monitoring.

Further studies including investigated healthy controls are mandatory to elucidate the diagnostic utility of salivary pepsin measurement in primary care setting.

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

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

Disclosure of Interest: A.J. Bredenoord: Received research funding from EndoIm, Medical Measurement Systems, Danone and Given and received speaker fee and/or consulting fees from MMS, Astellas, AstraZeneca and Almirall. All other 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 aceticamide and placebo groups, respectively. These results suggest that aceticamide may be effective in patients with associated reflux events. Aceticamide significantly reduced the reflex events and improved reflux symptoms in patients whose symptoms were associated with reflux events. Co-administration of aceticamide 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. Pawelek A, et al. The gastric accommodation response to meal intake deter-

OP054 A RANDOMIZED CONTROLLED TRIAL TO ASSESS THE CLINICAL EFFECTIVENESS AND SAFETY OF ESOMEPRAZOLE 20 MG ONCE DAILY VS. VONOPRAZAN 20 MG ONCE DAILY FOR RESOLUTION OF GASTRO-ESOPHAGEAL REFUX DISEASE SYMPTOMS IN NEWLY DIAGNOSED PATIENTS

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Introduction: Gastro-oesophageal reflux disease (GORD) is a frequent and troublesome disease mainly in young adults. Vonoprazan (VPZ) has potent acid inhibitory efficacy. We assessed clinical efficacy for Gastro-oesophageal reflux disease (GORD) symptom.

Aims & Methods: Aceticamide was a single-blind, randomized controlled, open-label, parallel-group trial conducted to assess the clinical efficacy of Esomeprazole (EPZ) 20 mg once daily vs. VPZ 20 mg once daily for the resolution of GORD symptoms in newly diagnosed patients.

Patients ≥ 20 years of age with upper gastrointestinal symptoms of at most moderate 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 regression (GOS = 0) at weeks 2 and 4 treatment (p < 0.05). Both treatment were generally well tolerated, but a patient in the VPZ group withdrew because of the adverse events.

Discussion: Despite VPZ has potent acid inhibitory efficacy, EPZ 20 mg once daily provides significant clinical efficacy for the resolution of GORD symptoms 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).

The 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.

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

References

OP055 EFFICACY AND SAFETY OF THE ENDOLUMINAL DEVICES OF GASTROESOPHAGEAL REFUX WITH BAND LIGATION

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Introduction: Gastro-oesophageal reflux disease is characterized by reflux of the gastric contents causing troublesome esophageal and extramural symptoms that could affect adversely the quality of life. About 10–40% of patients with GERD fail to show adequate symptomatic response to the standard dose of PPI. Several mechanisms could explain refractivity to GERD as improper PPI closing, patient non-compliance, esophageal hypersensitivity, residual acid reflux, bile reflex, nocturnal acid breakthrough. Alternative therapeutic options include laparoscopic fundoplication, lower esophageal magnetic bands, endoscopic therapy which are expensive, and about 10% of patients experience persistence of heart burn, or develop dysphagia.

Aims & Methods: We aimed to evaluate the safety and efficacy of endoluminal rubber band ligation in the management of 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 regur-
gitation 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 boclofen 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, dyspnea, oedema, bleeding. Large hiatal hernia more than 2 cm, paraoesophageal hernia, active Heliocobacter pylori infection, esokinophilic 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, mean GERD related quality of life questionnaire (GERD-QOL) value was 35.4 ± 6.9, depth of Z- line 34 ± 1.1 cm, 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, significantly improved after 6 months, 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 signifi-
cantly 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
1. Inadomi JM, McIntyre L, Bernard L and Hendrick AM. Step-down from multiple- to single-dose proton pump inhibitors (PPIs): a prospective study of patients with heartburn or acid regurgitation completely relieved with PPIs. Am J Gastroenterol 2003; 98: 1940.
Intervention: LSG is the most commonly performed bariatric procedure in the US and Canada and the Asia-Pacific region. However, LSG can result in new GERD and may worsen preexisting 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.5–10

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 successful swallowing and no oropharyngeal symptoms on maximum tolerated 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, 215 usec, at 20Hz. Postop follow-up endpoints included clinical symptoms, improvement in GERD symptoms and esophageal acid exposure. Most patients reported. No dysphagia or other GI side effects were reported.

Results: 12 patients, 66% (8/12) women at 8 centers have been treated. Median age (IQR 34–55) years. LSG patients (8/12) were on or did not require double-dose PPIs. At their last follow-up (median = 12 months), 75% (6/8) were off-PPI and one each was using PPIs on < 50% of days and standard dose once a day. The last follow-up Gastroesophageal Reflux Disease Score for chronic therapy failure for kidney transplants and not GERD symptoms. Median esophageal pH at baseline was 16.4% (IQR 8.5–22.4), which improved to 1.3% (IQR 0.4–2.2) at last follow-up after 6 months of treatment (n = 6; p = 0.01). All patients improved esophageal acid exposure (p < 0.05) and 10 patients had normalized acid exposure and 16 patients 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 (p < 0.05). No SAEs related to the device or procedure were reported. No dysphagia or other GI side effects were reported.

Conclusion: Preliminary results on patients with LSG and GERD with bothersome GERD symptoms on maximal medical therapy were evaluated. 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
Abstract No: OP058

A. Katagiri1, T. Baba1, F. Ishida1, H. Inoue3, M. Oda4, K. Mori5

The overall accuracy of ECV-CAD was comparable to that of expert endoscopists. Therefore, it is uncertain whether ECV-CAD can achieve a diagnostic ability as high as that of expert endoscopists.

Aims & Methods: The aim of this study was to compare the diagnostic ability of ECV-CAD with that of human endoscopists in characterization of colorectal lesion. The algorithm of ECV-CAD is based on texture analysis, which can quantify the pattern of endoscopic images, and vessel features. ECV-CAD provides a 2-class diagnostic processes for neoplastic or non-neoplastic diagnoses. To validate the diagnostic ability of ECV-CAD, we selected 4 expert endoscopists (with an experience of > 200 cases of EC) and 3 novices (with an experience of < 20 cases of EC). The EC images used for the evaluation with ECV-CAD were randomly allocated to the assessors. The assessors recorded their diagnosis (non-neoplasms or neoplasms) with its confidence level (high or low). For ECV-CAD, a probability of >90% was considered as a high-confidence computed diagnosis. The sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of distinguishing neoplasms from non-neoplasms, as well as the ratio of high-confidence diagnosis were calculated. Furthermore, the diagnostic ability when the diagnosis was made in high confidence was also calculated.

Results: The overall accuracy of ECV-CAD was 87.8%, whereas the accuracy for high-confidence cases was 93.5%. These values were higher than those for training sets. The accuracy for training sets was 84.2% and 90.8% for expert endoscopists and 83.3% and 94.4% for novices, respectively. The details of the diagnostic abilities are shown in the Table.

Table: Diagnostic Abilities

<table>
<thead>
<tr>
<th>Adenomas overall, N</th>
<th>Proximal colon adenomas, N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found at Index</td>
<td>Missed and found by EC</td>
</tr>
<tr>
<td>CC Index</td>
<td>53</td>
</tr>
<tr>
<td>EC Index</td>
<td>93</td>
</tr>
</tbody>
</table>

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 making 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

LONG-TERM MANAGEMENT OF IBD - ROOM G

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

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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 (combotherapy). 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 model of multiple covariates, to predict the probability to receive thiopurines, anti-TNFs or combotherapy at baseline. Hazard ratios for the risk of 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) unexposed to thiopurines or anti-TNFs, 111,113 PY exposed to thiopurines, 60,736 PY exposed to anti-TNFs and 11,514 PY exposed to combotherapy. Among them, 166, 56, 31 and 13 patients developed lymphoma, respectively. In multivariate analyses, patients exposed to thiopurines or anti-TNFs monotherapy had an increased risk of lymphoma as compared to unexposed patients (Hazard ratio (HR) 4.83 (2.51-9.5)). Patients exposed to combotherapy had a more than four-fold increased risk of lymphoma as compared to unexposed patients (HR: 4.83 (2.51-9.8)).

Conclusion: The risk of lymphoma associated with combotherapy 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 combotherapy.

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.
INCIDENT CANCER IN INFLAMMATORY BOWEL DISEASE: RISK FACTORS IN A LONG TERM MULTICENTER NESTED CASE-CONTROL IBD STUDY AT 4 YEARS


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12Gastroenterology Unit, University of Rome Tor Vergata, Rome/Italy
13GI Unit, Ospedale Cervello, Palermo/Italy
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Abstract: Cross-sectional study of a cohort of 2416 IBD patients followed up for 24 years (2012-2014) showed a higher risk of cancer in IBD vs non-IBD patients, whereas cancer risk was similar in CD and UC patients.

Methods: We used a nested case-control study to compare cancer incidence in 217 IBD patients (117 CD, 100 UC) with 145 controls (after age and sex matching). Patients with and without cancer were compared using univariate and multivariate logistic regression analysis.

Results: Cancer incidence was higher in IBD patients than in controls, with a hazard ratio of 1.42 (95% CI 1.08-1.86) for all cancers. This increased risk was also found for CRC (hazard ratio 1.75, 95% CI 1.31-2.33) and for lymphoma (hazard ratio 3.52, 95% CI 1.36-8.99).

Conclusions: Our findings support the need to investigate the possible role of CD and UC in the development of cancer and to develop personalized surveillance strategies for patients with IBD.

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

References:

Support: This study was supported by grants from the Italian National Research Council (PRIN 2012) and from the Italian Ministry of Health (Ricerca Corrente).
Aims & 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). 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 2003 to 2013, and followed up until 31 December 2014. A propensity score was used for thiopurines, anti-TNFs or combotherapy at baseline. Hazard ratios of infections were estimated based on Cox regression models, stratified on age at cohort entry (aged 18–64 years and ≥ 65 years) and with treatments considered as time-dependent variables. Serious and opportunistic infections were classified according to infection sites and pathogens, respectively.

Results: 173 077 IBD patients were included and followed over 4.9 years in median, accounting for 512 805 person-years (PY) unexposed to anti-TNFs or thiopurines, 108 315 PY exposed to thiopurines monotherapy, 57 464 PY exposed to anti-TNFs monotherapy and 11 089 PY exposed to combotherapy. Among them, a total of 4926 (1.16%) 932 serious infections occurred in patients aged 18–64 years and 120 and 47 opportunistic infections occurred, respectively. After adjustment (based on propensity score, age, time-varying exposure to corticosteroids and past history of serious infections), exposure to thiopurines monotherapy was associated with an increased risk of serious infections compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs and combotherapy compared to thiopurines monotherapy. After adjustment (based on propensity score, age, time-varying exposure to corticosteroids and past history of serious infections), exposure to thiopurines monotherapy was associated with an increased risk of serious infections compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs and combotherapy compared to thiopurines monotherapy. After adjustment (based on propensity score, age, time-varying exposure to corticosteroids and past history of serious infections), exposure to thiopurines monotherapy was associated with an increased risk of serious infections compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs and combotherapy compared to thiopurines monotherapy. After adjustment (based on propensity score, age, time-varying exposure to corticosteroids and past history of serious infections), exposure to thiopurines monotherapy was associated with an increased risk of serious infections compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs and combotherapy compared to thiopurines monotherapy. After adjustment (based on propensity score, age, time-varying exposure to corticosteroids and past history of serious infections), exposure to thiopurines monotherapy was associated with an increased risk of serious infections compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs and combotherapy compared to thiopurines monotherapy. After adjustment (based on propensity score, age, time-varying exposure to corticosteroids and past history of serious infections), exposure to thiopurines monotherapy was associated with an increased risk of serious infections compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs and combotherapy compared to thiopurines monotherapy.
and 438 patients at the five, ten and 20 years follow up, respectively. Of these patients, 199 (139 UC, 60 CD) and 191 (133 UC, 58 CD) answered the SF-36 at all follow-up visits. 54 (38.9%) and 17 (28.3%) had stable scores. Of 133 UC patients and 58 CD patients, who answered the SF-36 at all follow-up visits, 31 (23.3%) and 13 (22.4%) had stable scores.

### Table: N-IBDQ total scores and General Health dimensional scores

<table>
<thead>
<tr>
<th>Follow-up year</th>
<th>UC Men</th>
<th>UC Women</th>
<th>CD Men</th>
<th>CD Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 years</td>
<td>108</td>
<td>148</td>
<td>88</td>
<td>72</td>
</tr>
<tr>
<td>10 years</td>
<td>191</td>
<td>187</td>
<td>178</td>
<td>186</td>
</tr>
<tr>
<td>20 years</td>
<td>191</td>
<td>187</td>
<td>186</td>
<td>178</td>
</tr>
</tbody>
</table>

**Table 2: Hazard ratios for any serious or opportunistic infections according to medication exposure**

<table>
<thead>
<tr>
<th>Serious infections, all</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed to thiopurines or anti-TNFs</td>
<td>1.29 (1.0–1.9)</td>
<td>1.27 (1.1–1.6)</td>
<td>2.40 (2.2–2.6)</td>
<td>2.31 (2.0–2.5)</td>
<td>3.82 (2.6–5.5)</td>
</tr>
<tr>
<td>Exposed to anti-TNFs monotherapy</td>
<td>1.17 (0.4–2.9)</td>
<td>1.09 (0.4–2.8)</td>
<td>1.76 (1.4–2.2)</td>
<td>2.18 (1.7–2.6)</td>
<td>3.22 (1.2–8.8)</td>
</tr>
<tr>
<td>Exposed to thiopurines or anti-TNFs</td>
<td>8.59 (2.1–35.1)</td>
<td>6.42 (1.4–30.0)</td>
<td>2.24 (0.9–5.5)</td>
<td>2.40 (0.9–5.9)</td>
<td>2.06 (0.4–9.7)</td>
</tr>
<tr>
<td>Exposed to anti-TNFs monotherapy</td>
<td>2.82 (1.0–7.4)</td>
<td>2.45 (1.3–4.5)</td>
<td>2.10 (1.6–2.7)</td>
<td>1.95 (1.5–2.6)</td>
<td>1.24 (1.0–1.5)</td>
</tr>
</tbody>
</table>

**OP065: PROGNOSTIC FACTORS FOR LONG-TERM INFLIXIMAB TREATMENT IN CROHN’S DISEASE PATIENTS: A 20-YEAR SINGLE CENTER EXPERIENCE**


1. *Laboratory for Therapeutic and Diagnostic Antibodies, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven/Belgium*

| Aims & Methods: The aim of this study was to identify patient- and disease-related factors influencing the real-life long-term response of infliximab in CD and UC patients. Initially, 946 patients participated. A validated model was pre-tested with bootstrapping with 1000 replications. The c-statistic was used to assess the predictive accuracy of the regression model.

**Abstract No: OP063**

**Disclosure of Interest:**


1. *Laboratory for Therapeutic and Diagnostic Antibodies, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven/Belgium*

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**Introduction:** The long-term efficacy of infliximab (IFX) in Crohn’s disease (CD) patients is suboptimal and prognostic factors for real-life long-term efficacy are insufficiently studied.

**Aims & Methods:** The aim of this study was to identify patient- and disease-related factors influencing the real-life long-term response of infliximab in CD and UC patients. Initially, 946 patients participated. A validated model was pre-tested 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%) 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 rates were 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). p < 0.0001. Multivariate Cox regression identified disease duration < 1 year (hazard ratio (HR) 2.5 (95% CI 1.2–5.2), p = 0.02), isolated IL1 disease location (HR 2.0 (1.1–3.5), p = 0.02), prior anti-TNF use (HR 2.3 (1.1–4.8), p = 0.03), hemoglobin < 13.5 g/dL (HR 2.3 (1.2–4.4), p = 0.02), absence of TDM use (HR 8.0 (4.1–15.6), p = 1x10⁻¹⁸), and first IFX dose optimization within first year (HR 7.5 (4.9–12.7), p = 5x10⁻¹⁵) as independent predictors of IFX failure-free survival. All 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 95.3% (95% CI 94.2–96.4) 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% (8.4–44.0) for the high risk group (≥4 risk factors). (p = 8x10⁻¹⁸). 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 free survival. 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, Jansen, Mitsubishi Tanabe, MSD, Takeda, Tillotts, Zeria - Consultancy: Abbvie, Boehringer-Ingelheim, Ferring, Jansen, MSD
G. Van Assche: - Financial support for research: Abbvie, MSD - Lecture fees: Abbvie, Ferring, MSD, Janssen - Travel reimbursement: Ainhoa, MSD, Takeda
A. Gils: - Financial support for research: FWO grant G.0617.12, 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, Tillotts - Consultancy: Abbvie, MSD, Takeda, Ferring, Gentechent/roche, shire, Pfizer, Galapagos, Mundipharma, Hospira, Cellgen corporation, Janus
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 CIRCULAR ENTERAL NUTRITION FOR THE MAINTENANCE OF REMISSION IN PEDIATRIC CROHN’S DISEASE PATIENTS
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2Hospital Dom Doestafia, 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 inpatient treatment, strafying patients as well as disease flares with similar efficacy compared to steroid therapy and no side effects. Some reports indicate a role for EN as maintenance therapy, but usually on top of other therapies. Thus, we aimed to test feasibility and efficacy of cyclic EEN as sole maintenance therapy.

Aims & Methods: Nine patients with active luminal paediatric Crohn’s disease, L1 (n=2) or L3 (n=7), followed at Necker Hospital between 2012 and 2014 were included in this prospective pilot study. After 8 weeks of exclusive enteral nutrition with Monduin IBID, patients who came into complete CRP-negative remission were proposed to continue on cyclic EEN therapy as sole treatment in an open manner. Cyclic EEN consists of a 6 weeks phase of normal feeding followed by a 2 weeks phase of exclusive enteral nutrition, without any conco-

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

OP067 CHANGES IN MUCOSAL-ASSOCIATED INTESTINAL BACTERIOFA AND FECAL BACTERIA IN INFILTRATING BOWEL DISEASE PATIENTS AND HEALTHY SUBJECTS: A PILOT STUDY
M. P.L. Guarrino1, L. Puigmit2, A. Altomare3, F. Del Chierico2, S. Cocca1, M. Cicala1
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2Parasitology and Metagenomics Unit, Bambino Gesu Children’s Hospital and Research Institute, Rome/Italy

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Introduction: The present study was to evaluate the mucosal and fecal microbiota composition in healthy controls (CTRLs) and IBID patients, in a case-control study exploited by 16s rRNA targeted metagenomics-based approach (phylootyping, PH). Fecal specimens were collected from 14 IBID patients [10 Crohn’s disease (CD), 4 ulcerative colitis (UC)] and from 11 healthy subjects. Microbiota composition was assessed by 16s rRNA gene, 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 V1-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 sequence similarity level of 97% by QIIME and aligned by UCLUST for OTUs matching against Greengenes database (v.13.8).

Results: In adult IBID 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 IBID patients showed an increment of Proteobacteria and decrease of Bacteroidetes, the difference was not significant compared to CTRLs. Particularly, a predominant presence of Enterobacteriaceae in IBID and a predominant presence of Ruminococcaceae, Rikenellaceae and Prevotellaceae in CTRLs were prevalent (P<0.05). Patient finding, 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.

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Introduction: Adherent-invasive Escherichia coli bacteria in the GI TRACT OF CRONH’S DISEASE PATIENTS
M. Galtier1, L. De Sordi2, A. Sivignon2, A. De Vallée2, D. Maura1, C. Neuf1, O. Rahmoun1, K. Wannerberger1, P. Desreumaux3, N. Barnich4
1Dpt Of Microbiology, Institut Pasteur, Molecular Biology of the Gene in Extremophiles Unit, Paris/Paris
2Universite d’Avernier Inserm U1051, Clermont-Ferrand/France
3Université Lille Nord De France, Division of Bacteriology, Lille/ France
4Univ. Lille, Inserm, LIRIC, UM9095, Lille/France
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Introduction: Adherent-invasive Escherichia coli (AIEC) are abnormally predomi-

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

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Introduction: Adherent-invasive Escherichia coli bacteria in the GI tract of Crohn’s disease patients potentially act to initiate or maintain chronic intestinal inflammation. A sufficiently powered randomized controlled trials is currently conducted by the GETAID pediatrique to confirm this pilot data.

Disclosure of Interest: F. Ruemmele: Nestle Nutrition Institute, Nestle Health Science
All other authors have declared no conflicts of interest.

Conclusion: This study demonstrates for the first time prolonged clinical, biologi-

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Disclosure of Interest: All authors have declared no conflicts of interest.
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 colonisation 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 bacteriophages were driving a long-term digestive tract colonization of AIEC LF82 bacteria which in turns reduces colitis symptoms.

**Conclusion:** Bacteriophages targeting AIEC bacteria with high efficiency 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 bacteriophages provides therefore, a new “microbiota friendly” way to efficiently target gut pathogens.

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

**OP069** CIPROFLOXACIN RESISTANCE IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH ESBL-PRODUCING ENTEROBACTERIACEAE COLONIZATION


1 Internal Medicine Gastroenterology, Riga Stradiņš University; Riga/Latvia
2 Riga Stradiņš University, Riga/Latvia
3 University of Latvia, Riga/Latvia
4 Riga East Clinical University Hospital, Riga/Latvia

**Contact E-mail Address:** vita@skuja.lv

**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 colonizing 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. Moreover, patients with ciprofloxacin resistance were compared to patients with ciprofloxacin-susceptible bacteria. In 1 case CTX-M and TEM gene combination was observed and in 2 cases only ESBL resistance CTX-M, TEM and SHV gene combination was observed. In 7 cases, TEM and SHV gene combination was observed and in 2 cases only SHV gene was present. Conclusion: 1. High gut colonization rate (11%) with ESBL-producing bacteria in UC patients, mostly E. coli, expressing CTX-M gene. 2. High resistance to ciprofloxacin (57%) in UC patients. 3. CTX-M gene associated with resistance to ciprofloxacin.

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

**References**


**OP070** CARD9 IMPACTS COLITIS BY ALTERING GUT MICROBIOTA METABOLISM OF TRYPТОPHAN INTO ARYL HYDROCARBON RECEPTOR LIGANDS

B. Lamas1, M. Lave-Richard2, M. Michél2, V. Leducq2, C. Brisonneau2, G. Da Costá1, L. Beaugerie2, P. Langella2, H. Sokol1

1 Centre ENS Tautavel, CNRS UMR7326, University of Toulouse, Toulouse/France
2Micalis, UMR 1157, CNRS UMR CNRS 7203, UPMC, Paris/Parc
3Micas, UMR 1319, Jouy-en-Josas/France
4Department Of Gastroenterology, APHP St Antoine, Paris/France

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**Introduction:** Inflammatory bowel diseases (IBD) develop as a result of a combination of genetic predisposition, dysbiosis of the gut microbiota, and environmental influences. Caspase recruitment domain 9 (CARD9), one of the numerous IBD susceptibility genes, encodes an adaptor protein 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 DDS. AHR activity in intestinal activation and increased sensitivity to colitis observed in CARD9-/- mice. 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. Alterations: Card9 deletion has an effect on the gut microbiota in mice and its transmission to WT GF recipients 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 response to catabolised microbial molecules, 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 UC: A RANDOMISED CONTROLLED FOCUS STUDY AIMED TO CHARACTERISE THE MICROBIOMIC CHANGES UNDERLYING FMT IN UC PATIENTS WITH ENSUING A RANDOMISED CONTROLLED FOCUS STUDY

P. Paramsothy1, N. Kaakoush2, M.A. Kamm3, J. Faith1, J. Clemente1, A. Walsh1, J. Van Den Bogaerde1, D. Samuel4, R. W. Leong5, S. Connor6, Ng7, R. Paramsothy6, E. Lin8, J. Colombel4, T.J. Borody8, H. Mitchell2

1 Centre for Digestive Diseases, Sydney/Australia
2 Bankstown-Lidcombe Hospital, Sydney/Australia
3 St Vincent’s Hospital, Sydney/Australia
4 Centre for Digestive Diseases, Sydney/Australia
5 Micalis, UMR 1319, Jouy-en-Josas/France
6 St Vincent’s Hospital, Sydney/Australia
7 Centre for Digestive Diseases, Sydney/Australia
8 University of New South Wales, Sydney/Australia
9 Centre for Digestive Diseases, Sydney/Australia
10 University of New South Wales, Sydney/Australia
11 Centre for Digestive Diseases, Sydney/Australia
12 Centre for Digestive Diseases, Sydney/Australia

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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 (ECGO 2016 & DDW 2016)1. This part of the FOCUS study aimed to characterise the microbial changes underlying FMT in UC, to 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 subsequently offered 8 weeks of open label FMT. Each FMT enema was derived from 2-5 UC patients with remission of disease activity. Fecal samples were collected from patients at week 0, 4
and 8, open label mid and end of treatment (if applicable), and 8 weeks after FMT; colonic biopsies were collected at week 0 and 8, and end of open label treatment (if applicable). Faecal samples were also collected from individual donors and donor batches. DNA was extracted from faecal samples and 16S ribosomal RNA gene sequencing performed using 2x300 bp Illumina MiSeq chemistry (F27 & 519R). Raw sequences were analysed using MOTHUR, and statistical tests performed on counts and relative abundances.

Results: Faecal and colonic samples were collected from 70 study patients. 14 donors contributed to 21 donor batches. 314 patient and 113 donor (individual plus batch) faecal samples along with 160 patient colonic samples were analysed. 26976 ± 540 clean sequences per faecal sample and 26893 ± 881 per colonic biopsy were obtained with rarefaction curves suggesting sampling had reached saturation. In both faecal and colonic samples e-oxidation significantly increased at all FMT treatment time points relative to baseline (p < 0.005); this persisted 8 weeks after FMT in the faecal samples. On PCA, Cluster, and PERMANOVA analyses FMT significantly influenced patient microbial profiles, with the shift towards healthy donor microbiota most notable at the genus and OTU levels. LEME analysis of both faecal and colonic samples showed a decrease in patient Bacteroidaceae and an increase in donor Prevotella with FMT, independent of clinical outcome. A range of other microbial taxa were identified as transplanted or displaced with FMT across all taxonomic levels. Patients receiving FMT who achieved remission had greater baseline faecal and colonic mucosal e-oxidation levels than those who did not achieve remission, and also had greater resultant diversity with and after FMT treatment. Specific taxa were consistently significantly associated with FMT remission across both faecal and colonic samples: taxa within Bacteroides were associated with remission, while OTUs within Faustobacterium and Sutterella were associated with lack of remission.

Conclusion: Baseline patient microbial diversity in UC appears to be predictive of therapeutic response to FMT. Intensive FMT is associated with increased mucosal microbiornial diversity, with the greatest diversity noted in patients achieving remission. Increased diversity persists 8 weeks after cessation of therapy. Specific bacterial taxa were associated with remission outcome of which are associated with treatment outcome. A high level of concordance was observed between the faecal 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 Centre for Digestive Diseases, where faecal microbiota transplantation is a treatment option for patients and has filed patents in this field.

All other authors have declared no conflicts of interest.

References

MONDAY, OCTOBER 17, 2016
14:00–15:30
FREE PAPER SESSION: THE FUTURE OF DIAGNOSTIC IN HBP AND UPPER GI – ROOM N1

OP072 RELAXIN-COATED IRON-OXIDE MAGNETIC NANOPARTICLES AS A NOVEL THERANOSTIC APPROACH FOR DIAGNOSIS AND TREATMENT OF LIVER FIBROSIS
R. Bansal1, B. Nagoniewicz1, J. Prakash1, G. Storm2
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2 Department Of Pharmacaceutics, Utrecht University, Utrecht/Netherlands

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Introduction: Hepatic fibrosis is a growing health problem with no effective and clinically approved therapy. Hepatic stellate cells (HSCs) are the key cells involved in the pathogenesis of liver fibrosis. Upon activation, HSCs undergo morphological and functional changes, and are transformed into contractile ECM-producing myofibroblasts leading to scar tissue formation. Relaxin (RLN) has been shown to inhibit HSC activation and contraction thereby ameliorate liver fibrosis and portal hypertension. However, RLN has very poor pharmacokinetics and administration of high or frequent doses can lead to detrimental side effects due to vasoconstriction.

Aims & Methods: In this study, we aimed to develop a nanoparticle-based delivery system for chemically reactive molecules of RLN for the diagnosis and treatment of liver fibrosis. We conjugated human RLN-2 to PEGylated magnetic nanoparticles (RLN-MNP) and characterized the size, shape and stability. We examined RLN-MNP for RLN conjugation and characterization of high or frequent doses can lead to detrimental side effects due to vasoconstriction.

Results: RLN-MNP was successfully synthesized and remained stable at 4°C. RLN-MNP showed specific binding and uptake to TGF-β activated human HSCs while MNP alone showed no binding/uptake. In vitro, RLN-MNP and unconjugated RLN significantly inhibited TGF-β induced 3D collagen gel contraction and HSCs migration. Significant up-regulation of RXFP1 in TGF-β activated HSCs and CCL4-induced liver fibrosis mouse model was observed. In vivo, after 8 weeks CCL4-induced liver fibrosis mouse model, both RLN and RLN-MNP strongly attenuated fibrosis by inhibiting HSC activation, ECM production and angiogenesis. Importantly, RLN-MNP, but not unconjugated RLN, increased Nitric oxide release by significant up-regulation of iNOS. On the other hand, unconjugated RLN induced systemic side effects by inducing systemic NO release (in serum) while RLN-MNP did not.

Conclusion: This study presents a novel strategy to deliver RLN specifically to HSCs, key pathogenic cells involved in liver fibrogenesis, for the diagnosis and treatment of liver fibrosis.

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

References
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 bleed</td>
<td>5/10 (50.0%)</td>
<td>4/14 (28.6%)</td>
</tr>
<tr>
<td>NBVV</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 for patients with ultrasound detected recurrent bleeding. The use of additional physiological stimuli during routine esophageal manometry improves diagnostic yield and symptom reproducibility. Methods: Prospective series of patients referred for esophageal HRM between November 2014-April 2016. All patients had undergone prior endoscopy with findings of normal or mild (LA grade A esophagitis). WS and STMs used were performed in the upright seated position. Diagnosis of major and minor esophageal motor disorders were based on CC version 3.0 for water swallows (2) and modified for solid swallows as appropriate (3). All medications known to interfere with GI motility were stopped for at least one week prior to the study. Symptoms reported by the patients during HRM study were analyzed for any corresponding manometric abnormalities. Symptom associated dysfunction (SAD) was defined as a symptom event reported during or up to 10 seconds after concurrent esophageal dysmotility during STM.

**References**

1. Fox et al., **DDW** 2014.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
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 and evaluated it. Finally, we carried out ESD and compared the image with the pathology results. In conclusion, our findings suggest that GC cells could generate miR-21-rich exosomes that are delivered to surrounding normal cells to promote malignant neoplasms. For now, little is known about how cancer cell-derived exosomes and miRNAs in exosomes modulate the microenvironment to optimize conditions for tumor progression and metastasis. Aims & Methods: We aimed to investigate whether cancer cell-derived exosomal miRNAs 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.

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 BLI mode and the LCIþAIM method. In the classification of visualization ability, 12 lesions were Clear, 22 lesions were Visible, 38 lesions were Invisible by BLI mode. On the other hand, 33 lesions were Clear, 34 lesions were Visible, 5 lesions were Invisible by LCIþAIM method. In the visualization ability of the surface fine structure, LCI+AIM method is significantly clearer than BLI mode (p < 0.05).

Conclusion: When we use AIM, indigocarmine accumulates in pit of the duct, and duct structures become clear by the acetic acid. By LCI mode, we can observe the vascular pattern of the lesion clearly. So by the combination of AIM and LCI, we can observe the lesion three-dimensionally. By this method, we can compare histopathology with an endoscopic image intuitively, so we believe that a magnifying endoscopy diagnosis of the gastric cancer is enabled even if we do not use various confusing classifications.

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

Reference
Results: Of the 6,300 survey completers, 5,931 were retained for analysis (49.2% female; mean age = 47.4, range 18–92; 1,949 US, 1,994 UK, 1,988 Canada) after 369 incomplete responders were eliminated. Due to the quota-based sampling method, sex or age group proportions did not differ between countries. Rome IV vs. Rome III IBS prevalence rates (census-correlated estimates in parentheses) were 6.1% (7.8%) in Canada, 6.6% (8.5%) in the US, 10.7% (11.7%) in Canada, and 5.5% (5.5%) vs. 10.1% (10.6%) in the UK. There were no IBS prevalence differences between countries, but Rome IV IBS prevalence was significantly lower than Rome III IBS in all countries (p < 0.0001) than with Rome III (16.6% IBS-C, 20.6% IBS-D, 60.1% IBS-M and 2.1% IBS-U).

Table: Table: Population Rome III and Rome IV IBS rates (%) by sex and age groups in the US, UK and Canada survey samples (without census weighting).

<table>
<thead>
<tr>
<th>Country</th>
<th>Rome III</th>
<th>Rome IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 18–34</td>
<td>Age 35–49</td>
<td>Age 50–64</td>
</tr>
<tr>
<td>US Females (n = 962)</td>
<td>15.6</td>
<td>16.6</td>
</tr>
<tr>
<td>US Males (n = 987)</td>
<td>7.2</td>
<td>9.3</td>
</tr>
<tr>
<td>UK Females (n = 976)</td>
<td>14.2</td>
<td>15.4</td>
</tr>
<tr>
<td>UK Males (n = 1018)</td>
<td>4.9</td>
<td>7.2</td>
</tr>
<tr>
<td>Canada Females (n = 980)</td>
<td>14.6</td>
<td>16.8</td>
</tr>
<tr>
<td>Canada Males (n = 1008)</td>
<td>6.3</td>
<td>10.3</td>
</tr>
</tbody>
</table>

Conclusion: These first-ever national population prevalence estimates for Rome IV IBS show that IBS prevalence and demographic distribution is equivalent in the US, UK and Canada, and confirm that the disorder is female-predominant and less prevalent in younger 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: 1. Rome Foundation.]


OP078 URINARY KALLIKREIN-10 PREDICTS INCURRABILITY FOR GASTRIC CANCER

Introduction: Recent material and technical development enables us to get many throughput biomarkers 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 incurrability of GC, we conducted this study using urine samples from GC patients and healthy control. Results: A proteome analysis identified 26 markers 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 (uKLK10) and protease 3 were positively associated with tumor stage progression. Moreover, urinary KLK10 (ulKLK10) 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: 2.53 (95%CI, 1.23–5.21), P = 0.007). Urinary KLK10 distinguished operability of GC with an area under the curve (AUC) of 0.85 (95%CI 0.73–0.98). Conclusion: uKLK10 is a promising non-invasive biomarker for incurable GC.

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

MONDAY, OCTOBER 17, 2016 14:00–15:30

FROM SYMPTOMS TO DIAGNOSIS IN IBS – ROOM N2

OP079 POPULATION PREVALENCE OF ROME III AND ROME IV IRRITABLE BOWEL SYNDROME (IBS) IN THE UNITED STATES (US), CANADA AND THE UNITED KINGDOM (UK)

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Introduction: Rome IV criteria include several adjustments in diagnostic requirements for IBS compared to Rome III. Here we will describe how this will affect the prevalence and demographic distribution of IBS.

Aims & Methods: We used data from a large internet survey of the general population in 3 countries to measure and compare Rome IV vs. Rome III IBS rates and the demographics of the disorder. A community sample of 6,300 individuals aged 18 and older in the US, UK and Canada (2,100 in each country) completed the secure online survey. Quota-based sampling was used to ensure equal proportion of sex (50%/50%) and age groups (40% aged 18–39, 40% aged 40–64, 20% aged 65+), across countries, and to control education distributions (30% maximum with college degree or equivalent). The survey included the Rome IV Diagnostic Questionnaire for Adults, Rome IV diagnostic modules for IBS, and demographic questions. Latest national census figures were used to calculate correction weights for age (in 5 year bins) and gender proportions and obtain IBS prevalence estimates for each country.

Results: Of the 6,300 survey completers, 5,931 were retained for analysis (49.2% female; mean age = 47.4, range 18–92; 1,949 US, 1,994 UK, 1,988 Canada) after 369 incomplete responders were eliminated. Due to the quota-based sampling method, sex or age group proportions did not differ between countries. Rome IV vs. Rome III IBS prevalence rates (census-correlated estimates in parentheses) were 6.1% (7.8%) in Canada, 6.6% (8.5%) in the US, 10.7% (11.7%) in Canada, and 5.5% (5.5%) vs. 10.1% (10.6%) in the UK. There were no IBS prevalence differences between countries, but Rome IV IBS prevalence was significantly lower than Rome III IBS in all countries (p < 0.0001) than with Rome III (16.6% IBS-C, 20.6% IBS-D, 60.1% IBS-M and 2.1% IBS-U).


OP080 FUNCTIONAL HEARTBURN OVERLAPS WITH IRRITABLE BOWEL SYNDROME MORE OFTEN THAN GERD - DEVELOPMENT OF A PREDICTIVE MODEL FOR CLINICAL PRACTICE

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7DiMat., Gastroenterology Unit, DiMl, Gastroenterology Unit, University of Genoa, Genoa/Italy
8Department Of Internal Medicine, IRCCS San Martino DIMI, Genova/Italy
9Department Of Medical and Surgical Sciences, S.Orolso-Malpighi University Hospital, Bologna/Italy
10Dept Internal Medicine, Universita di Genova, Genova/Italy

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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 (MH-IIP) 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 defined in GERD and FH has not yet been assessed.
Aims & Methods: Our aim was to assess the prevalence of IBS as well as anxiety and depression in patients subdivided into IBS and FBD groups by means of upper GI endoscopy and MII-pH monitoring. We also aimed to assess the prevalence of various clinical and endoscopic characteristics in IBS and FBD patients in order to develop a predictive model for distinguishing FH from GERD in patients presenting with typical reflux symptoms, potential utility in clinical practice. Patients underwent a structured interview based on questionnaires for GERD (GERDQ), IBS (RIIAD), anxiety and depression (HADS). Upper GI endoscopy and 24h-MII-pH monitoring were performed in all cases. In patients with IBS, fecal calprotectin was measured and colonooscopy was scheduled for values >100 μg/kg to exclude organic disease. Multivariate logistic regression analysis was performed to identify independent risk factors for FH. A predictive model for FH diagnosis based on clinical and endoscopic findings was developed by applying the purposeful selection of covariates. The coefficients estimated in the multivariate logistic regression analysis were used to predict FH diagnosis. The performance of the predictive model was then assessed by examining measures of discrimination and calibration. Discrimination was considered as the ability of the predictive model to differentiate 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 presenting with heartburn was built.

Results: Of the 701 consecutive heartburn patients who entered the study, 458 (65%) had GERD whereas 243 (35%) had FH. IBS was found in 143/458 (31%) GERD but in 187/243 (77%) FH patients (p < 0.001). At multivariate analysis IBS, anxiety, and smoking resulted independent risk factors for FH whereas hiatial hernia resulted protective. We developed a predictive model based on clinical and endoscopic characteristics (IBS, Smoking, Anxiety, Age ≥ 43, Heartburn > 12 mo, H. pylori +, Oesophagitis ≤ IIAAH). The area under ROC curve in an external validation cohort of 51 patients was 0.920. Considering the previously established cut-off, sensitivity and specificity of the predictive model in diagnosing FH against GERD were 84.3% and 78.9%, respectively. A calculator to help clinicians in automatically computing the predicted probability of FH versus GERD in patients presenting with heartburn was built (URL: http://app.calculoid.com/de/ calculator/2012).

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

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

A35

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.


A. Torblom: Consultant/Advisory Board member for Almirall, Danon and Shire.
M. Simrén: Unrestricted research grants from Danone, and Ferrin Pharmaceuticals (Advisory Board, member for AstraZeneca, Danone, Nestle, Chi Hansen, Almirall, Allergan, Albiro, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall.
All other authors have declared no conflicts of interest.
**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 patient 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, Albireo, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall; B. Jonéfält: Speaker for Abbvie, MSD and MEDA; 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 America 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.

**Sensitivity (95% CI) Specificity (95% CI) Positive LR (95% CI) Negative LR (95% CI)**

**Rome III criteria and normal Hb and CRP**

<table>
<thead>
<tr>
<th>Rome III criteria and normal Hb and CRP</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Positive LR (95% CI)</th>
<th>Negative LR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rome III criteria and normal Hb and CRP</td>
<td>90.0% (34.8–63.4%)</td>
<td>90.0% (33.2–93.6%)</td>
<td>4.32 (2.76–6.76)</td>
<td>0.09 (0.46–0.72)</td>
</tr>
<tr>
<td>Rome III criteria and HADS score ≥8</td>
<td>69.6% (5.3%–99.9%)</td>
<td>69.6% (5.3%–99.9%)</td>
<td>4.32 (2.76–6.76)</td>
<td>0.09 (0.46–0.72)</td>
</tr>
<tr>
<td>Rome III criteria and high somatisation</td>
<td>94.5% (91.7–97.8%)</td>
<td>94.5% (91.7–97.8%)</td>
<td>8.48 (2.33–10.0)</td>
<td>0.08 (0.70–0.91)</td>
</tr>
<tr>
<td>Rome III criteria, normal Hb and CRP, and high somatisation</td>
<td>22.2% (13.3%–33.6%)</td>
<td>95.0% (91.7%–97.8%)</td>
<td>4.32 (2.76–6.76)</td>
<td>0.09 (0.46–0.72)</td>
</tr>
<tr>
<td>Rome III criteria, no nocturnal passage of stool, and HADS score ≥8</td>
<td>18.2% (9.8%–29.6%)</td>
<td>99.0% (96.3%–99.9%)</td>
<td>17.3 (4.45–67.6)</td>
<td>0.83 (0.72–0.90)</td>
</tr>
</tbody>
</table>

**Abstract No: OP083**

**Aims & Methods:** We collected complete symptom, colonoscopy, and histology data from 318 consecutive, unselected adult patients with lower gastrointestinal 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. **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.
Table

<table>
<thead>
<tr>
<th></th>
<th>Diagnosed IBS-D (n = 859)</th>
<th>Undiagnosed IBS-D (n = 370)</th>
<th>Controls (n = 56,932)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p-value: Diagnosed vs. controls</td>
<td>p-value: Undiagnosed vs. controls</td>
<td>p-value: Undiagnosed vs. controls</td>
</tr>
<tr>
<td>Any provider visits</td>
<td>7.23 (0.31)</td>
<td>5.17 (0.35)</td>
<td>4.14 (0.02)</td>
</tr>
<tr>
<td>Gastroenterologist visits</td>
<td>7.19 (0.62)</td>
<td>7.01 (0.01)</td>
<td>4.25 (0.03)</td>
</tr>
<tr>
<td>Emergency room visits</td>
<td>2.69 (0.12)</td>
<td>2.06 (0.15)</td>
<td>1.70 (0.01)</td>
</tr>
<tr>
<td>General practitioner visits</td>
<td>0.02 (0.12)</td>
<td>0.12 (0.03)</td>
<td>0.17 (0)</td>
</tr>
<tr>
<td>Hospitalisations</td>
<td>14.00 (0.03)</td>
<td>8.08 (0.03)</td>
<td>0.11 (0)</td>
</tr>
</tbody>
</table>

**Introduction**: Endoscopic submucosal dissection (ESD) has been established as a standard treatment modality for 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**: Recurrence rate was 1.9% in ESD patients, 0.7% in gastrectomy patients (p = 0.08); 1.0%, 3.1% and 1.4% in AC, EC and BEC groups in ESD patients, (p = 0.062) and 2.0% and 1.4% in the AC+EC and BEC groups in ESD patients (p = 0.069), which were not significantly different between criteria groups. In concrete, recurrence rate was 1.1% and 0% in AC group of ESD and gastrectomy patients, respectively, 3.1% and 1.9% in EC group, and 1.4% and 0% in BEC group. 394 of 468 (84.2%) ESD patients were within criteria. (AC+EC and BEC).

**Conclusion**: The recurrence rate was neither significantly different between ESD and 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 operation risk.

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

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

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**Introduction**: 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.

Introduction:

A MULTICENTER RETROSPECTIVE STUDY
OP088 EVALUATION OF METASTATIC POTENTIAL CAUSED BY
INTERSEGMENTATION IN GASTRIC CANCER

Disclosure of Interest:

Aims & Methods: The aims of this study were to identify risk factors for non-curative resection and metastachronous 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: recurrences were also classified with the recently published European Society of Gastrointestinal Endoscopy guidelines. Univariate analysis (independent samples t-test, Mann-Whitney U test or chi-square test as appropriate) and multivariate logistic regression were performed to identify risk factors. Odds ratios (OR) were computed with 95% confidence intervals (CI). Survival analysis was performed using Kaplan-Meier curves and log-rank test. Significance level was defined as p < 0.05.

Results: In 184 lesions (288 segments) followed between 2005-2014, the median follow-up was 40 months. End-bloc and complete resection rates were 93.5% and 93.8%, respectively. Overall adverse events occurred in 13%. Mean follow-up time and longer procedure and more advanced histology in pre-resection biopsies were associated with non-curative resection (p < 0.05) but only intramucosal carcinoma on pre-resection biopsies was identified as a significant risk factor on multivariate analysis (adjusted OR 3.04, 95% CI 1.02–9.06). Histological upgrade (from low-grade dysplasia to high-grade dysplasia or from high-grade dysplasia to carcinoma) occurred in 49.5% of the cases. Metachronous lesions occurred in 18.4% and the incidence rate was 4.7 lesions per 100 patient-years. The mean time to first occurrence of metachronous detection was 24 months (interquartile range 9-56.25 months). Older age at diagnosis was identified as the only predictor of metachronous development in logistic regression (OR 1.46, 95% CI 1.09–1.97). Overall survival was 94.5% and 89.5% at 1 and 3 years, respectively; disease-specific survival was 99.4%, with only one patient dying of gastric cancer. Survival was significantly higher in patients with curative resections (log-rank 4.538, p = 0.033). In the non-curative resection group, patients submitted to surgery were significantly younger (mean age 66.7 ± 9.4 versus 73.6 ± 7.5 in the follow-up group, p = 0.037) and were less frequently classified as ASA III/IV (23.1% versus 31.1%, p = 0.062). However, survival rates were similar to those in patients with a shorter follow-up period (p = 0.052). In the gastrectomy specimens, there was no residual neoplasia in 75%. Comparing survival according to ESGE criteria, survival in patients with high-risk resection was significantly worse than in patients with low-risk resection (log rank 7.539, p = 0.006), while the differences were not significant in the survival of patients with low and local-risk resection (log rank 0.133, p = 0.715).

Conclusion: The identified risk factors for non-curative resection help to improve patient counseling for endoscopic resection and to guide patient selection for endoscopic resection and also patient information regarding the concept of No-touch isolation techniques might prevent the spread of cancer cells in colorectal and pancreatic cancer, in the influence of submucosal operation during ESD for gastrectomy does not make risk of LNM and prognosis worse.

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

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

References:


MONDAY, OCTOBER 17, 2016
14:00–15:30
GASTRIC FUNCTION IN HEALTH AND DISEASE – ROOM L8

OP091 CALORIC AND NON-CALORIC ARTIFICIAL SWEETENERS HAVE DISOCSOCIAL EFFECTS ON ANTRAL SATIETY AND PLASMA MITOMIN LEVELS IN HEALTHY VOLUNTEERS
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Introduction: Activation of gastrointestinal (GI) sweet taste receptors by caloric sweeteners such as glucose or fructose induces the secretion of GI peptides to regulate food intake. The effect of non-caloric sweeteners on GI peptide secretion and antral satiety is controversial. We have recently shown that motilin-induced gastric phase III contractions of the migrating motor complex (MMC) signal hunger feelings. The mechanism underlying interruption of the MMC by specific sweet tastants has not yet been studied. It is conceivable that this requires sweet taste receptor activation and accompanying changes in the release of GI peptides.

Aims & Methods: The aim was to determine the effect of caloric and non-caloric sweeteners on GI motility and GI peptide secretion as well as on hunger feelings and satiety feelings. We were therefore using induced mixed model analysis.

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

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

Reference
Aims & Methods: The aim of this study was to investigate the effect of LG on MMC, GA, GE and hunger or satiation in healthy volunteers (HVs). The study was an open-label, crossover trial conducted in 10 lean HVs. Liraglutide (Victoza®; Novo Nordisk, Belgium, 0.6 mg) was administered subcutaneously 14 hours before the start of the study protocol. No administration was done in the placebo arm. The study consisted of protocol 1 (MMC) and protocol 2 (GA/GE). In both protocols a high-resolution impedance manometry probe was advanced via the nose to the duodenum. Protocol 1: Gastroduodenal motility was registered for the duration of 1 MMC cycle. Antral and duodenal motility index (MI) were calculated (number of contractions/average amplitude contractions/average duration contractions)/5 min. Average MI was calculated by averaging 6 consecutive antral or duodenal cycles. Occurrence of antral or duodenal phase III contractions was evaluated. Protocol 2: After a stabilization period, HVs ingested a liquid test meal (200 ml, 300 kcal; 89% carbohydrate, 11% protein) labeled with 13C-sodium octanoate. GA was measured as the intragastric pres- sure over 5 channels in the fundus compared to baseline 5 minutes before the drink. LG administration completely suppressed MMC (placebo) to 5% (LG) (p<0.001). Similarly, phase III contractions were lower after LG for both phases III (p<0.007 and 0.005 respectively). Protocol 2: LG administration did not affect the IGP drop but significantly delayed the GE t1/2 (p<0.005) (Table). In the control condition all volunteers had a phase III within 4 hours after the meal. After LG this number decreased to 70% (AR2)% (ns). LG administration completely switched the origin of phase III contractions with a gastric origin from 65% (placebo) to 5% (LG) (p<0.001). The antral MI of both first and second phase III contractions was significantly lower after LG (p<0.01 and 0.002 respectively). Similarly, the duodenal MI was also lower after LG for both phases III (p=0.002 and p=0.05, respec- tively). Hunger or satiation ratings [JT3] were not affected by LG treatment in both protocols.

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

Disclosure of Interest: All authors have declared no conflicts of interest.
Results: We enrolled 20 patients (mean age 42y (range 18–70), 11f). Lower oesophagogastric pressure was significantly higher in the baclofen treated arm compared to the placebo arm (17.8±1.4 vs. 12.8±1.4 mmHg, p < 0.001). The number of transient LOS relaxations was lower (6 ± 1 vs. 8 ± 2, p = 0.04) and the percentage of transient LOS relaxations was no different in straining episodes between placebo and baclofen arm, but the percentage of straining episodes associated with rumination was significantly lower in the baclofen arm (14.6±3.8 vs. 31.29±5.96, p = 0.0003). The number of postprandial regurgitation symptoms marked by the patients 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 (1–0), 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.

IOP096 GASTRIC ELECTRICAL STIMULATION (GES) FOR REFRACTORY RUMINATING: RESULTS OF A PROSPECTIVE MULTICENTRE RANDOMIZED BLINDED CONTROLLED CROSS-OVER TRIAL

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8 Gastroenterology, Hopital Nord, Maruelle/ France
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11 Francophone, CRU Jean Moinier, Reims/France
12 Gastroenterology Department, Rennes University Hospital, Rennes/France
13 Caremeau Gastroentérologie, Nimes/France
14 Dept. De Medecine Digestive, CH Estang Medecine Digestive, Clermont Ferrand Cedex/France
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Introduction: Open trials have suggested that GES could be effective for the relief of symptoms associated or not with gastroparesis (GE). But, short randomized trials carried out in gastroparetic patients led to negative results. Our aim was to perform a large multicenter randomized double-blind controlled trial in patients with refractory rumination associated or not with gastroparesis, to confirm or not the efficacy of GES.

Aims & Methods: Aims & Methods: Aims & Methods: In human patient tumor samples, a total of 85% and 66% of patients harbored a mutated ITGA5 (ITGA5), a receptor for the ECM protein fibronectin, for its prognostic and therapeutic significance in pancreatic neoplasms. In vivo, ITGA5 expression 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 in PSCs and human pancreatic tumor cells (Panc-1). Knockdown (60%) of ITGA5 led to a dramatic reduction of several ECM molecules, including fibronectin. This study confirms that baclofen is an effective treatment option for patients with rumination syndrome, probably through its effect on LOS pressure.

Aims & Methods: Aims & Methods: Aims & Methods: 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 profibrotic myofibroblasts (cancer-associated fibroblasts (CAF)) in tumor stroma and therefore become key target in pancreatic cancer therapy (1). CAFs secret growth factors, exosomes and proteins that increase the neoplastic potential and invasion. Bcl-3 is a transcription factor that is altered in pancreatic cancer, and indicates that Bcl-3 has an important pro-tumorigenic role in pancreatic cancer development and progression.

Conclusion: In summary, our data provide the first insights into the function of Bcl-3 in pancreatic cancer, and indicate that Bcl-3 has an important pro-tumorigenic role in pancreatic cancer development and progression.

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

IOP098 INTEGRIN ALPHAS AS A NOVEL PROGNOSTIC AND THERAPEUTIC TARGET IN PANCREATIC TUMOR STROMA

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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 profibrotic myofibroblasts (cancer-associated fibroblasts (CAF)) in tumor stroma and therefore become key target in pancreatic cancer therapy (1). CAFs secret growth factors, exosomes and proteins that increase the neoplastic potential and invasion. Bcl-3 is a transcription factor that is altered in pancreatic cancer, and indicates that Bcl-3 has an important pro-tumorigenic role in pancreatic cancer development and progression.

Conclusion: In summary, our data provide the first insights into the function of Bcl-3 in pancreatic cancer, and indicate that Bcl-3 has an important pro-tumorigenic role in pancreatic cancer development and progression.

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: In conclusion, the present study reveals ITGAs 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.

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

Conclusion: These findings provide mechanistic insights into EMT in pancreatic cancer by (a) identifying HULC as a highly induced IncRNA by TGF-b, (b) demonstrating that HULC promotes EMT, (c) identifying that miR-622, as a down regulated miRNA by TGF-b, can target HULC, and (d) showing a functional role for miR-622 in EMT via targeting HULC. These observations imply that miR-622 would suppress invasion and metastasis by inhibiting EMT signaling through targeting HULC and suggest potential strategies to inhibit invasion and metastasis in human pancreatic cancer.

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

Disclosure of Interest: All authors have declared no conflicts of interest.
OIK10 RELA CONTROLS KRS-DRIVEN PANCREATIC CARCINOGENESIS BY MODULATING ONCOGENE-INDUCED SENESCENCE VIA THE CXCL1/KC/CXCR2 AXIS

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Introduction: The IKK/NF-κB pathway has been shown to be a crucial mediator of tumour growth and progression, exhibiting both tumour-promoting and tumour-suppressive properties. How IKK/NF-κB regulates tumour cell behaviour and tumour cell–neuron interactions remains unclear.

Methods: To study the invasion of tumour cells along neurites we have combined 3D co-culture assays of dorsal root ganglia (DRG) and tumour cells in line with time-lapse microscopy and 3D co-culture assays of dorsal root ganglia (DRG) and tumour cells with time-lapse microscopy and specifically track the directional movement of individual tumour cells along neurites extending from DRGs. Quantification of the change in tumour cell trajectory with time-lapse microscopy reveals that neurite outgrowth from the DRG induces the tumour cells to migrate towards the DRG and allow to quantitate length, velocity, forward migration and endpoint analysis in order to track the locomotion of individual tumour cells.

Results: Neural invasion (NeI) is associated with an unfavourable course of the disease and constitutes a major cause of neuropathic pain, thus limiting the quality of life. NeI is considered as a mixed interaction between tumour cells and nerves and involves both, the unidirectional tracking and invasion of tumour cells along neural routes but also implicates tumour mediated changes in neural plasticity resulting in nerve hypertrophy and increased nerve density in PDAC.

Conclusion: We have described several 3D approaches using line with time-lapse microscopy to understand tumour cell invasion and its impact on neuronal plasticity in PDAC. Using a combination of 3D co-culture assays of DRG and PDAC, we are able to study tumour cell invasion and associated changes in neuronal plasticity in PDAC.

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

References:
2. Maier HJ, Wagner M, Schips TG, Salem HH, Baumann B and Wirth T. IKK/NF-κB: Mediators of oncogene-induced senescence (OIS) by regulating the CXCL1/CXC-2 axis. However, as soon as OIS is bypassed during progression of tumorigenesis, NF-κB supports tumour progression by enhancing proliferation of the transformed pancreatic cancer cells.

OIP102 MODELLING TUMOR CELL NERVE INTERACTIONS IN PANCREATIC CANCER

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Introduction: Neural invasion (NI) has emerged as a key pathologic feature of pancreatic adenocarcinoma (PDAC) and represents a distinct route of tumour cell dissemination. NI is associated with an unfavourable course of the disease and also constitutes a major cause of neuropathic pain, thus limiting the quality of life. NI is considered as a mixed interaction between tumour cells and nerves and involves both, the unidirectional tracking and invasion of tumour cells along neural routes but also implicates tumour mediated changes in neural plasticity resulting in nerve hypertrophy and increased nerve density in PDAC.

Aims & Methods: Here we describe several 3D approaches using line with time-lapse microscopy to understand tumour cell invasion and its impact on neuronal plasticity in PDAC. Using a combination of 3D approaches using line with time-lapse microscopy to understand tumour cell invasion and its impact on neuronal plasticity in PDAC.

Results: Neural invasion (NeI) is associated with an unfavourable course of the disease and constitutes a major cause of neuropathic pain, thus limiting the quality of life. NeI is considered as a mixed interaction between tumour cells and nerves and involves both, the unidirectional tracking and invasion of tumour cells along neural routes but also implicates tumour mediated changes in neural plasticity resulting in nerve hypertrophy and increased nerve density in PDAC.

Conclusion: We have described several 3D approaches using line with time-lapse microscopy to understand tumour cell invasion and its impact on neuronal plasticity in PDAC. Using a combination of 3D approaches using line with time-lapse microscopy to understand tumour cell invasion and its impact on neuronal plasticity in PDAC.
colon of CDEIS responding patients. The molecular profile appears to be differ-
entiated from anti-TNF treatment.


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

#### 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-to-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 colonoscopic evaluations (i.e. at UNITI-I or 2 baseline [BL] and WK4, and IM-UNITI WK0-44) 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 65 mg/kg, or PBO). Thereafter, UST induction responders [primary randomized maintenance population] were re-randomized to subcutaneous (SC) UST 90 mg every 8 wks (UST) or 12 wks (UST). UST induction responders [primary randomized maintenance population] were re-randomized to subcutaneous (SC) PBO, UST 90 mg every 12 wks (PBO). At maintenance WK0 (i.e. induction WK8), UST induction responders [primary randomized maintenance population] were re-randomized to subcutaneous (SC) PBO, UST 90 mg every 8 wks (UST) or 12 wks (UST). UST induction responders [primary randomized maintenance population] were re-randomized to subcutaneous (SC) PBO, UST 90 mg every 12 wks (UST).

#### Results:

The substudy primary endpoint was met, as UST induction significantly greater reduction in SES-CD from BL at induction WK0 vs. PBO. UST induction responders vs. PBO at induction WK0 achieved maintenance endoscopic end-points at WK44. The endoscopy 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 WK8. Results from 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 end-point vs. PBO. Together, these data support the efficacy of UST in inducing & maintaining endoscopic healing of the mucosa in CD.

#### Conclusion:


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### Table 1a: Induction Week 8 (UNITI-I&2)

<table>
<thead>
<tr>
<th>SES-CD Change from BL, mean (SD)</th>
<th>PBO (N = 97)</th>
<th>UST (N = 155)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical meaningful endoscopic improvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29.9%</td>
<td>47.7%</td>
</tr>
<tr>
<td><strong>Endoscopic Response</strong></td>
<td>13.4%</td>
<td>20.6%</td>
</tr>
<tr>
<td><strong>Endoscopic Remission</strong></td>
<td>4.1%</td>
<td>7.7%</td>
</tr>
<tr>
<td><strong>Mucosal Healing</strong></td>
<td>4.1%</td>
<td>9.0%</td>
</tr>
</tbody>
</table>

*P < 0.05 3 Primary endpoint 1 SES-CD reduction ≥5 from induction BL 2 SES-CD reduction ≥50% from induction BL 3 SES-CD total score ≤5 4 Complete absence of ulcers

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 endoscopy 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 WK8. Results from 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 end-point vs. PBO. Together, these data support the efficacy of UST in inducing & maintaining endoscopic healing of the mucosa in CD.

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### Table 1b: Maintenance Week 44 (IM-UNITI)

<table>
<thead>
<tr>
<th>SES-CD Change from BL, mean (SD)</th>
<th>PBO (N = 51)</th>
<th>UST (N = 74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Clinical meaningful endoscopic improvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25.5%</td>
<td>44.6%</td>
</tr>
<tr>
<td><strong>Endoscopic Remission</strong></td>
<td>4.2%</td>
<td>24.1%</td>
</tr>
<tr>
<td><strong>Mucosal Healing</strong></td>
<td>9.8%</td>
<td>20.3%</td>
</tr>
</tbody>
</table>

*P < 0.05 3 Primary endpoint 1 SES-CD reduction ≥5 from induction BL 2 SES-CD reduction ≥50% from induction BL 3 SES-CD total score ≤5 4 Complete absence of ulcers

**Table 1: Key efficacy parameters

<table>
<thead>
<tr>
<th>Variable/unit/patient</th>
<th>Placebo (N = 44)</th>
<th>Ustekinumab (N = 128)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical remission</td>
<td></td>
<td></td>
<td>0.0077</td>
</tr>
<tr>
<td>(CDAI &lt; 150), %, ITT-NRI</td>
<td>23</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>PRO2, mean change from baseline, ITT-LOCF</td>
<td>17.6</td>
<td>33.8</td>
<td>0.0045</td>
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</tbody>
</table>

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

#### 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 to 450, CDEIS: 400 to 1000) were randomized to receive 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-100) underwent corticosteroid tapering after Week 10. Anti-TNF naïve patients were permitted to discontinue 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 y), 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 18% of placebo recipients (p = 0.0007), and led to improvement in PRO2 score, and quality of life (IBDQ 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 PRO2 score, and quality of life (IBDQ changes from baseline) compared to placebo (p = 0.05).

Table 1: Key efficacy parameters

<table>
<thead>
<tr>
<th>Variable/unit/patient</th>
<th>Placebo (N = 44)</th>
<th>Filgotinib (N = 128)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical remission</td>
<td></td>
<td></td>
<td>0.0077</td>
</tr>
<tr>
<td>(CDAI &lt; 150), %, ITT-NRI</td>
<td>23</td>
<td>47</td>
<td></td>
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</tbody>
</table>
OP106 TOFACITINIB HAS INDUCTION EFFICACY IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS, REGARDLESS OF PRIOR TNF INHIBITOR THERAPY


Aims & Methods: We investigated the effect of prior tumour necrosis factor inhibitor (TNFi) therapies or disease activity (baseline Mayo score) on clinical efficacy endpoints and patient-reported outcomes (PROs) in pooled data from OCTAVE Induction 1 and 2. Adults with moderately to severely active UC (baseline Mayo score ≥5, rectal bleeding subscore ≥1 and endoscopic subscore ≥2) and prior failure/intolerance to ≥1 of corticosteroids, thiopurines or TNFi were randomised (4:1) to receive tofacitinib 10 mg or PBO for up to 9 weeks (wks). Efficacy endpoints at Wk 8 included remission (primary endpoint; Mayo score <2), no subscore >1 and rectal bleeding subscore of 0, mucosal healing at Wk 8 (Mayo endoscopic subscore ≤1), clinical response (decrease from baseline Mayo score ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1). All endoscopic scores were assessed at baseline and Wk 8.

Results: A total of 824 patients across 11 countries were randomised (n = 549 to tofacitinib and n = 275 to PBO). Baseline Mayo score, prior TNFi exposure and prior failure/intolerance were significantly more frequent in the tofacitinib group. Across all prior TNFi exposure or failure subgroups, the superiority of tofacitinib 10 mg BID vs PBO was significant for clinical response, remission and mucosal healing. The treatment effect on clinical response was greater for patients with prior TNFi failure (primary vs secondary) or disease severity and was significant regardless of prior TNFi exposure.

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>Endpoint</th>
<th>Placebo</th>
<th>Tofacitinib</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission, n (%)1</td>
<td>159 (17.6)</td>
<td>14 (6.0)</td>
<td>11.7 (7.5, 15.5)***</td>
</tr>
<tr>
<td>Prior TNFi exposure1</td>
<td>90 (23.7)</td>
<td>13 (12.5)</td>
<td>12.2 (7.8, 16.6)***</td>
</tr>
<tr>
<td>Prior TNFi failure1</td>
<td>53 (11.4)</td>
<td>1 (0.8)</td>
<td>10.6 (7.3, 13.9)***</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)1</td>
<td>106 (24.1)</td>
<td>13 (11.5)</td>
<td>12.5 (10.0, 15.0)***</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)1</td>
<td>19 (7.5)</td>
<td>1 (1.4)</td>
<td>8.2 (0.0, 16.4)***</td>
</tr>
<tr>
<td>Baseline Mayo score &lt;5</td>
<td>91 (28.3)</td>
<td>6 (7.3)</td>
<td>11.0 (5.5, 16.5)***</td>
</tr>
<tr>
<td>Baseline Mayo score ≥5</td>
<td>68 (11.7)</td>
<td>5 (3.5)</td>
<td>8.2 (4.3, 12.1)***</td>
</tr>
<tr>
<td>Mucosal healing, n (%)1</td>
<td>271 (97.9)</td>
<td>32 (13.7)</td>
<td>13.3 (11.1, 15.6)***</td>
</tr>
<tr>
<td>Prior TNFi exposure1</td>
<td>112 (95.1)</td>
<td>5 (4.7)</td>
<td>10.8 (8.6, 13.0)***</td>
</tr>
<tr>
<td>Prior TNFi failure1</td>
<td>119 (92.3)</td>
<td>16 (13.3)</td>
<td>8.3 (5.9, 10.7)***</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)1</td>
<td>38 (12.9)</td>
<td>5 (4.1)</td>
<td>8.6 (2.8, 14.5)***</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)1</td>
<td>57 (20.0)</td>
<td>11 (9.2)</td>
<td>10.8 (6.5, 15.1)***</td>
</tr>
<tr>
<td>Baseline Mayo score &lt;5</td>
<td>145 (45.2)</td>
<td>17 (20.7)</td>
<td>24.4 (14.3, 34.8)***</td>
</tr>
<tr>
<td>Baseline Mayo score ≥5</td>
<td>126 (21.6)</td>
<td>9 (19.9)</td>
<td>11.7 (8.9, 14.9)***</td>
</tr>
<tr>
<td>Clinical response, n (%)1</td>
<td>521 (57.6)</td>
<td>72 (30.8)</td>
<td>26.8 (23.0, 30.5)***</td>
</tr>
<tr>
<td>Prior TNFi exposure1</td>
<td>254 (52.0)</td>
<td>20 (23.2)</td>
<td>29.3 (24.5, 34.1)***</td>
</tr>
<tr>
<td>Prior TNFi failure1</td>
<td>267 (64.0)</td>
<td>43 (41.3)</td>
<td>22.2 (17.7, 26.7)***</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)1</td>
<td>237 (51.0)</td>
<td>29 (23.4)</td>
<td>27.6 (19.8, 35.3)***</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)1</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)1</td>
<td>116 (45.8)</td>
<td>19 (25.7)</td>
<td>20.2 (8.5, 31.9)***</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)1</td>
<td>102 (54.5)</td>
<td>20 (9.9)</td>
<td>33.6 (19.5, 47.7)***</td>
</tr>
</tbody>
</table>

Conclusions: Tofacitinib has demonstrated efficacy vs placebo, 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.

**OP106**Table 1 Continued

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

CDAI: Crohn’s Disease Activity Index; ITT: Intent-to-treat; NRI: Non-responder imputation; LOCF: Last observation carried forward; PRO2: Patient Reported Outcome; 82: number of daily usual soft stool count + 7x (daily mean abdominal pain score); IBDO: Inflammatory Bowel Disease Questionnaire; ECLIPSE: Endoscopic Disease Activity of 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 CD. 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.


cRNA: Interest: 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.


Full analysis set, non-responder imputation ***Not significant; **p <0.01; *p < 0.05; ***p < 0.001; ***p < 0.0001 vs placebo 95% confidence interval was based on normal approximation for the difference in binomial proportions *N=488 for tofacitinib 10 mg BID and N=130 for placebo; **N=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=151 for placebo; statistical significance based on the Cochran-Mantel-Haenszel chi-squared test stratified by study, prior treatment with tumour necrosis factor inhibitors, corticosteroids use at baseline and geographic region BD, twice daily; CI, confidence interval; TNFi, tumour necrosis factor inhibitor; Wk, week.
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 trial named COLLECT in 131 patients with moderate to severe 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 trial named COLLECT in 131 patients with moderate to severe ulcerative colitis. Patients were on mandatory steroid therapy and could be taking sulphasalazine, aminosalicylates, or thiopurines at stable doses. European trial named COLLECT in 131 patients with moderate to severe ulcerative colitis (UC) patients refractory to conventional therapy.

Results: At entry into the OLE, the partial Mayo Score (pMS) for patients on placebo, ozanimod 0.5 mg, and 1 mg were 4.6, 4.5, and 3.3 respectively. At the time of the data-cut in the OLE, the pMS had improved in all groups (1.7, 1.7, and 1.9) at Week 44. The greatest improvement was reported in patients who received placebo or ozanimod 0.5 mg in the TOUCHSTONE trial with a change in pMS at Week 44 of −2.6, −2.7 and −1.3 in the placebo, 0.5 mg and 1 mg groups. Improvement occurred rapidly, in the first 4 to 8 weeks of the OLE. The greatest improvement was reported for patients who received placebo or ozanimod 0.5 mg in the TOUCHSTONE trial with a change in pMS at Week 4 of −1.8, −1.1, and −0.8 and a change in pMS at Week 8 of −2.4, −1.9 and −1.1 in the placebo, 0.5 mg and 1 mg groups. At the Week 44 visit in the OLE, 119/131 (90.9%) had little or no active disease based on the physician global assessment (PGA 0 or 1), 129/131 (98.5%) had little or no blood in the stools (RBS 0), and 105/131 (80.2%) had little or no increase in their number of stools (Stool Frequency score of 0 or 1). The most common adverse events (AEs) (>2%) during OLE were UC flare, anemia, upper respiratory tract infection, nasal pharyngitis, back pain, arthralgia, headache, alanine aminotransferase (ALT) or aspartate aminotransferase (AST) elevation. The only serious AEs in ≥2 patients were anemia, and ulcerative colitis flare. ALT and AST elevation. The only serious AEs in ≥2 patients were anemia, and ulcerative colitis flare. ALT and AST > 3x upper limit of normal occurred in 4 (3.0%), 1 (0.8%), and 3 (2.3%) of patients in the placebo, 0.5 mg, and 1 mg groups respectively.

Conclusion: Long-term treatment with ozanimod continues to be safe and well tolerated with good compliance and evidence of durable efficacy.
Aims & Methods: Ten pigs were randomly assigned to the self-assembling peptide RADA-16 (4 [Arg-Ala-Asp-Ala]) or the control group after undergoing a 5 cm long circumferential endoscopic submucosal dissection of the lower esophagus. Endoscopic diagnosis of esophagitis and esophageal varices, weight variation, and histological measurements of fibrosis, granulation tissue, and neopithelium 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. 4.5 mm (2–5.5) in the control group (p = 0.13). The median (IQR) stricture index on esophagograms at day 14 was 0.25 (0.14–0.48) and 0.26 (0.14–0.33) in treatment and control groups, respectively (p = 0.42). Median (IQR) weight variation during the study was +0.2 (–7.4–18.3) 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
A retrospective study from Sept-2013 to Sept-2015 was made at our institution in patients requiring evaluation of bile duct disease or therapy for biliary stones. Gastrointest Endosc 2011; 74: 805–14.

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

Reference
Table (OP114)

<table>
<thead>
<tr>
<th>Characteristics of Included Trials</th>
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<td>Montano Loza, 2007</td>
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<td>Sotoudehmanesh, 2007</td>
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<td>Dobronte, 2012</td>
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<td>Dobronte, 2014</td>
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<td>Lvenick, 2016</td>
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**Methodology**

<table>
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<tr>
<th>Intervention</th>
<th>Indomethacin</th>
<th>Placebo</th>
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<tr>
<td>81 63 86 30 19</td>
<td>16 29 21</td>
<td>18 29 21</td>
</tr>
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<tr>
<th>Location</th>
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<tr>
<td>Mexico-MultiCenter</td>
<td>Clinical, amylase</td>
<td>N/A</td>
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<tr>
<td>Iran-Single Center</td>
<td>Clinical, amylase</td>
<td>N/A</td>
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<tr>
<th>Definition of post-ERCP pancreatitis</th>
<th>Indomethacin</th>
<th>Placebo</th>
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<tr>
<td>Pain, amylase, prolonged admission</td>
<td>No</td>
<td>No</td>
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<tr>
<th>Randomization</th>
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<th>Placebo</th>
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<tr>
<td>Total randomized</td>
<td>55 58</td>
<td>66</td>
</tr>
<tr>
<td>Total analysed</td>
<td>51 58</td>
<td>67</td>
</tr>
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<table>
<thead>
<tr>
<th>Pancreatic stent used?</th>
<th>Indomethacin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (10 cases in indomethacin group; 9 cases in placebo group)</td>
<td>No</td>
<td>N/A</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Baseline demographics</th>
<th>Indomethacin</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>Mean age (y)</td>
<td>75 221</td>
<td>130 347</td>
</tr>
<tr>
<td>% Female</td>
<td>65 56</td>
<td>63 34</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Procedure demographics</th>
<th>Indomethacin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Difficult cannulation</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Pain, amylase, prolonged admission</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Placebo</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</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.

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 and 100 mg PR before and during ERCP.

Results: 196 patients were enrolled and 71 patients did not have EST. The analysis included 125 patients who had undergone EST with 60 in the PPI group and 65 in SC group. The mean age was 70.9 (SD = 14.8) years with 62 (49%) men.

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.

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, 20 mL/kg bolus after the procedure, and 3 mL/kg/h for 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 9.3% (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 during the infusion via internal but not an endoscope.

Conclusion: In our series, the incidence of PEP was 9.3%, and a non-significant risk reduction trend was observed in patients undergoing intensive hydration, with no severe pancreatitis being observed in this group. Worsung contrast injection is an alternative to ERCP for the treatment of PEP, Lower serum amylase and lipase levels at 4 hours after ERCP were excellent predictors for absence of PEP at 24 hours, displaying a negative predictive value of 100%.

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 OCTANOYLATED GHELIN LEVELS AND HEDONIC FOOD INTAKE

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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 system) 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 hunger 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 (10μmol/kg) or distilled water (placebo) was recorded using functional magnetic resonance imaging (fMRI). 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 libitum chocolate milkshake drink test. fMRI 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 p<0.001 uncorrected < 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 using radiomunnoassays.

Results: Compared to placebo, intragastric QHCl infusion significantly increased neural activity in 5 different clusters within the ROIs, with local maxima in the cortex, medial orbitofrontal cortex and hippocampus. A decrease of neural activity in 5 different clusters within the ROIs, with local maxima in the cortex, medial orbitofrontal cortex and hippocampus. A decrease of neural activity in 5 different clusters within the ROIs, with local maxima in the cortex, medial orbitofrontal cortex and hippocampus.

Conclusion: 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 hunger 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 (10μmol/kg) or distilled water (placebo) was recorded using functional magnetic resonance imaging (fMRI). 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 libitum chocolate milkshake drink test. fMRI 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 p<0.001 uncorrected < 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 using radiomunnoassays.

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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Introduction: Irritable Bowel Syndrome (IBS) is a heterogeneous 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 therapy via internet but not an endoscope.

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. Results: Of 27 patients who commenced therapy 22 completed the entire course of therapy and post-therapy measures. There was no difference in baseline scores for any measure between completers and non-completers. Scores for both abdominal symptom and psychological traits were substantially and significantly improved at the end of therapy (Table 1).

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>-0.98</td>
</tr>
<tr>
<td>Catastrophising</td>
<td>19.8 (11.3)</td>
<td>-11.5 (11.9)</td>
<td>-0.97</td>
</tr>
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</table>

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 (p = 0.53, p = 0.01) and depression (p = 0.53, p = 0.01) and to a lesser extent with change in anxiety (p = 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 catastrophising with change in abdominal symptoms opens avenues for further understanding of the mechanisms of 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.

References

Disclosure of Interest: None declared.

Disclosure of Interest: None declared for the following authors:

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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Contact E-mail Address: fabio.turco81@yahoo.it

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 are related to psychiatric conditions such as depression and anxiety. Brain-gut communication is more complex than previously thought and not fully understood involving 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 which are regulated by probiotic-induced dysbiosis animal model. Young male mice received a mixture of nonabsorbable antimicrobials (ampicillin, streptomycin and cyclohexamide), which has been associated to the microflora composition alteration2, for 2 weeks. Afterwards, animals were treated with probiotic (Lactobacillus Casei DG, 10⁷ cells) or vehicle up to 7 days. Whereupon, various behavioral testing were performed. After sacrifice, mice intestine was cut in segments (duodenum, jejunum, ileum) and the expression of pro-inflammatory markers (IL-1β,
OP120 QUORUM SENSING MOLECULES OF GUT MICROBIOTA INFLUENCE ON HOST SATIETY AND HUNGER

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2Dep Of Medicine, University of Padova, Padova/Italy

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Introduction: Accumulating evidence suggests that the gut microbiota controls host satiety and hunger (1). Even if quantitative modifications of the gut microbiota have been described in obesity, bacterial-derived soluble factors are likely involved in host dietary habits.

Aims & Methods: In this study we investigated the role of quorum sensing molecules (the autoinducers, AI) used for communication within gut microbial communities (2), in modifying food intake in the host. Adults CD1 male mice were fed a high-fat diet (HFD, 35% energy by fat) or a normal diet (4% energy by fat) and then daily rectally dosed with vehicle or 30 mg/kg weight of purified AI namely N-(3-oxoodecanoyl)-L-homoserine lactone (AHL-12) or 2-Heptyl-3-hydroxy-4(3H)quinoline (PQS). Two weeks later we determined: a) gut microbiota composition by quantitative PCR (qPCR) on cecal DNA; b) enteroendocrine cells (ECC) density in colonic mucosa by immunohistochemistry (IHC) for synaptophysin; c) mRNA levels specific for taste receptors and for anorectic or orexigenic peptides by qRT-PCR on colon and hypothalamus; d) food intake, body weight gain, oral glucose tolerance test. Results: In HFD-fed mice rectally administration of AHL-12 or PQS reduced the gut microbiota composition and normalized the ECC density in colonic mucosa, altered by diet. AI administration increased the mRNA levels of Tafs2r5, Tafs2r3 and Tafs2r105 whereas did not affect Tafs2r131 and Tafs131 allistic variants of bitter taste receptors. Moreover, AHL-12 and PQS significantly increased mRNA levels of anorectic peptides namely Cholecystokinin, Leptin and Nutrtenosin in the gut and Brain-Derived Neurotrophic Factor in the hypothalamus. Intraperitoneal administration of AHL-12 or PQS had no effects, supporting an intestinal direct action. Accordingly, the rectal but not the peritoneal administration of PQS and to a lesser extent AHL-12 significantly reduced food intake, decreased fat-diet induced body weight gain and improved oral glucose tolerance test.

Conclusion: We speculate that gut microbial AI mediates satiety through activation of taste receptors expressed by ECCs and the release of gut peptides involved in host dietary habits.

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

References
4. Aso1, K. Nakamura1

OP122 ACOTIAMIDE-SENSITIVE IMPAIRED RECEPTIVE RELAXATION OF LOWER ESOPHAGEAL SPHINCTER IN PATIENTS WITH ESOPHAGOGRADIENT 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 immediately declined in normal subjects, LES pressure in the supine position, while swallowing ten 5-mL liquid boluses. 13 patients with EGJOO and 19 patients with normal esophageal pressures (mean age 30 ± 4 years, 11 of whom were women) and 19 participants with normal esophageal pressures (mean age 50 ± 3.0 years, 11 of whom were women) were enrolled. Basal LES pressure (BLES) and the integrated relaxation pressure (IRP) were measured. The measurement of PWS-induced LES relaxation (mmHg) was calculated as the difference between BLES and the mean LES pressure in the 5-s period before meal.

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 ± 1.4 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 significantly lower in EGJOO subjects, but was absent in patients with EGJOO.

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

References
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Disclosure of Interest: All authors have declared no conflicts of interest.
The mean LES pressure induced by PWS was 33.0 ± 1.6 mmHg, and did not differ between the PWS and HLES groups (32.7 ± 1.6 mmHg). Acotiamide was administered to address severe symptoms in six out of 13 patients with EGJO. Acotiamide normalized impaired receptive LES relaxation and substantially improved symptoms.

Conclusion: Symptomatic subjects have receptive LES relaxation, but this is impaired in EGJO. Acotiamide normalizes IRP in EGJO, 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
ENDOSCOPIC MANAGEMENT OF UPPER GASTROINTESTINAL CANCER – ROOM U1

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 cervical 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 from both groups. We evaluated adverse events including strictures 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 1.7:1. 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 patients with 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. Chemoradiotherapy as additional treatments were conducted in 1 patient. No local recurrence was observed during an average duration of follow-up of 34 months. In the control group, the average age was 72.7 years old, and the male-to-female ratio was 3.2:1. The average maximum size of lesions was 24.2 mm, and the histological depth of invasion was EP/LPM, MM/SM1, 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 was administered in 6 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 gold standard technique, submucosal tunneling endoscopic resection (STER) was used 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 esophagogastrectic junction, as well as to analyze the clinicopathological factors that affect the feasibility of STER. Patients with large SMTs of 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.

Among the 145 patients (96.8%) (26.9%) complained specific symptoms, while 106 patients (73.1%) had non-specific complaints. In the STER group, the mean tumor size and transverse diameter were 5.8 cm and 2.2 cm. Meanwhile, in the TS group, the mean tumor long and transverse diameters were 6.2 cm and 1.1 cm, respectively. The number of SMTs, depth of invasion, and number of patients with irregular shape were 81 (55.9%). All of the tumors were located in esophagus (84, 57.9%), and EGI (61, 42.1%). There was no significant difference between the two groups in age, gender, symptoms, tumor size, tumor location, tumor shape, tumor histology type, and tumor histological depth of invasion was EP/LPM, MM, and SM2 in 306, 67, and 32 cases, respectively. The mean tumor size and transverse diameter of larger than 7.0 cm, transverse diameter lager than 3.5 cm and irregular shape were 3 significant risk factors for STER-related piecemeal resection, while tumor with transverse diameter lager than 3.5 cm was the risk factor for STER-related complications. The mean tumor size and transverse diameter irregular shape is feasible, but associated with a relatively high risk of difficulty in retrieval of tumors.

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

OP125 CHARACTERISTICS OF METACHRONOUS GASTRIC ADENOMAS OCCURRING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC ADENOMAS AND CANCERS
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Introduction: With the progress of endoscopic diagnosis and treatment, endoscopic treatment has come to be used for gastric adenomas and early gastric cancers (EGCs). Endoscopic submucosal dissection (ESD) has become accepted as a minimally invasive treatment for superficial gastric neoplasms. However, the development of metachronous neoplasms has been occasionally detected during follow-up after ESD. The clinicopathologic characteristics of these lesions occurring after ESD were investigated.

Methods: From August 2006 to December 2015, stomach ESD was performed for 375 patients with 426 lesions of gastric adenoma and differentiated-type EGC at Aichi Cancer Center Aichi Hospital. Periodic upper gastrointestinal endoscopy, blood tests, and chest and abdominal computed tomography were performed every 12 months after treatment. During the follow-up period, 31 metachronous lesions (27 patients) were discovered at endoscopy more than 1 year after initial ESD. The characteristics of these lesions were examined retrospectively.

Results: The median age at initial ESD was 72 (range, 56–82) years. The male to female ratio was 23:4. On endoscopy, all patients were found to have atrophic gastritis of the open-type according to the Kimura-Takemoto classification. Helicobacter pylori testing was positive in 18 patients (66.7%), negative in 8 patients (33.3%). On the 1st biopsy, patients, 17 underwent H. pylori eradication therapy after initial ESD, and it was successful in 16 (94.1%). The median duration from initial ESD to the detection of a metachronous lesion was 25.9 months, (range, 12.4–83.8) months. The locations of the lesions were classified as follows: upper third (U), middle third (M), and lower third (L). Of 29 primary lesions (27 patients) 1 lesion (3.4%) was U, 11 lesions (37.9%) were M, and 17 lesions (58.6%) were L. The gross type was 0-I in 31 lesions (41.1%), 0-IIc in 1 lesion (3.4%), and 0-II in 12 lesions (41.3%). The median tumor size was 10 (range, 3–30) mm. In ESD, en bloc resection was performed for 28 lesions (96.6%). Aspiration pneumonia occurred in one patient after ESD, but the patient was successfully treated by intravenous antibiotics. There were no treatment-related deaths. On pathological examination, 21 were tubular adenomas, and 8 were differentiated adenomas. Histologically, curative resection was obtained in 27 cases (93.1%). In contrast, the location of 31 metachronous lesions was U in 9 lesions (29%), M in 8 lesions (25.8%), L in 14 lesions (45.2%). The gross type was 0-IIa in 16 lesions (51.6%), 0-IIb in 1 lesion (3.2%), 0-IIc in 13 lesions (41.9%), and 0-IIa+IIb in 1 lesion (3.2%). The median tumor size was 9 (range, 1.5–38) mm. En bloc resection was performed for 28 lesions (90.3%). Aspiration pneumonia occurred in one patient and was successfully treated by intravenous antibiotics. There were no treatment-related deaths. On pathological examination, 21 were tubular adenomas, and 8 were differentiated adenomas.

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/flat and depressed type), 
tumor size, or histology between primary and metachronous lesions. However, 
locally advanced lesions (P = 0.029). Furthermore, there were significant differences in U/P (P = 0.016) and U/L (P = 0.014). There 
was a slightly higher frequency of metachronous lesions in the U area.
Conclusion: Metachronous lesions tended to develop in the U area. These results 
suggest that we should carefully observe the U area by surveillance endo-
scopy 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 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER WHICH HAS PATHOLOGICAL FACTORS HIGHLY RELATED WITH LYMPH NODE METASTASIS: DEVELOPMENT AND VALIDATION OF “ECURA 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 recommend-
Aims & Methods: This multicenter study aimed to establish a scoring system (eCura system) for deciding the potential risk of LNM after ESD with patholo-
gical factors related with LNM. Of the 15,785 consecutive patients who under-
went ESD for EGC from January 2000 to 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. Cox proportional hazards proportional to β regression coeffi-
cient values for the factors determined in the multivariate analysis. Second, for validating the risk-scoring system, the validity by survival analysis was evaluated in 905 patients without additional treatment.
Results: In the validation stage, based on Cox 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 (0–1 point), intermediate (2–4 points), and high (5–7 points). The C statistic (95% confidence interval (CI)) of the system for LNM was 0.74 (0.62–0.87) and the bootstrapping analysis showed similar results (95% CI, 0.62–0.86). In the validation stage, cancer-specific survival differed signifi-
cantly among these groups (99.6%, 95.5%, and 90.1%, respectively, at 5 years; p < 0.001). Cox proportional hazards regression analysis showed that the high-risk [hazard ratio (95% CI) = 15.5 (4.03–59.4), p < 0.0001] and intermediate-risk [4.03–59.4, p < 0.0001] groups had significantly higher cancer-specific mortal-
ity compared with the low-risk group. Moreover, the C statistic of the system for cancer-specific mortality was 0.78.
Conclusion: This scoring system predicted cancer-specific survival, which may be helpful to value the risk of LNM in patients after ESD that does not meet the curative criteria.
Disclosure of Interest: All authors have declared no conflicts of interest.

OP127 COMPARISON OF EMR AND ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RESECTION OF EARLY STAGE GASTRIC CANCER: WHICH ONE IS BETTER?
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Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are now being increasingly used for the treatment of gastro-
intestinal 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 muscularis 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 cancers with high-grade dysplasia, 3 minute submucosal cancers, 6 submucosal deep cancers and 2 carcinoid tumors sub-
mitted to ESD, were compared to 98 patients (mean patient age 62.7, range 18–88 years, male: female ratio 52/46) who underwent EMR (20 involved ade-
neumors, 42 intraepithelial cancers with low-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 0.5 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, postoperative 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. The en-bloc rate was significantly lower in EMR group (2%, 2/98) (p < 0.01). In the ESD 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 recur-
rence in the ESD group (p = NS). The post-operative bleeding rate was 3.9/2% (5/ 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 perspective 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 risk-patients when performed by less experienced endoscopists.
Disclosure of Interest: All authors have declared no conflicts of interest.
Reference

OP128 LONG-TERM OUTCOME OF THE INCIDENCE RATE OF METACHRONOUS GASTRIC CANCERS AFTER HELICOBACTER PYLORI ERADICATION – A FOLLOW-UP AND ANALYSES OF JGSG TEST STUDY GROUP ENROLLED PATIENTS
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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 (1). 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 patients were recommended to receive an eradication therapy. Patients have been followed-up once a year endoscopically. Among 40 patients with the most follow-up case is in 15th observation year. A long-term 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, 13 years 10 months after the enrollment). When these 4 lesions were detected, 3 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 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 observation 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.
Reference
1. Fukuse K, et al. Effect of eradication of Helicobacter pylori on incidence of meta-
SYMPTOMATIC HEPATIC CYSTS, A RANDOMIZED CONTROLLED TRIAL

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Introduction: Aspiration sclerotherapy is a therapeutical option for large symptomatic hepatic cysts. However, inadequate cyst reduction is frequently reported. Somatostatin analogues are able to curtail cyst volume. We hypothesized that the long-acting somatostatin analogue pasireotide (SOM230) with aspiration sclerotherapy would 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 after 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 (PDL-Q) that assesses frequency and severity of 14 disease-specific symptoms leading to a proportional cyst diameter. All other 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.

RESULTS: Proportional cyst diameter reduction at six weeks compared to controls was 23.6% [IQR 9.6–31.8%] versus 21.8% [IQR 9.6–31.8%; p = 0.96]. 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 PDL-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: All other authors have declared no conflicts of interest.

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Table (OP130)

Risk factors for enterococcal cholangitis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Enterococcus spp. isolation (N = 109)</th>
<th>Non-enterococcus spp. isolation (N = 82)</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>76 (43–97)</td>
<td>71 (44–97)</td>
<td>0.96 (0.57–1.61)</td>
<td>1</td>
</tr>
<tr>
<td>Male gender</td>
<td>65 (60%)</td>
<td>55 (67%)</td>
<td>1.39 (0.84–2.27)</td>
<td>0.144</td>
</tr>
<tr>
<td>Onset after 48 h admission</td>
<td>21 (19%)</td>
<td>19 (22%)</td>
<td>0.70 (0.41–1.21)</td>
<td>0.244</td>
</tr>
<tr>
<td>Biliary tract malignancies</td>
<td>54 (50%)</td>
<td>38 (46%)</td>
<td>1.24 (0.75–2.04)</td>
<td>0.467</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>22 (20%)</td>
<td>19 (23%)</td>
<td>1.13 (0.64–2.05)</td>
<td>0.77</td>
</tr>
<tr>
<td>Prior cholecystitis</td>
<td>12 (11%)</td>
<td>4 (5%)</td>
<td>1.34 (0.78–2.36)</td>
<td>0.300</td>
</tr>
<tr>
<td>CBD stone</td>
<td>48 (44%)</td>
<td>38 (46%)</td>
<td>1.24 (0.78–2.00)</td>
<td>0.503</td>
</tr>
<tr>
<td>Gallstone or biliary sludge</td>
<td>63 (58%)</td>
<td>53 (65%)</td>
<td>1.24 (0.78–2.00)</td>
<td>0.503</td>
</tr>
</tbody>
</table>

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Introduction: Knowledge of pathogenic spectrum for cholangitis is important for adequate empirical 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 (±9.7) years. Enterococcus species were isolated in 128 episodes from bile and/or blood culture. Age over 75 years old (Odds Ratio [OR] = 1.98; 95% Confidence Interval [CI] 1.10–3.48; P = 0.028), prior endoscopic sphincterotomy (OR = 5.676; CI 2.73–11.87; P < 0.001), presence of device in biliary tract (OR = 3.141; CI 1.59–6.183; P = 0.0099), biliary reconstruction (OR = 5.895; CI 1.301–26.71; P = 0.015), stayed in Intensive Care Unit in past admission (OR = 2.033; CI 0.912–4.532; P = 0.088), presence of device in biliary tract (OR = 2.588; CI 1.342–4.992; P = 0.005) were independent risk factors for Enterococcus species isolation by the univariate analysis. Multivariate analysis revealed that prior endoscopic sphincterotomy (OR = 4.480; 95% CI 1.970–11.26; P = 0.005) and biliary reconstruction (OR = 8.945; 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.

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.
exposure. Exogenous estrogens are used extensively to alleviate symptoms of menopause, but their long-term effect on biliary tract cancer diagnosis is not known.

Aims & Methods: This was a population-based cohort study conducted in Sweden between July 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 factors of history of delivery, thrombotic events and hysterectomy, creating 8 strata of normal matching (nearest neighbor) was performed for age, smoking status, alcohol use, obesity and diabetes within each stratum. Record linkage to the Swedish Patient Register allowed collection of potential confounding factors and status of the matching variables. The cohort was followed to the date of biliary tract cancer and death by linkage to The Swedish Cancer Register and the Cause of Death Register. Logistic regression models were estimated to calculate odds ratios and matching 95% confidence intervals for the association between MHT exposure and biliary tract cancer. All analyses were stratified by MHT regimen (estrogen/progestogen/progesterone combinations). All matching variables were included in the logistic models. Additionally, the risk of developing symptomatic gallstone disease was evaluated using a similar logistic regression model.

Results: The final cohort included 290,186 MHT exposed, and 870,165 unexposed, women. The total reported cancer consisted of more than 1.1 million women and follow-up was performed over 7 years. The odds of gallbladder cancer were decreased in MHT exposed women (OR 0.65, 95% CI 0.40–0.97), whereas no clear association between MHT-exposure and cancers of the extrahepatic bile ducts was seen (OR 0.87, 95% CI 1.01–1.16). 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 0.85, 95% CI 0.66–1.02). Additionally, MHT exposure significantly increased the risk of gallstone disease (OR 7.09, 95% CI 6.6–7.3).

Conclusion: In this large cohort study did not support a clear association between MHT and BTC. Furthermore, the reduced risk of GBC after MHT exposure is likely to be explained by increased risk of symptomatic gallstone disease resulting in cholecystectomy. Thus, this study supports the role of gallstones as an intermediate step in the development of GBC.

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

References

OP132 MUC3NA, A PROMISING TUMOR MARKER FOR DIAGNOSIS OF EXTRAHEPATIC CHOLANGIOCARCINOMA
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Introduction: The prognosis of extrahepatic cholangiocarcinoma (ECC) was poor for the lack of early diagnosis due to their anatomical location and insidious onset, and little effective tumor markers. Our previous study showed Mucin3A (MUC3A) was the main differential protein in bile with proteomics technology unsupervised and absolute validations (TRAQ) in patients with ECC and 20 patients with sphenoid of oyster dysfunction (SOD).
Aims & Methods: 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 tissue specimens by immunohistochemistry method. The relationship between MUC3A and the clinicopathologic features of ECC were investigated. (2) Serum MUC3A was detected 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 with CEA, CA19-9 in 20 patients with ECC and 20 patients with SOD.
Results: (1) The positive cells rates of MUC3A in ECC specimens were significant higher than normal in bile duct tissue specimens (83.3% vs. 35.0%, P < 0.01). The expression of MUC3A was significant correlated with metastasis of lymph node infiltration and UICC stage of carcinoma, differentiation grade of carcinoma (P < 0.05). (2) The preoperative serum values of MUC3A in patients with ECC were significant higher than patients with SOD (57.8 ± 19.6 vs. 25.1 ± 6.9 ng/ml, P < 0.01). Compared with the preoperative results, postoperative MUC3A in patients with ECC were significantly decreased (26.8 ± 4.6 vs. 57.8 ± 19.6 ng/ml, P < 0.01). ROC curve analysis showed serum MUC3A could distinguish ECC with SOD while 40.7 ng/ml as the cut-off value (AUC = 0.907, 84.6% specificity, 90% sensitivity). (3) The serum MUC3A has marked differences when the analyses were stratified for estrogen or estrogen/progestogen combinations. All matching variables were included in the logistic models. Additionally, the risk of developing symptomatic gallstone disease was evaluated using a similar logistic regression model.
Conclusion: MUC3A is high expression in tumor tissue of ECC, and related to the differentiation grade and stage of tumor. The MUC3A in peripheral blood is valuable to preoperative diagnosis of ECC. MUC3A is expected to become one of the most promising tumor markers for ECC.

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

OP133 KINETICS OF PULMONARY ANGIOGENESIS IN MOUSE COMMON BILE DUCT LIGATION-INDUCED LIVER FIBROSIS
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Introduction: Hepatopulmonary syndrome (HPS) is a severe pulmonary complication of liver disease for which no medical treatment is available. In rats, common bile duct ligation (CBDL) has been documented as a model for human HPS, which is characterized by pathological pulmonary angiogenesis. Studies in genetically modified mice could offer opportunities for further research. However, in this species the development of pulmonary angiogenesis in biliary cirrhosis has not been outlined yet.
Aims & Methods: We aimed to elucidate the temporal changes in proangiogenic signature of hepatic and pulmonary vascular cells after CBDL in mice and in addition identify potential proangiogenic factors contributing to the pathobiology of HPS. Male Swiss mice underwent CBDL or sham surgery and were sacrificed at a weekly basis for 6 consecutive weeks. Pulmonary inflammation was studied by cytology on broncho-alveolar lavage fluid, myeloperoxidase assay and luminecx bead based assay on lung tissue. Liver and lungs were collected for protein analysis and histology to assess liver fibrosis and hepatic and pulmonary angiogenesis. Scanning electron microscopy was performed on vascular corrosion casts to visualize pulmonary changes.
Results: CBDL progressively induced liver fibrosis from week 1 (F0–1) to week 6 (F4). This was accompanied by a gradual increase in hepatic immunopositivity for Endoglin and von Willebrand Factor, two markers of endothelial cell activation (P < 0.001). Hepatic liver fibrogenic and vascular endothelial growth factor (VEGF) receptor 1 and 2 were significantly increased at week 6, whereas placental growth factor (PIGF), which is exclusively involved in pathological angiogenesis, was already upregulated at week 2 (P < 0.001). In the pulmonary compartment, CBDL resulted in neutral and increased pro-inflammatory mediators from week 2 to 6 (all P < 0.001). Pulmonary immunoreactivity for Endoglin and von Willebrand Factor progressively increased from week 4 to 6, while PIGF was already increased from week 2 onwards (all P < 0.0001). Scanning electron microscopy revealed regions of abnormal vascular architecture, mainly located at the pleural side, decreased intercapillary distance (P < 0.0001) and increased capillary density (P < 0.001) in lungs of cirrhotic mice. Conclusion: CBDL in mice is associated with pathological pulmonary angiogenesis and may represent a model for human HPS. In addition, we pointed to PIGF as an early indicator of pathological hepatic and pulmonary angiogenesis.
Disclosure of Interest: S. Raevens: Sarah Raevens is sponsored by the Research Foundation Flanders (FWO14/ASP/200). S. Lefere: Sander Lefere is sponsored by the Research Foundation Flanders (FWO15/ASP/146). X. Verhelst: Xavier Verhelst is sponsored by the Research Foundation Flanders (FWO15/ASP/146). H. Van Vlierberghe: Hans Van Vlierberghe is senior clinical investigator of the Research Foundation Flanders. All other authors have declared no conflicts of interest.

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, inflammation or adenomyoma). Cholecystectomy is only indicated for neoplastic polyps, as they are (pre)malignant.1 Annually, over 23,000 cholecystectomies are performed in the Netherlands.2 However, there is scarce pathologic data on the prevalence of gallbladder polyps and attribution of neoplastic or nonneoplastic nature.
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 over the period 2003–2013. The search 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 excerpts concerning primary gallbladder surgery containing a polyp or (focal) wall thickening > 5 mm were included. 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 polyp was classified as neoplastic. Prevalence of gallbladder
polyps and the attribution of neoplastic polyps and nonneoplastic polyps was calculated. In 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 1737 patients were excluded due to primary non-gallbladder surgery, leaving 4012 unique cholecystectomies. In 2083 cholecystectomies (0.9%), a polypoid lesion was present. Which results in a calculated prevalence of polyps in 944/100,000 patients who underwent cholecystectomy. Of the polyps, 1172 (56.8%) were adenomatous polyps (13.3%), adenocarcinomas, and 57 (2.7%) other malignancies. Nine hundred and ten (43.7%) poly were nonneoplastic; 375 (18%) cholesterol polyp, 334 (16%) adenomyoma’s, 70 (3.7%) hyperplastic polyps, 54 (2.6%) mucosal polyps, 42 (2.0%) inflammatory polyps, 18 (0.9%) papilloma’s 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
clarify the mechanisms responsible for liver atrophy, pathological analysis should be carried out within the first week after the liver was harvested. 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 6 (d0, w2, w6, respectively). In specimens of embolized lobe (E) and non-embolized lobe (control, Cont), we measured the distance between the portal vein and central vein (PV-CV) area, and hepatocyte number per lobule and apoptotic activity. Immunohistochemical reactions of microtubule-associated-protein-light chain 3 beta (LC3) as autophagy and glutamine synthetase (GS) and cytochrome c1E1 (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 significantly reduced in E at w4 and w6 (P < 0.001). Apoptotic 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 areas 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 lobule 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

OPI40 EFFECT OF CHRONIC THIOACETAMIDE TREATMENT ON HEPATIC HEMODYNAMIC PARAMETERS IN RATS: EVALUATION BY MAGNETIC RESONANCE IMAGING
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Introduction: For the investigation of hepatic hemodynamics in animal models invasive methods are conventionally used. This study seeks to evaluate a non-invasive Magnetic Resonance Imaging (MRI) method as a reliable diagnostic tool in the widely used model of Thioacetamide (TAA)-induced liver injury.

Aims & Methods: (1) To quantitatively assess hepatic hemodynamic parameters (portal vein area, portal blood flow velocity and portal blood flow volume) and arterial blood flow volume using MRI technique in rats; (2) To investigate the influence of the hepatotoxic agent TAA on these hemodynamic parameters. 54 male Wistar rats were studied. 15 of which were left untreated and 39 received TAA in their drinking water (0.03g TAA / 100 ml H2O). The TAA dosage was limited to 2 weeks based on the body weight changes. From the 39 treated rats 15 received TAA for 12 weeks and 24 for 16 weeks. The following parameters were measured by a 9.4 Tesla preclinical MR scanner: portal vein area, portal blood flow velocity, portal blood flow volume and aortal blood flow volume. Specifically gradient-echo fast phase contrast sequences were used with both cardiac and respiratory gating. All MRI measurements were performed under continuous Isoflurane anesthesia. The degree of liver injury was estimated by standard histological criteria. Histological evaluation was performed in all 54 rats while hemodynamic measurements could be evaluated in 50 rats. For statistical analysis Kruskal-Wallis test was used.

Results: From the rats which received TAA for 12 weeks 100% (15/15) developed fibrosis of the liver, liver fibrosis was up to stage F2 (group 12w/fib). From the rats which...
received TAA for 16 weeks, 46% (11/24) developed liver fibrosis with a Desmet score of 1-3 34% (8/24) had liver cirrhosis with a Desmet score of 4 (group 16w/cir). The untreated rats (15/54) served as control group (group con).

Introduction: Of the 226 patients completing the TAXIT maintenance phase, 125 (55%) underwent endoscopy after one year maintenance treatment. This subanalysis of TAXIT optimization, continued concentration-based dosing was not superior to clinical efficacy endpoints (TAXIT) randomized controlled trial [1] showed that targeting patients’ infliximab trough concentrations during the maintenance phase of TAXIT were higher in patients with mucosal healing. Thus predictors were assessed only in the Hungarian patients. Infusion reaction did not occur in the Czech population 384 consecutive IBD patients were included in the present cohort.

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

Tuesday, October 18, 2016 08:30–10:00

OPTIMISING ANTI-TNF THERAPY – ROOM G

OP141 CORRELATION OF ENDOCUTOPIC 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 attempt 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) after 1 year maintenance treatment. For ulcerative colitis (UC), healing was defined as a Mayo endoscopic subscore of 0 or 1. Rates of mucosal healing were compared for both arms in TAXIT (clinically-based arm 1 and concentration-based dosing arm 2) and infliximab trough concentrations were correlated to the degree of healing.

Results: Of the 226 patients completing the TAXIT maintenance phase, 125 (55%) underwent endoscopy after one year and 55 in arm 1 and 70 in arm 2. In arm 2; n = 50 (95%) 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 = 0.1). The rates of mucosal healing were also compared in CD patients in arm 1 (83%) vs. 88% in arm 2 (p = 0.69) and in UC patients separately (15/17 in arm 1 vs. 14/18 patients 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 (28/41 or 68%) (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 of infliximab during maintenance phase of TAXIT were 5.31 μg/ml in patients with mucosal healing and 4.26 μg/mL in patients without mucosal healing (p = 0.07).

Conclusion: The primary endpoint of TAXIT, clinical and biochemical remission, compared 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.

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Introduction: Safety data of the immunogenicity coming from the ‘real life’ use of CT-P13, the first biosimilar to infliximab, in inflammatory bowel disease (IBD) are still lacking.

Aims & Methods: Our aim was to assess the frequency and characteristics of infusion reactions during CT-P13 therapy in 13 Hungarian and 1 Czech IBD centres. Demographic data were collected and a harmonized monitoring strategy was applied. Trough (TL) and anti-drug antibody (ADA) concentration were regularly measured by ELISA at baseline and before every subsequent infusion. Predictors, characteristics, therapy and outcomes of infusion reactions were prospectively evaluated.

Results: 384 consecutive IBD patients were included in the present cohort. Twenty-eight Hungarian IBD patients (9.6%) developed infusion reaction during the treatment. Infusion reaction did not occur in the Czech population thus predictors were assessed only in the Hungarian patients. Infusion reaction occurred most frequently during the 2nd and 3rd infusion. The most frequent symptoms of infusion reactions were flushing, dyspnea and chest pain. CT-P13 therapy had to be stopped in 78.6% of the cases and was switched to adalimumab in 42.8% of the patients. However in 21.4% CT-P13 therapy was continued with the use of supplementary intervention. Previous anti-TNF exposure did not influence the induction therapy. Predictors, characteristics, therapy and outcomes of infusion reactions were prospectively evaluated.

Conclusion: Patents with previous exposure to anti-TNFs and ADA positivity during the induction therapy were more likely to develop infusion reactions. CT-P13 biosimilar is safe with low rate of infusion reaction.

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

OP143 AZATHIOPRINE DOSE REDUCTION INFLAMMATORY BOWEL DISEASE PATIENTS ON COMBINATION THERAPY: A PROSPECTIVE STUDY


Reference

and endoscopic and/or biomarkers remission) for at least 6 months. All patients had an IFX trough level over 2 μg/mL and were on stable doses of AZA (2 to 2.5 mg/kg) and IFX (5 mg/kg every 8 weeks). In cohort A, AZA and IFX were continued unchanged; in cohort B, the dose of AZA was halved, with a minimum dose of 50 mg/d; in cohort C, AZA was stopped and IFX continued as monotherapy. Primary endpoint was failure defined as a clinical relapse (CDAI > 220 with fecal calprotectin > 450 μg/g stools) and/or need to change the original therapeutic regimen because of adverse events. trough levels of IFX (TRI) and antibodies (ATT) were measured before each infusion.

Results: 81 patients (45 CD and 36 CD, mean age: 29.7 years, mean disease duration: 24 months) were included (28 in cohort A; 27 in cohort B; 26 in cohort C). The clinical characteristics, duration of combination therapy, biomarkers levels and TRI were similar in the three cohorts at the time of inclusion. Five patients (17.8%) in cohort A, three in cohort B (11.5%), and 8 in cohort C (30.7%) experienced failure at one year (p = 0.1 across group). Three patients in cohort A had to stop AZA or to reduce the dose due to myelotoxicity or digestive intolerance. In cohort A, the mean TRI concentrations were similar at the time of inclusion (3.65 vs 3.45 μg/mL, respectively). In cohort B, the mean TRI increased significantly after the reduction of AZA dose (3.95 vs 3.6 μg/mL, respectively) while there was a significant reduction in the mean 6-TGN levels (310 pmol vs 128 pmol, respectively; p = 0.03) at one year whereas in cohort C, there was a significant reduction in TRI (4.2 vs 2.1 μg/mL; p = 0.02). Four patients (14.2%) in cohort A, four patients in cohort B (14.8%), and 11 in cohort C (42.3%) experienced an unfavourable evolution of IFX pharmacokinetic defined by a decrease of TRI < 1 μg/mL or undetectable TRI with positive ATI (p = 0.022 between A and C; p = 0.039 between B and C; p = 0.87 between A and B). By ROC analysis (AUCROC: 0.93), a threshold of 6-TGN < 105 pmol was associated with an unfavourable evolution of IFX pharmacokinetics (sensitivity: 67%; specificity: 92%; Likelihood ratio: 7.67).

Conclusion: AZA dose reduction in IBD patients on combination therapy is as effective as maintenance of AZA at the same dose and may improve AZA safety profile. A threshold of 6-TGN < 105pmol was associated with an unfavourable evolution of IFX pharmacokinetics.

Disclosure of Interest: E. Del Tedesco: MSD S. Paul: Theradiag, MSD X. Roblin: MSD, Theradiag, HAC Pharma All other authors have declared no conflicts of interest.

Table (OP144): Clinical and serological evolution after dose de-escalation

<table>
<thead>
<tr>
<th></th>
<th>T-1 (n = 33)</th>
<th>T0 (n = 43)</th>
<th>T1 (n = 43)</th>
<th>T2 (n = 26)</th>
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<tr>
<td>Median (IQR) time from T0</td>
<td>18.0 weeks (13.5–26.1)</td>
<td>14.0 weeks (12.3–19.0)</td>
<td>30.5 weeks (26.8–34.5)</td>
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<tr>
<td>Median (IQR) ADA serum level</td>
<td>11.6 μg/mL (9.1–15.1)</td>
<td>11.5 μg/mL (9.3–14.3)</td>
<td>7.5 μg/mL (5.8–9.5) p &lt; 0.001</td>
<td>7.2 μg/mL (5.4–8.6) p &lt; 0.001</td>
</tr>
<tr>
<td>Median (IQR) C-reactive protein</td>
<td>1.6 mg/L (0.4–4.9)</td>
<td>1.4 mg/L (0.6–3.3)</td>
<td>1.3 mg/L (0.6–5.1) p = 0.217</td>
<td>1.7 mg/L (0.6–4.1) p = 0.139</td>
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<tr>
<td>Median (IQR) PRO2 serum level</td>
<td>44.5 g/L (42.6–47.0)</td>
<td>44.1 g/L (42.7–47.0)</td>
<td>43.7 g/L (41.6–47.2) p = 0.893</td>
<td>42.4 g/L (40.9–45.0) p = 0.339</td>
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<tr>
<td>p-values: relative to T0, Wilcoxon Signed Rank test; IQR: interquartile range</td>
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OP145 EFFICACY AND SAFETY OF BIOSIMILAR INFLIXIMAB AFTER ONE-YEAR: RESULTS FROM A PROSPECTIVE NATIONALWIDE COHORT

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Introduction: Although dose escalation is widely used to optimize biological therapy in case of clinical relapse, less is known about possibilities to de-escalate therapeutic regimen because of adverse events. trough levels of IFX (TRI) and antibodies (ATI) were measured before each infusion.

Results: We identified 43 patients with dose de-escalation to ADM 40 mg ETW (32 male, 39 CD, 4 UC, median age 37 years). All patients received monotherapy with ADM every other week, which was initiated a median of 28 months prior to dose de-escalation. Median PRO2 was 0, and median CRP level 1.4 mg/L. Reasons for dose de-escalation were ADM associated adverse events (AE, n = 1), serum levels above 2 μg/mL (n = 9), or a combination of both (n = 33). Most frequently reported AE were skin manifestations (52%), arthralgia (24%) and recurrent infections (21%). While ADM serum level dropped significantly 4 and 8 months after dose de-escalation, CRP levels remained stable (Table). In patients with CD a significant increase in PRO2 was observed.

Conclusion: In this retrospective cohort analysis, 61% of patients were able to continue ADM therapy at a dose of 40 mg ETW. Furthermore, in half of the patients who experienced ADM related AE at baseline, the AE disappeared completely. Regardless of ADM serum levels, disease remission should be objectively assessed prior to dose de-escalation, since an elevated baseline CRP predicted the relapse following de-escalation with subsequent need for increase of ADM dose.

Disclosure of Interest: S. Vermeire: Grants from MSD, Takeda and Abbvie, lecture fees from Abbvie, MSD, Falk, Tilittos, Ferring, Centocor, Takeda, Hospira; consultancy for Ferring, Abbvie, Shire, Genentech/Roche, Celgene, Janssen, MSD, Takeda, Galapagos, Hospira, Mundipharma, Pfizer. 

M. Ferrante: Research grant from Janssen Takeda, lecture fees from Tilittos, Ferring, Boehringer-Ingelheim, Janssen, Chiesi, Falk, Zeria, Mitsubishi Tanabe, MSD, Takeda, and does consultancy for Abbvie, Ferring, MSD, Boehringer-Ingelheim and Janssen.

All other authors have declared no conflicts of interest.
The inclusion of additional biologicals to the treatment sequence resulted in a undiscounted health gain was 0.3 QALY per patient. In all countries, biosimilar dominated the originator infliximab-adalimumab-vedolizumab sequence. The standard care. The biosimilar infliximab-adalimumab-vedolizumab sequence varied between Hungary and standard care treatment sequence vs. standard care or to other biological sequences in nine European countries (Belgium, France, Germany, Hungary, Italy, the United Kingdom, Spain, 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 based 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 time horizon (10-year). Discount rates for both costs and benefits complied with the national pharmacoeconomic guidelines.

**Results:** The incremental cost-utility ratio (ICUR) of the biosimilar infliximab in 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:** All authors have declared no conflicts of interest.
OP150 NOVEL 4-THIAZOLIDINONE DERIVATIVES AS CYTOPROTECTIVE AGENTS AGAINST NSAID-INDUCED INJURY

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Introduction: Hydrogen sulfide (H₂S) and prostaglandins are an important mediator of mucosal defense and suppression of its synthesis by NSAIDs leads to increased susceptibility to enteropathy. H₂S also exerts a number of anti-inflammatory effects. Therefore, the ability of H₂S to promote the healing of the damage tissue and to resolution of inflammatory response has been exploited in the development of novel therapeutic agents.

Aims & Methods: The purpose of our study was to investigate the role of 4-thiazolidinone derivatives (compounds Les-5054 [5-[3,5-Di-tert-butyl-4-hydroxy-phenyl]-2-mercapto-acrylic acid]) as a novel H₂S donors in promoting the resolution of inflammation and injury in small intestine. The study was conducted on 40 white rats weighing 180–250 g according to the ethical requirements concerning the work with the laboratory animals. Animals were divided into 4 groups: I – control; II – small intestinal injury produced by indomethacin (IM) in the ulcerogenic dose (35 mg/kg, subcutaneously) per 72 h; II, IV – compounds Les-5054 and Les-5055 were administered three times per 72 h intragastrically at a single dose 10 mg/kg on the background of NSAID-induced injury. Then the rats were sacrificed and in small intestinal mucosa were measured the NOS and arginase activity, concentration of nitrite anions and MDA, activity of enzymes of the antioxidant protection system (SOD and catalase) and MPO activity; the concentration of L-arginine and H₂S in blood plasma.

Results: IM injection manifested by erosions and hemorrhages and leads to the following changes: the activity of iNOS increased more than threefold (P < 0.01) as compared with independent action of indomethacin. Parameters of MDA concentration and catalase activity increased for 35% (P < 0.01), H₂S concentration increased for 20.4% (p = 0.020), with no statistical differences in GI events. AC users had higher death risk (OR 1.5; 95%CI: 1.1–2.2) compared to AP users. Dual AP users had higher risk of ischemic events (OR 2.1; 95%CI: 1.1–3.7). Rebleeding event rates were 85 and 120 events per 1000 pt-year with AP and AC users respectively. The corresponding event rates were 71 and 82 per 1000 pt-year for vascular events, and 93 and 144 respectively for deaths.

Conclusion: Nearly 40% of patients presented a new adverse event related with AP/AC treatment during the follow-up. The risk of death is higher in patients on AC therapy compared with AP users. Resumption of AP/AC therapy is associated with higher risk of rebleeding and lower risk of death without any influence of AP or AC treatments later than 7 days is associated with significant higher risk of ischemic events.

Disclosure of Interest: A. Lunas: Professor Lunas has been an advisor for AstraZeneca, Bayer and Pfizer. All other authors have declared no conflicts of interest.

OP149 RISK OF REBLEEDING, VASCULAR EVENTS AND DEATH AFTER GASTROINTESTINAL BLEEDING IN ANTICOAGULANT AND/OR ANTIPLATELET USERS

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Introduction: Patients who develop gastrointestinal (GI) bleeding during anticoagulant (AC) and/or antiplatelet (AP) therapy represent a clinical challenge. Consideration of a higher risk of short-term or long-term considerations of these treatments will have important clinical implications concerning the risk of vascular, GI bleeding and death events. Differences on the risks between AP or AC users after drug resumption are not well established.

Aims & Methods: We aimed to determine the rate of rebleeding, vascular events and death in a cohort of patients treated with AP or AC agents who developed a major GIB (upper or lower) event. To compare these risks depending on the treatment adopted after the GIB event.

Methods: Retrospective long-term observational cohort study of patients who developed GIB while on AP and/or AC treatment from March 2008 to August 2013. Drug use information was prospectively collected during the GIB event. Data concerning the follow-up period, which ended on December 31st 2013 were obtained from databases from different Spanish Health care areas. Primary outcomes were vascular event, GI rebleeding and death from any cause. Statistical analyses were performed using SPSS software version 22.0.

Results: Patients were included (mean age 78.7 ± 8.9; 56.6% males; 52.8% (409/774), 38.5% (298/774), 8.7% (67/774) were on AP, AC or AP+AC therapy respectively. 22.6% of patients presented rebleeding, 17.1% ischemic event and 26.9% death during the follow up (median 23 months). Following the index GIB, mortality was interrupted in 80.1% (572/714) of patients and discharged (median time 6 days (1–370). Resumption of therapy was associated with higher risk of rebleeding (3.5% vs 24% p < 0.001) but lower risk of death (43.7% vs 19.9% p < 0.001). Early resumption of therapy (<7 days) vs delayed (≥7 days) was associated with higher rate of GI rebleeding (20.4% vs p = 0.020), with no statistical differences in GI events. AC users had higher death risk (OR 1.5; 95%CI: 1.1–2.2) compared to AP users. Dual AP users had higher risk of ischemic events (OR 2.1; 95%CI: 1.1–3.7). Rebleeding event rates were 85 and 120 events per 1000 pt-year with AP and AC users respectively. The corresponding event rates were 71 and 82 per 1000 pt-year for vascular events, and 93 and 144 respectively for deaths.

Conclusion: Nearly 40% of patients presented a new adverse event related with AP/AC treatment during the follow-up. The risk of death is higher in patients on AC therapy compared with AP users. Resumption of AC/AP therapy is associated with higher risk of rebleeding and lower risk of death without any influence of AP or AC treatments later than 7 days is associated with significant higher risk of ischemic events.

Disclosure of Interest: A. Lunas: Professor Lunas has been an advisor for AstraZeneca, Bayer and Pfizer. All other 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 presenting NSAID 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 control user in a ratio of 1:1 to non-aspirin users in 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 morality 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 month. Among the subjects who were never prescribed aspirin, 491,852 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 (HR = 0.80 to 0.85), and showed significant reduction in overall mortality (HR = 1.74). In the subgroup analyses, aspirin use showed significantly higher incidence of GI bleeding (HR = 1.80), and showed marginally significant higher mortality among those diagnosed with GI bleeding (HR = 1.03, 95% CI = 1.02 to 1.05). The results remained unchanged in the sensitivity analyses.

Conclusion: This is a population-based study to concurrently compare the risk and benefit of long-term use of aspirin. We concluded that long-term use of low-dose aspirin will increase the risk of GI bleeding, and moderate increase the 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.
POEM as a safe alternative to Heller Myotomy. However, the safety of POEM is still the subject of extensive analysis and multiple adverse events (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. Methodology: Patients who underwent POEM performed for the treatment of achalasia and SEDs were included 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&II vs. type III/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. Overall, 113 patients (6.1%) experienced 179 severe AEs. A total of 48 inadvertent mucosotomies occurred and represented the most common AE of POEM (31% of all AEs, overall incidence 2.8%). Mild, moderate and severe AEs occurred in 107 (74.5%), 26 (19%) and 9 (6.5%) patients, respectively. Among the 9 severe AEs, 2 were esophageal leaks, 1 perforation, 1 aspiration pneumonia, 1 empyema, 1 pneumomediastinum, 1 cardiac arrhythmia and 2 delayed bleeding. There were no deaths related to POEM. When patients with AEs were compared with a control group (case-control analysis), there was no difference between the 2 groups in terms of Charison comorbidity index/ASA class, prior therapy, sigmoid esophagus, operator specialty, direction of myotomy (anterior vs. posterior), type of used needle, extent and length of myotomy, and operator experience. The time of procedure was significantly longer in cases as compared to controls (123 min ± 49 vs. 103 min ± 38, p = 0.002). Length of stay was significantly higher in patients who experienced AEs (4.9d ± 2.7d, p < 0.001).

Conclusion: POEM as a safe therapeutic modality with a 7.5% 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
Disclosure of Interest: procedure.

The vast majority of initial clinical failure can be solved with endoscopic and efficacy of POEM for the management of achalasia and other motility dis-

Introduction: 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.

Conclusion: S. Roman: Sabine Roman is a consultant for Medtronic and Sandhill Scientific F. Mion: Francois Mion is a consultant for Medtronic M. Khashab: Mouen Khashab 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?

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 esopha-
gical spasm (1.1%), 1 atracorner esophagus (0.3%); in 48 patients (13.8%) acha-
lasia 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 conserva-
tively. 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 resection, 3 received no treatment because of mild symptoms. Clinical success slightly decreased with time, being 97%, 97%, 95%, 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. 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 effect-
ively controlled with PPI in all the patients but 2 who complained with heart-
burn 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 dis-

Disclosure of Interest: All authors have declared no conflicts of interest.
In this large multicenter study, POEM was safe and effective for reflux esophagitis and abnormal pH acid exposure. Multivariate analysis demonstrated prior HM (adjusted OR 2.91, p = 0.05) was significantly associated with clinical failure. The length of myotomy is comparable to that of patients with no prior HM. Follow-up data were available in 153 patients. Clinical response was defined by decrease in ES to ≤3. Adverse events (AEs) were graded according to the 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 s4RPR. The HM group had higher proportion of patients with prior PD (44% vs. 28%; p = 0.01). The length of myotomy was similar between the two groups. Technical success rates were comparable between HM group (89%/91%; 2 failures due to extensive submucosal fibrosis) and control group (100%) in control group (p = 0.49). Procedure time was similar between the two groups. The mean follow-up was 8.5 months (IQR 3.2–14.7) and was similar in both groups. 20 AEs occurred in 19 patients (7/18%) in HM group and 12 (13%) 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 10%, p = 0.34) AEs were similar. One severe AE (anastomotic leak) occurred 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 = 0.002). 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. Multivariate analysis demonstrated prior HM (adjusted OR 2.91, p = 0.05) was marginally associated with clinical failure after POEM. Post-POEM symptoms of reflux esophagitis and abnormal pH acid exposure were similar between the two groups.

Conclusion: In this large multicenter study, POEM was safe and effective for 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 group). 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 ≥ 7)]. Clinical response was defined by decrease in ES to ≤3. Adverse events (AEs) were graded according to the ASGE lexicon. Technical success, clinical success and AEs were compared between the two groups.

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

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Disclosure of Interest:
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Introduction: In this large multicenter study, POEM was safe and effective for achalasia patients with and without prior HM. Although rate of technical success in patients with prior HM is lower than those without prior HM, the safety profile of POEM is comparable to that of patients with no prior HM.

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OP160 EXPRESSION OF CD161 ON CD4+ T CELLS PROMOTES HBV-ASSOCIATED LIVER FIBROSIS THROUGH CD161-LLT1 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 54 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 prepared for further flow cytometric and real-time PCR analyses. 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. Results: Compared to HC, the percentage of CD4+CD161+ T cells significantly increased among IA patients while dramatically decreased among IT patients; however, 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-alpha, TNF-alfa, IL-17, IL-21 and IL-4 whereas produced less IL-10 and IL-22 than CD4+CD161– T cells. In comparison with CD4+CD161+ T cells, in vitro culture of CD4+CD161– T cells revealed that CD161 expression increased the activity of acid Sphingomyelinase (aSM) and subsequent PI3K, MAPK, and mTOR pathways of CD4+ T cells. Both knocking down of CD161 and using imipramine to inhibit aSM could down-regulate CD4+ T cell-proliferation and production of IFN-gamma and IL-17, especially for IL-17. 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-alpha, TNF-alfa, IL-17, IL-21 and IL-4 whereas produced less IL-10 and IL-22 than CD4+CD161– T cells. In comparison with CD4+CD161+ T cells, in vitro culture of CD4+CD161– T cells revealed that CD161 expression increased the activity of acid Sphingomyelinase (aSM) and subsequent PI3K, MAPK, and mTOR pathways of CD4+ T cells. Both knocking down of CD161 and using imipramine to inhibit aSM could down-regulate CD4+ T cell-proliferation and production of IFN-gamma and IL-17, especially for IL-17. Conclusion: CD161 on CD4+ T cells or LLT1 on HSCs could partly reverse the aforemen- tioned effects. In HSCs-CD4+CD161– T cell co-culture system, expression of CD161 on CD4+CD161– T cells. In comparison with CD4+CD161+ T cells, in vitro culture of CD4+CD161– T cells revealed that CD161 expression increased the activity of acid Sphingomyelinase (aSM) and subsequent PI3K, MAPK, and mTOR pathways of CD4+ T cells. Both knocking down of CD161 and using imipramine to inhibit aSM could down-regulate CD4+ T cell-proliferation and production of IFN-gamma and IL-17, especially for IL-17.

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

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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 FORCPEPS IN CHARACTERIZING COLORECTAL POLYPS LESS THAN 10 MM: A PROSPECTIVE BLINDED STUDY

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Introduction: Optical biopsies of colorectal 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. This study aims to assess FUSE versus FVC in dysplasia surveillance in an IBD population. The dysplasia yield of targeted versus random colon biopsies will also be assessed. Methods: A prospective, single-center, randomized, order, back-to-back crossover tandem colonoscopy study was conducted comparing FUSE versus FVC in an IBD surveillance population. Crohn’s disease (CD) and ulcerative colitis (UC) subjects were recruited from the IBD Sydney Cohort population-based database, all of whom met the inclusion criterias of published IBD surveillance guidelines. Subjects not due their surveillance colonoscopy were excluded. The primary outcome was the per-dysplasia miss rate of the first colonoscopy identified by the second colonoscopy with chromoendoscopy. Secondary outcomes were per-subject dysplasia miss rate, mean dysplasia lesions found, procedural times, and dysplasia yield of targeted- versus random colon biopsies. The trial was registered with the Australia New Zealand Clinical Trials Registry (ACTRN12616000047493).

Results: In total 104 tandem (52-paired) colonoscopies were conducted with 27 subjects randomized to FVC first and 25 to FUSE first. Both settings were not statistically significantly different for age, IBD disease, CD versus UC, and additional dysplasia risk factors. The dysplasia prevalence rate of the cohort was 30.8%. The dysplasia miss rates for FVC and FUSE were 71.4% versus 56.6%, respectively. (P = 0.014). The per-subject analytic, the dysplasia miss rate was 75.0% using FVC and 25.0% using FUSE (P = 0.046). FUSE identified a mean of 0.37 dysplastic lesions versus 0.12 for FVC (P = 0.007). Targeted biopsies increased dysplasia identification (26/163, 16.0%) versus random biopsy detection (2/687, 0.3%, P < 0.0001). Chromoendoscopy identified 10/28 (35.7%) of dysplastic lesions. The total colonoscopy times were similar (21.2 minutes versus 19.1 minutes, P = 0.32) but colonoscopy withdrawal time was significantly longer (15.8 minutes versus 12.0 minutes, P = 0.03) for FUSE and FC respectively.

Conclusion: FUSE Full Spectrum Endoscopy outperformed conventional forward view- ing colonoscopy in inflammatory bowel disease subjects undergoing dysplasia surveillance. A high dysplasia prevalence was identified most likely due to multiple colonoscopy passes and the use of multiple advanced imaging modalities comprising white-light colonoscopy, FUSE and chromoendoscopy. Improved dysplasia identification rates may reduce colorectal cancer mor- tality and increase interval colonoscopies. Improved dysplasia yield of targeted biopsies versus random colon biopsies was confirmed. Disclosure of Interest: R. W. Leong: Endosochse USA investigator-initiated study All other authors have declared no conflicts of interest.

Table (OP162): Diagnostic performance of WavStat4, Endoscopic assessment and combined algolithmic assessment for characterization fo colorectal polyps less than 10 mm in size and prediction of surveillance intervals

<table>
<thead>
<tr>
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<th>WavStat alone</th>
<th>Combination of WavStat + endoscopic assessment (algorithmic approach)</th>
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<tbody>
<tr>
<td></td>
<td>WLE+S-NBI</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>97.6% (95% CI 0.88-0.95)</td>
<td>85.0% (95% CI 0.77-0.89)</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)</td>
</tr>
<tr>
<td>NPV</td>
<td>96.8% (95% CI 0.85-0.89)</td>
<td>91% (95% CI 0.75-0.84)</td>
</tr>
<tr>
<td>PPV</td>
<td>54.7% (95% CI 0.28-0.47)</td>
<td>66% (95% CI 0.44-0.79)</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%</td>
</tr>
</tbody>
</table>
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 version4 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 NBI and 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: 26 patients 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 96.8% 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 81.2% of patients. An algorithmic approach combining Wavstat4 and endoscopic assessment had a high NPV with accurate prediction of surveillance intervals correctly.

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

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

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Aims & Methods: The aims of the current study were to explore the impact of the presence of T cell clonal expansions in the inflamed tissue at time of surgery on the 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 (performed at M6), associated with an extensive bio-banking. Clinical, biological and endoscopic parameters were collected at month 6. Endoscopic recurrence was defined by a Rutgeerts score >1. Biopsies of ileal mucosa were collected on surgical specimens and by endoscopy six months after surgery. T cell Receptor (TCR) analysis was performed on DNA extracted from biopsies by next generation sequencing (Adaptive Biotechnology 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. Recent MEMO patients seven patients were included. The REMIND cohort analysis showed: 33 (68%) 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 10000 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 score>1) at M6, when compared to patients without recurrence. 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 these 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, Ferring All other authors have declared no conflicts of interest.

Reference
colon cancer microbiome using mass spectrometry imaging in a prospective cohort of CRC patients.

**Aims & 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 collected under aseptic conditions from cancers and adjacent normal tissue and frozen at −80°C. Using 16S rRNA sequencing analysis of corresponding tissue samples (performed in Mothur and Stamp), target bacteria including *Fusobacterium spp*, *E. coli* and *Bifidobacteria* were identified. A chemical database of target spectra was 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 lipids. Taxon-specific data were mapped onto these images using chemical spectra identified by REIMS. Candidate microbial lipids were validated using cell co-culture experiments and analysis with REIMS. Multivariate analysis was performed and supervised Linear Discriminant Analysis was performed using Cell Co-Culture with REIMS. Candidate microbial lipids were validated using cell co-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 differentially expressed regions based on co-registration of the chemical data with 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 = 0.97.5. Increased long chain fatty acids were seen in malignant tissue. 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 *Bacteroidetes*, *Bifidobacteriales* and *Enterobacteriaceae*. These were positively validated using cell culture REIMS.

**Conclusion:** 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.

**OP167 COMPREHENSIVE CIRCULATORY TRANSCRIPTOMIC AND PROTEOMIC PROFILING IN NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASES: A MULTI-CENTRE COHORT STUDY**

**R. Kalla**, A. T. Adams¹, J. Lindstrom², Ibd Character Consortium¹, J. Satsangi¹

**Aims & Methods:** Gene expression patterns from whole blood RNA and proteomic profiles from serum were assessed from patients using targeted RNA-seq (Ion AmpSeq Transcriptome Human Gene Expression platform) and Olink multiplex protein 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 transcriptomes 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 5678 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 ¼ 2.3x10⁻⁷), VBPI (p ¼ 2.9x10⁻⁶) and S100 proteins (S100A9, p ¼ 7.8x10⁻⁶ and S100A1, p ¼ 7.9x10⁻⁶). 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 proteins upregulated in IBD included MMP12 (Homo sapiens, p ¼ 4.1x10⁻⁴) and S100A12 (p ¼ 1.7x10⁻⁴) and downregulated in IBD were CXCL9 (p ¼ 5.8x10⁻⁶) and S100A12, p ¼ 3.4x10⁻⁷). Proteomic profiles were available and correlated with RNA expression. 39 proteins showed significant correlation with gene expression including OSM (rho ¼ 0.51, Hausdorff corrected p ¼ 1.4x10⁻⁴), CXCL9 (rho ¼ 0.41, p ¼ 3.4x10⁻⁷) and other markers such as CCL4 showed poor correlation (rho ¼ 0.16, p ¼ 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 ¼ 619, AUC 0.64, p for comparison ¼ 2.7x10⁻⁴ vs. MMP12) and albumin (AUC 0.66, p ¼ 0.004 vs MMP12). 6 proteins differentially UC from CD including MMP12 (p ¼ 4.6x10⁻⁴). In CD, MMP12 levels were lower in those with small bowel involvement compared to CD without small bowel involvement (p ¼ 0.009) while in UC, MMP12 levels were significantly higher in extensive disease (Paris classification E1 and E2 vs. E3, p ¼ 5.8x10⁻³).

**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 Ferrying Speaker Fees J. Lindstrom: J has served as a speaker, a consultant and a advisory board member for MSD, Tillot, Ferring, Abbvie, Celltrion, Orion Pharma, Takeda, Napp Pharm, Meda, AstroPharma, Hikma and Pfizer.

G. Fomollon: Advisor: Griffols, Abbvie, MSD. Travel Grants: Abbvie, 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.
## Table 1 (OP168): Demographics, procedural outcomes, bowel cleanliness and adenoma detection.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>WE N = 408</th>
<th>WI N = 408</th>
<th>AI N = 408</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females, n (%)</td>
<td>184 (45.1)</td>
<td>185 (45.3)</td>
<td>183 (44.9)</td>
<td>0.990</td>
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<tr>
<td>Males, n (%)</td>
<td>224 (54.9)</td>
<td>223 (54.7)</td>
<td>225 (55.1)</td>
<td>0.088</td>
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<tr>
<td>Age, mean (SD)</td>
<td>61.4 (6.2)</td>
<td>61.0 (6.3)</td>
<td>60.9 (6.2)</td>
<td>0.261</td>
</tr>
<tr>
<td>Body Mass Index, mean (SD)</td>
<td>26.4 (4.1)</td>
<td>26.4 (4.4)</td>
<td>26.4 (4.4)</td>
<td>0.753</td>
</tr>
</tbody>
</table>

### Indications for colonoscopy, n (%)

<table>
<thead>
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<th>WI</th>
<th>AI</th>
<th>ANOVA</th>
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<tbody>
<tr>
<td>Screening FIT+</td>
<td>242 (59.3)</td>
<td>242 (59.3)</td>
<td>222 (54.4)</td>
<td>0.012</td>
</tr>
<tr>
<td>Screening FOBT+</td>
<td>18 (4.4)</td>
<td>19 (4.7)</td>
<td>19 (4.7)</td>
<td>0.364</td>
</tr>
<tr>
<td>Family history of colorectal cancer</td>
<td>47 (11.5)</td>
<td>47 (11.5)</td>
<td>45 (11.0)</td>
<td>0.249</td>
</tr>
<tr>
<td>Primary colonoscopy</td>
<td>101 (24.8)</td>
<td>100 (24.5)</td>
<td>122 (29.9)</td>
<td>0.099</td>
</tr>
</tbody>
</table>

### Procedural outcomes

<table>
<thead>
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<th>AI</th>
<th>ANOVA</th>
</tr>
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<tbody>
<tr>
<td>Cecal intubation rate (final), n (%)</td>
<td>402 (98.5)</td>
<td>400 (98.0)</td>
<td>399 (97.8)</td>
<td>0.823</td>
</tr>
<tr>
<td>Cecal intubation time, min</td>
<td>10.1 (5.4)</td>
<td>9.4 (5.7)</td>
<td>9.7 (6.7)</td>
<td>0.157</td>
</tr>
<tr>
<td>Withdrawal time without polypectomy, mean (SD), min</td>
<td>9.5 (3.2)</td>
<td>9.5 (3.6)</td>
<td>9.8 (3.1)</td>
<td>0.507</td>
</tr>
<tr>
<td>Total procedure time, mean (SD), min</td>
<td>24.8 (11.7)</td>
<td>24.6 (12.0)</td>
<td>23.3 (11.0)</td>
<td>0.842</td>
</tr>
<tr>
<td>Withdrawal endoscopists’ correct guesses of insertion method</td>
<td>119 (29.2)</td>
<td>135 (33.1)</td>
<td>116 (28.4)</td>
<td>0.091</td>
</tr>
<tr>
<td>Overall Boston Bowel Preparation Scale (BBPS) score, mean (SD)</td>
<td>7.9 (1.5)</td>
<td>7.4 (1.6)</td>
<td>7.5 (1.7)</td>
<td>0.924</td>
</tr>
<tr>
<td>Right colon BBPS score (SD)</td>
<td>2.6 (0.6)</td>
<td>2.4 (0.6)</td>
<td>2.4 (0.7)</td>
<td>0.815</td>
</tr>
<tr>
<td>Infused water during insertion, median (range), mL</td>
<td>570 (50-6500)</td>
<td>400 (50-2000)</td>
<td>0 (0-1000)</td>
<td>0.566</td>
</tr>
<tr>
<td>Aspirated water during insertion, median (range), mL</td>
<td>500 (0-6500)</td>
<td>50 (0-1000)</td>
<td>100 (0-900)</td>
<td>0.397</td>
</tr>
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### Adenoma detection

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<th>ANOVA</th>
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<tbody>
<tr>
<td>Overall ADR, n (%)</td>
<td>79 (19.4)</td>
<td>70 (17.2)</td>
<td>58 (14.2)</td>
<td>0.413</td>
</tr>
<tr>
<td>Right colon BBPS score (SD)</td>
<td>1.79 (1.2)</td>
<td>1.99 (1.9)</td>
<td>1.79 (1.3)</td>
<td>0.143</td>
</tr>
</tbody>
</table>

### Disclosures of Interest: S. Cadoni: Recipient of the 2013 ESGE Research Grant. All other authors have declared no conflicts of interest.
OP106 EFFICACY OF ENDOCUFF-ASSISTED COLONOSCOPY IN THE DETECTION OF COLORECTAL POLYPS USING THE NEWLY INTRODUCED OE-TECHNOLOGY

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Introduction: Polyp detection is crucial in colorectal cancer screening. Despite advances in conventional colonoscopy, the detection rate of colorectal polyps has not substantially improved, even with the use of advanced optical technologies. The EndoCuff is a mucosal compression device that is attached to the colonoscope. This device has been shown to improve polyp detection during colonoscopy.

Aims & Methods: The study aimed to investigate the efficacy of Endocuff-assisted colonoscopy in the detection of colorectal polyps using the newly introduced OE-technology.

Results: A total of 239 patients underwent colonoscopy with or without Endocuff assistance. The Endocuff-assisted group had a significantly higher polyp detection rate (6.1% vs. 3.2%, P < 0.013) and the adenoma detection rate increased by 15% (55% vs. 40%, P < 0.001). There were no statistically significant differences in other factors.

Conclusion: Endocuff-assisted colonoscopy enabled a significantly higher polyp detection rate compared to conventional colonoscopy. This improvement suggests that Endocuff-assisted colonoscopy could be an effective option for improving polyp detection.

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

OP107 DEVELOPMENT AND VALIDATION OF A SIMPLE CLASSIFICATION SYSTEM FOR IN VIVO DIAGNOSIS OF COLORECTAL POLYPS USING THE NEWLY INTRODUCED OPTICAL ENHANCEMENT (OE) TECHNOLOGY

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Introduction: Optical enhancement (OE) will be introduced at UEGW 2016 as a novel endoscopic imaging technique that adjusts emitted light to enhance mucosal vascular pattern and surface pattern morphology. This study assessed for the first time the utility of OE to predict colorectal polyp histology.

Aims & Methods: Primary objective was to develop and validate a simple classification system that allows differentiation of hyperplasic and adenomatous colorectal polyps and provides information for endoscopic mucosal resection or endoscopic polyp removal. The classification considers both patient-related factors and endoscopic predictors of advanced histology. Careful case selection which considered both patient-related factors and endoscopic predictors of advanced histology is critical to optimize the outcomes of endotherapy for LNPFCPs.

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

Reference

OP101 FREQUENCY AND PREDICTORS OF ADVANCED HISTOLOGY IN LARGE NON-PEDUNCULATED COLORECTAL POLYPS: EXPERIENCE-BASED DATA AT A UNIVERSITY HOSPITAL

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Introduction: Endoscopic resection of large non-pedunculated colorectal polyps (LNPFCPs) is challenging, with a significant proportion of them containing malig- nant dysplastic or adenocarcinoma. The aim of this study was to examine the frequency of LNPFCPs in clinical practice, endoscopic and histopathologic features and predictors for advanced histology.

Aims & Methods: We previously studied all endoscopists (9 faculty and 14 trainees) at Maastricht UC+. On detection, diagnosis and endoscopic resection of colorectal neoplasms using a stepwise training program: Phase 1: Training on detection and diagnosis of colorectal neoplasms, with special attention for non-pedunculated (flat and depressed) colorectal neoplasms using lectures, videos and individual feedback. Phase 2: Training in endoscopic resection techniques using videotraining and hands-on training with experienced colonoscopists. Then, we embarked in a prospective study of all consecutive colonoscopies performed at our institution from February 2008 to February 2012. Quality indicators (e.g. intubation rate, adenoma and polyp detection rate and resection rate) were monitored. We recorded patient characteristics (age, gender) and lesion characteristics, i.e., location, size, shape using Paris classification (including photo documentation) and histopathological diagnosis. We defined LNPFCPs as large (>20 mm) non-pedunculated (i.e. sessile, flat, depressed, combinations) colorectal neo- plasms. (Rutter et al, Gut 2015). We paid special attention to laterally spreading tumors (LSTs), defined as superficially growing lesions along the mucosa instead of growing up- or downwards. We conducted a logistic regression analysis to identify predictors for advanced histopathology, defined as high-grade dysplasia or early colorectal cancer (pT1).

Results: A total of 7166 neoplasms were identified in 9353 patients (mean age 59.0 years, 46.0% male), of which 1761 (19.5%) patients (mean age 68.3 years, 56.3% male) were LNPFCPs. The majority (65.9%) of LNPFCPs were located in the proximal colon. Mean size was 30 mm (20–100 mm). Ninety-six LNPFCPs (46.8%) were sessile and 109 (53.2%) LSTs. LNPFCPs contained more advanced histopathology: sessile serrated adenoma/adenocarcinoma (36.5%), high-grade dysplasia adenoma (17.1%), early colorectal cancer (17.1%), sessile serrated adenoma/polyp (6.6%), hyperplasia (8.8%), and traditional serrated adenoma (0.5%). Sessile-LNPFCPs more often contained advanced histopathology than LST-LNPFCPs (61.5% vs. 34.9%, p < 0.001). After adjusting for age and gender, distal location (OR 3.1, 95% CI 1.6–6.0, p < 0.001), size of lesion (OR 2.7 for LNPFCP ≥40 mm compared to 20–29 mm, 95% CI 1.1–6.2, p = 0.023) and sessile shape (OR 2.3, 95% CI 1.2–4.4, p < 0.001) were all independent predictors for advanced histopathology. The overall referral rate to surgery increased from 3.2% in the first half of the study period to 16.7%. Delayed bleeding occurred in 6 (5.6%) cases after endoscopic resection, none requiring surgical intervention. No perforations were reported.

Conclusion: In this real-life prospective cohort, 1.9% of all patients undergoing a colonoscopy had a LNPFCP. Lesion size, sessile shape and distal location were independent predictors of advanced histology. Careful case selection which considers both patient-related factors and endoscopic predictors of advanced histology is critical to optimize the outcomes of endotherapy for LNPFCPs.

Disclosure of Interest: S. Sanduleanu: Consultancy: Pentax Europe All other 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 lifetime 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: 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 PCCRC 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 1,195 life-years, compared to being ones detected at colonoscopy. Cumulative participation rate, positivity rate, number of colonoscopies and DY were evaluated using logistic regression model adjusted for age and gender.

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

Table 1 (OP172): Logistic regression model adjusted for age and gender

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<td>Location</td>
<td>LGD (n = 108)</td>
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<tr>
<td>Proximal</td>
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<tr>
<td>Distant</td>
<td></td>
</tr>
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<td>Size</td>
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*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 of 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 population registers of the Netherlands (2006–2010); 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 colonoscopy (3.5% vs 2.2%; p < 0.001) and 7.3% 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% for 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.

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 of John’s disease (59.1% vs 58.3%), 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 for Crohn’s disease in adults between 2004 and 2014 were identified. The influence of demographic factors, comorbidity and infused anti-TNF therapy on mortality, surgery and emergency readmissions was examined using multivariable 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 0.53 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 (2.26–8.94), p < 0.001) and were more likely to receive surgery than those aged 18–34. Increasing comorbidity (15.38
OP75 IS THE ‘RESET’ EFFECTIVE FOR CROHN’S DISEASE PATIENTS REFRACTORY TO ANTI-TNF THERAPY?

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Introduction: Anti-TNF-α agents (anti-TNFα) are currently the most effective therapeutic options for Crohn’s disease (CD). Some of CD patients under anti-TNF therapy, however, need surgery because of disease progression. Surgical resection (‘Reset’) usually leads to the elimination of the intestinal regions with the most severe activity. 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 received anti-TNFα therapy after surgery and 31 patients received preoperative anti-TNFα (TNFα-refractory 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. as 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-refractory group showed significantly higher rate of relapse than those of 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 was found to be an independent predictor of relapse (odds ratio 7.5, 95% confidence interval 1.1–43.8, 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 after surgery. Those patients may need additional treatment besides anti-TNFα therapy or increase in the dosage amount of the anti-TNFα after surgery. Those patients may need additional treatment besides anti-TNFα therapy or increase in the dosage amount of the anti-TNFα after surgery. Those patients may need additional treatment besides anti-TNFα therapy or increase in the dosage amount of the anti-TNFα after surgery.

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 hundred and ninety-two (192) patients who underwent surgery for Crohn’s disease terminal ileitis were enrolled. The patients were interviewed by telephone and responded to the generic European Quality of Life (EQOL) questionnaire and the Body Image Questionnaire (BIQ). 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 EQOL score and its single items (quality of life and body image) were significantly higher (and thus, better) in the laparoscopy group patients. Similarly, all the BIQ items were significantly better in patients who had a minimally invasive surgery compared to those who had open surgery. At univariate analysis, total EQOL score was directly correlated with minimally invasive surgery period. Surgery and anti-TNF therapy during admission has increased between 2004 and 2014. Surgery during admission was associated with men and at 1 year with men, younger age and non-white ethnicity.

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

OP77 CLOSE RECTAL DISSECTION VERSUS TOTAL MESORECTAL EXCISION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDERGOING PROCTECTOMY

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Introduction: Proctocolectomy or completion proctectomy in inflammatory bowel disease patients is frequently complicated by disturbed perineal wound healing and presacral abscess formation. Close rectal dissection (CRD) has been implemented 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-refractory group showed significantly higher rate of relapse than those of 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 was found to be an independent predictor of relapse (odds ratio 7.5, 95% confidence interval 1.1–43.8, 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.

Results: Fifty-nine patients (17 UC/42 CD) were included (46.4% male, mean age 45.5 (±14.5)). CRD was performed in 8 UC (47.1%) and 32 CD patients (76.2%). In UC, significantly less perineal complications (17.6% versus 47.6%, p = 0.033) and a higher healing rate at 6 months (87.5% versus 64.3%, p = 0.066) were seen. No significant differences in outcome between the techniques in UC. Perineal complications occurred more frequently in CD patients who underwent TME compared to CRD (20.0% versus 56.3%, p = 0.045), with higher healing rates at 6 months after TME (90.0% versus 53.3%, p = 0.052). Perineal healing rate at 12 months was 87.5% in the TME group versus 65.5% in the CRD group (p = 0.443). Analysis of rectal mesentery showed an enhanced infiltration of CD45+ immune cells in CD patients with the balance between CD3+ lymphoid T cells and CD14+ myeloid cells skewed significantly towards the myeloid population (UC vs CD median 24% versus 53%, p = 0.01). In addition, macrophages in CD patients showed significantly less expression of the wound healing marker CD206, in line with a more pro-inflammatory and less wound healing profile of CD rectal mesentery. Strikingly, these alterations were maintained in patients with a defunctioning stoma.

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Disclosure of Interest: All authors have declared no conflicts of interest.
Evidence has been accumulating indicating that the appendix has an
important role in controlling the microflora and in immunological processes.

Aims & Methods: This was a multicenter retrospective cohort study, which included patients with IRA for UC who completed a 12-month follow-up period in 2014. IRA failure was defined as progressive disease, Crohn's disease, or severe complications requiring colectomy. Survival analysis was performed using a Cox-proportional hazards model.

Results: In total, 303 patients were included in the study: 134 failed IRA and 169 did not. The median follow-up time was 15 months (IQR 10–20). The estimated time without IRA failure was 26.8 years. Two-thirds of secondary IRA failures were due to progression to Crohn's disease or complications requiring colectomy. The risk of IRA failure was not associated with the duration of disease before IRA, but was significantly associated with the presence of Clostridium difficile infection (CDI). However, the most commonly prescribed antibiotics for CDI were associated with increased risk of IRA failure.

Conclusion: IRA is a useful tool for treating patients with refractory UC. However, the risk of IRA failure is high, particularly in patients with CDI. Alternative treatments should be considered to reduce the risk of IRA failure.

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

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OP180 THE RISK OF CLOSTRIDIUM DIFFICILE INFECTION IN PATIENTS WITH PERNICIOUS ANAEMIA: A RETROSPECTIVE COHORT STUDY USING PRIMARY CARE DATABASE

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Introduction: Previous studies have shown an association between proton pump inhibitor use and Clostridium difficile infection1. One suggested mechanism of this association is the very low stomach acid levels caused by these drugs, since gastric acidity is an important host defence against ingested pathogens. If acid suppression is the true cause of Clostridium difficile infection in patients receiving proton pump inhibitors, then the effect should be manifested in patients with achlorhydria (no acid production), a condition associated with pernicious anaemia. Elucidating this association would provide a clear understanding of the acid-suppression hypothesis underlying the increased risk of infection in patients who have received gastric acid suppressive therapy.

Aims & Methods: The aim of this study was to determine the risk of Clostridium difficile infection in patients with pernicious anaemia. We conducted a population-based cohort study using English linked primary and secondary care database (Clinical Practice Research Datalink) and secondary care database (Hospital Episode Statistics) records (1998–2012). The exposed group consisted of patients with a diagnosis of pernicious anaemia who had been treated with vitamin B12 therapy. Each exposed patient was matched by age (within 5 years), gender and general practice to non-pernicious anaemia patients, with the follow-up start date of the control being as their matched exposed patient. Cox regression analysis was used to estimate the hazard ratio (HR) and 95% confidence interval for the association between Clostridium difficile infection and pernicious anaemia, adjusted for potential confounders.

Results: We identified 20,058 patients with pernicious anaemia receiving vitamin B12 therapy and 196,895 controls. The crude incidence rate of CDI was 1.90 (95% CI 1.77–2.05) CDI per 1000 person-years for those with pernicious anaemia while it was 1.87 (95% CI 1.84–1.89) CDI per 1000 person-years for controls. Patients with pernicious anaemia had a fivefold greater risk of Clostridium difficile infection than controls (adjusted HR 1.52, 95% confidence interval 1.33 to 1.73).

Conclusion: Individuals with pernicious anaemia have an increased risk of Clostridium difficile infection. This study supports severe hypochlorhydria as the mechanism for the increased Clostridium difficile infection in people who have received long-term acid suppression medication. Disclosure of Interest: F. Othman. This study has been carried out as part of my PhD program at University of Nottingham, UK, funded by Scholarship Award from King Saud bin Abdulaziz University for Health Sciences Saudi Arabia. There is no other potential conflicts of interest. All other authors have declared no conflicts of interest.

References

OP181 THERAPY REFRACTORY UC PATIENTS MAY BENEFIT FROM APPENDICECTOMY: EARLY RESULT FROM THE PASSION STUDY

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Introduction: Evidence has been accumulating indicating that the appendix has an important role in patients with ulcerative colitis (UC) potentially reduc-

ing the need for medication and colectomy. However, prospective data are limited and the therapeutic mechanism is not yet understood. The objective of this study was to examine the effect of an appendectomy to modulate the disease course of therapy refractory UC patients.

Aims & Methods: Patients with therapy refractory UC, and referred for proctocolectomy, were invited to undergo laparoscopic appendectomy first. The primary endpoint was clinical response at 3 months and after 12 months. Secondary endpoints were remission, improvement in IBDQ score and failure. Results were measured by the Mayo score (partial clinical 0–9 and endoscopic 0–3) and IBDDQ score (32 to 224). Clinical response was defined as a decrease in the partial Mayo of ≥ 3 points. Remission was defined as a decrease in the partial Mayo to 0 and endoscopic remission. Improvement in IBDQ was defined as an increase of ≥ 20 points. Failure was defined as when patient refused colectomy or prescribed trial medication (eg. Vedolizumab, Etrolizumab).

Results: In total, 30 patients (57% female) with a median age of 40 (IQR, 33–47) underwent appendectomy to treat a mean preoperative total Mayo score of 9 (SD 3.3). The median baseline IBDDQ was 125 (SD 34). After 3 months, clinical response was seen in 16 (53%) patients of whom 7 (30%) were in remission (7 patients refused endoscopy at this time point). Improvement in IBDDQ 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 (64%) had a decrease of at least 30% in IBDQ. The mean baseline IBDQ was 125 (SD 34). After 3 months, clinical response was seen in 16 (53%) patients of whom 7 (30%) were in remission (7 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. However, follow-up of at least 2 years is warranted to exclude a possible placebo effect.

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

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OP182 THE RISK OF CLOSTRIDIUM DIFFICILE INFECTION IN PATIENTS WITH PERNICIOUS ANAEMIA: A RETROSPECTIVE COHORT STUDY USING PRIMARY CARE DATABASE

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Introduction: Previous studies have shown an association between proton pump inhibitor use and Clostridium difficile infection. One suggested mechanism of this association is the very low stomach acid levels caused by these drugs, since gastric acidity is an important host defence against ingested pathogens. If acid suppression is the true cause of Clostridium difficile infection in patients receiving proton pump inhibitors, then the effect should be manifested in patients with achlorhydria (no acid production), a condition associated with pernicious anaemia. Elucidating this association would provide a clear understanding of the acid-suppression hypothesis underlying the increased risk of infection in patients who have received gastric acid suppressive therapy.

Aims & Methods: The aim of this study was to determine the risk of Clostridium difficile infection in patients with pernicious anaemia. We conducted a population-based cohort study using English linked primary and secondary care database (Clinical Practice Research Datalink) and secondary care database (Hospital Episode Statistics) records (1998–2012). The exposed group consisted of patients with a diagnosis of pernicious anaemia who had been treated with vitamin B12 therapy. Each exposed patient was matched by age (within 5 years), gender and general practice to non-pernicious anaemia patients, with the follow-up start date of the control being as their matched exposed patient. Cox regression analysis was used to estimate the hazard ratio (HR) and 95% confidence interval for the association between Clostridium difficile infection and pernicious anaemia, adjusted for potential confounders.

Results: We identified 20,058 patients with pernicious anaemia receiving vitamin B12 therapy and 196,895 controls. The crude incidence rate of CDI was 1.90 (95% CI 1.77–2.05) CDI per 1000 person-years for those with pernicious anaemia while it was 1.87 (95% CI 1.84–1.89) CDI per 1000 person-years for controls. Patients with pernicious anaemia had a fivefold greater risk of Clostridium difficile infection than controls (adjusted HR 1.52, 95% confidence interval 1.33 to 1.73).

Conclusion: Individuals with pernicious anaemia have an increased risk of Clostridium difficile infection. This study supports severe hypochlorhydria as the mechanism for the increased Clostridium difficile infection in people who have received long-term acid suppression medication.

Disclosure of Interest: F. Othman. This study has been carried out as part of my PhD program at University of Nottingham, UK, funded by Scholarship Award from King Saud bin Abdulaziz University for Health Sciences Saudi Arabia. There is no other potential conflicts of interest. All other authors have declared no conflicts of interest.

References
microbiota-based drug candidate targeted at recurrent CDI, is sourced from human-derived microbes from extensively screened 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/2C 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 critical 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 log2 fold changes (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 Actinobacteria showed reduced signal strength in the DP compared with the DS. Bacteroidetes 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. The gene expression level in stools compared to mice receiving a conventional diet suggested the potential effect on global intestinal inflammation. No significant alterations were observed on histological sections following HMD. Microbiota analysis revealed a 1000-fold decrease in E. coli population in mice fed HMD compared to mice receiving a conventional diet. Bisulfite sequencing revealed a hypermethylation of the CEACAM6 promoter, especially on the HRE sites. This hypermethylation of the promoter was associated with a significant decrease in CEACAM6 expression as measured by qPCR and Western-blot. RNA-seq data confirmed the decrease in CEACAM6 expression and highlighted many mis-regulated genes following HMD, among them, many genes involved in adaptive immunities.

**Conclusion:** This work shows that the addition of a few vitamins and oligo-elements to the diet could interfere with the DNA-methylation metabolism leading to changes in expression genes such as a decrease in CEACAM6 and modify microbiota composition leading to eradication of the E. coli population in the intestine. A diet-based strategy could help decreasing AIEC colonization in CD patients by modulating CEACAM6 expression.

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

**OP183 COMPARATIVE GENOMICS AND SINGLE NUCLEOTIDE POLYMORPHISM DISTRIBUTION BETWEEN ADHERENT-INVASIVE ESCHERICHIA COLI (AIEC) AND NON-AIEC STRAINS FROM THE HUMAN INTESTINE**


**Introduction:** The molecular basis of 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 with BLAST, and ii) SPAdes- Kraken assembly and comparative genomics between pairs in relation to a genome of reference (AIEC U10146) 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 indices 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 +30,178bp 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 other 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 site-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.

**Table 1:** Comparative Signal Strength of Bacteria

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Signal Strength in DS vs. DP</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>Allistipes</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>Negativitae</td>
<td>Increased</td>
<td>0.03 (0.01, 0.06)</td>
</tr>
<tr>
<td>Clostridium</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 = drug product</td>
<td>DS = drug source</td>
<td>CIM = confidence interval of mean</td>
</tr>
</tbody>
</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:**


**Disclosure of Interest:** All authors have declared no conflicts of interest.
OP184 ENTEROHEMORRHAGIC ESCHERICHIA COLI TROPISM TO PEYER’S PATCHES OF LONG POLAR Fimbriae AND INHIBITION BY A PROBIOTIC YEAST

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2EA CIDAM, Clermont-Ferrand/France

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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 of EHEC with Peyer’s patches, are 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 and 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 measured using an in vitro model of specialized intestinal efferent lymphatics. 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-infecting bacteria were determined using a quantitative method. To investigate the effect of probiotic yeasts, mice were given the probiotic for 7 days before ileal loops assays were conducted with O157:H7 wild type.

Results: Lpf isogenic mutants (i) were not able to interact with ileal biopsies compared to the 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, demonstrating that expression of lpfA1 and 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 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 EHEC with Peyer’s patches.

Conclusion: We conclude that Lpf are involved in the interactions of EHEC with Peyer’s patches. Among the carbohydrates tested, only mannose specifically limited the interactions of EHEC with Peyer’s patches, indicating that expression of lpfA1 or/and lpfA2 genes is essential in EHEC infections and use of antibiotics remains controversial. Probiotic could be an alternative strategy.

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

TUESDAY, OCTOBER 18, 2016 08:30-10:00

OP186 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 efficiency, safety and prognosis.

Aims & Methods: The aim of this study is to evaluate QOLs, clinical efficiency 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 37.0%, median age 73±17.6years) 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±6.6 days) than in TDT group (8.5±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). The major complication (at least one solid) was significantly higher in SEMS group (89.2% vs 25.0%, p<0.001). The Colonic Stent Safe Procedure Research Group Colorectal Obstruction Scoring System (CROSS) score before decompression was not significant difference in both group (3.6±0.9 vs 4.2±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>Variable</th>
<th>SEMS (n=27)</th>
<th>TDT (n=42)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73±17.0</td>
<td>65±15.2</td>
<td>0.36</td>
</tr>
<tr>
<td>Age &gt;85 years</td>
<td>9 (33.3%)</td>
<td>7 (17.1%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Obstructed location</td>
<td>23 (85.2%)</td>
<td>38 (90.5%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Primary colorectal cancer</td>
<td>21 (77.8%)</td>
<td>28 (70.0%)</td>
<td>0.53</td>
</tr>
<tr>
<td>BT</td>
<td>Bridge to SEMS insertion</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Palliation</td>
<td>0</td>
<td>0</td>
<td>0.02</td>
</tr>
<tr>
<td>Emergent surgery</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Metastatic colorectal cancer</td>
<td>6 (22.2%)</td>
<td>12 (30.0%)</td>
<td>0.35</td>
</tr>
<tr>
<td>BTS</td>
<td>Bridge to SEMS insertion</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Palliation</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Emergent surgery</td>
<td>1</td>
<td>0</td>
<td>0.25</td>
</tr>
<tr>
<td>Technical Success</td>
<td>27 (100%)</td>
<td>40 (95.2%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Perforation</td>
<td>2 (7.4%)</td>
<td>6 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>-Continued</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
OP187 EVALUATION OF CLINICAL FACTORS ASSOCIATED WITH THE TECHNICAL DIFFICULTY OF SELF-EXPANDABLE METALLIC STENT PLACEMENT FOR MALIGNANT COLONIC OBSTRUCTION


Introduction: In January 2012, the National Health Insurance began covering endoscopic self-expandable metallic stent (SEMS) placement for malignant colonic obstruction, and now this procedure is widely used in Japan. However, the clinical factors affecting the technical difficulty of SEMS placement are unclear.

Aims & Methods: This study aimed to clarify the clinical factors associated with the technical difficulty of SEMS placement for malignant colonic obstruction. We established the Colonic Stent Safe Procedure Research Group to provide instructions on how to safely perform SEMS placement, and we then conducted its prospective, observational, single-arm, multicenter clinical trial between March 2012 and October 2013 in Japan. Forty-six facilities participated in this study. An uncovered WallFlex Enteral Colonic Stent (Boston Scientific Corporation) was placed in each patient. Technically difficult cases of SEMS placement were defined as those that had a procedure time longer than 45 min (i.e., 1.5-fold longer than the median procedure time). We evaluated the clinical data and extracted risk factors associated with the technical difficulty of SEMS placement by using univariate and multivariate analyses.

Results: A total of 518 consecutive patients were enrolled in this study. Seven patients were excluded and the remaining 511 patients constituted the per-protocol cohort. There were 310 men (57%) and the mean age was 70 years. Three hundred eleven patients (61%) underwent stenting as a bridge to surgery, and 200 (39%) underwent stenting for palliation. Technical success was achieved in 412 patients (76.0%); median procedure time in the cohort with technical success was 30 min (4–170 min). One hundred thirty-six patients (27%) were defined as technically difficult cases of SEMS placement. Clinical risk factors independently associated with the technical difficulty of SEMS placement were metastasis of peritoneal carcinomatosis (odds ratio [OR], 2.24; 95% confidence interval [CI], 1.26–3.96; p < 0.001), a Colorectal Obstructing Scoring System (CROSS) score of 0 before SEMS placement (OR, 2.00; 95% CI, 1.18–3.40; p < 0.01), tumor site in the right colon (OR, 3.33; 95% CI, 2.06–5.42; p < 0.001), stricture length > 5 cm (OR, 1.65; 95% CI, 1.01–2.70; p = 0.04), the placement of > 1 stent (OR, 5.96; 95% CI, 1.39–29.27; p = 0.02), and a length of > 6 cm for the first stent (OR, 2.21; 95% CI, 1.38–3.56; p < 0.01). However, the 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 = 0.04), digestive tract decompression (OR, 0.45; 95% CI, 0.25–0.81; p < 0.01), and a diameter of 25 mm for the first placed stent (OR, 0.32; 95% CI, 0.12–0.76; p = 0.02).

Conclusion: This large study demonstrated the high technical success rate of SEMS placement for malignant colonic obstruction. However, clinicians should perform this procedure very carefully in cases with metastasis of peritoneal carcinomatosis, severe stenosis with a CROSS score of 0, and/or long strictures treated with a laser stent.

Disclosure of Interest: M. Shimada: personal fees:Century Medical Inc., Boston Scientific Japan
T. Kuwai: personal fees: Boston Scientific Japan
S. Yoshida: personal fees: Century Medical Inc., Boston Scientific Japan, ZEON
H. Iiyama: Donation & Lecture fees:Century Medical Inc. Boston Scientific Corp., Caequip Medical Co Ltd
T. Matsuzawa: personal fees: Boston Scientific Japan
K. Koizumi: Lecture fee: Century medical inc,personal fees: Olympus Medical System

OP189 LONG-TERM SURVIVAL AFTER ENDOSCOPIC STENTING AS A BRIDGE TO SURGERY IN OBSTRUCTIVE COLON CANCER: A SINGLE CENTER STUDY

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Aims & Methods: This study aims to describe the long-term survival data in a large patient group, treated with a stent as a bridge to surgery (BTS) for colon cancer. 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 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 tumor 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 perio
tative mortality 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 the cases a laparoscopic resection of the tumor was performed. Five point two percent of the patients got primarily open surgery. In 5.2% of the patients a laparoscopic procedure was converted to laparotomy, because of adhe
sions or peritonitis. Stoma rates were low (5.2%).

Conclusion: Mortality due to surgical AAD resection has a negative impact on the effectiveness of CRC screening. The number of AAD screen detected decreased and thus perioperative mortality will have a negative impact on the effectiveness of CRC screening. We recommend that stenting before surgery is effective and safe in the treatment with curative intent of patients with obstructive colon cancer and reinforce the debate on stenting as a BTS.

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

References
The EpiCom-cohort is a European prospective population-based cohort of unselected patients uniformly diagnosed with inflammatory bowel disease (IBD) in 2010 in 31 Western and Eastern European centres1. Previously, this cohort has demonstrated differences in the treatment strategy of IBD patients between Eastern and Western European centre including that significantly more patients in Western Europe receive biological therapy2. Despite these differences in treatment no differences regarding disease outcomes including surgery and hospitalization rates and quality of life between the two regions have been found. Anaemia is a common systemic complication and/or extra-intestinal manifestation to IBD, as well as an indicator of the level of global IBD care and inflammation control.

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. Incident patients were followed prospectively from the time of diagnosis. 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 guidelines.

Results: A total of 827 patients aged 15 years or older from 29 centres (20 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 remained anaemic (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 remained anaemic (94% vs 30%). These differences did, however, not reach statistical significance (p = 0.09).

Conclusion: In this unselected, population-based inception cohort the frequency of anaemia was high at the time of diagnosis, especially for CD, but decreased during 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 MICISTA 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 (92%). 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 thiopurines (adjusted odds ratio (aOR) 5.1; 95% CI 1.9–13.4; p = 0.001) and methotrexate (aOR 4.1; 95% CI, 1.0–16.8; 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).

Conclusion: SVI are rare events in patients with IBD who do not receive immunosuppressants. Exposure to thiopurines or methotrexate, and IBD clinical activity increases substantially the risk. Among 100 patients treated with thiopurines for 10 years, 3 will develop SVI.

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

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Disclosure of Interest: Patients with long-standing colonic inflammatory bowel disease (IBD) bear an increased colorectal cancer (CRC) risk. Endoscopic surveillance allows early detection and removal of precancerous lesions such as low-grade dysplasia (LGD), and may subsequently prevent CRC. However, the long-term clinical significance of LGD is still debates. The consequent risk to develop CRC remains uncertain,
since most available studies are small and cover a relatively short follow-up period. We performed a systematic review of five RCTs in patients with moderate risk of CRC, revealing 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 patients with LGD who were diagnosed with IBD between 1991 and 2005 in the Netherlands. Subsequently, follow-up data were extracted until 2016. We deter-
mined the cumulative CRC incidence with Kaplan Meier curves censoring 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), to perform a logistic multiple regression expressing the risk in terms of Odd Ratio. Finally, the diagnostic accuracy was tested by a ROC curve.

Results: We identified 134 patients with moderate risk of CRC. During the follow-up period, 12.8% of patients developed CRC. The 5-year cumulative CRC incidence was 8.0% (95% CI 4.4–11.6%). Patients with a history of LGD had a higher cumulative CRC risk compared to patients without a history of LGD (hazard ratio 4.0; 95% confidence interval 1.4–11.7; p = 0.008). Furthermore, patients with a history of LGD and a history of colorectal polyps had a significantly higher cumulative risk for CRC (hazard ratio 8.77; 95% confidence interval 1.71–45, p = 0.009).

Conclusion: Patients with LGD and a history of colorectal polyps have a significantly higher cumulative risk for CRC compared to patients without a history of LGD. Patients with LGD and a history of colorectal polyps should be encouraged to undergo regular colorectal surveillance to detect and remove preneoplastic lesions.

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

OP196 PREDICTORS OF FIRST COLONIC 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 with IBD 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 IBD patients with negative results of their first colonoscopy. 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 their first colonoscopy and 82 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% 1.07–37.9), 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 thiopurines (OR, 6.04; CI 95% 1.04–33; p = 0.03) and 5-aminosalicylic acids (OR, 5.27; CI 95% 0.84–87.86; p = 0.03) at the time of the colonoscopy. We developed a score based on these five variables 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 colonoscopy 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-aminosalicylic acids. 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 Abbott, 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 Abbott, MSD, Ferring Pharmaceuticals, Janssen, and research support from Abbott, Biocodex and Ferring Pharmaceuticals. All other authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016

10:30-12:00

COLORECTAL CANCER SCREENING: STATE-OF-THE-ART – ROOM K

OP198 PREDICTORS AND TRENDS IN Fecal HEMOGLOBIN CONCENTRATION: LONG-TERM FOLLOW-UP OF FIT-NEGATIVE SCREENEEES IN POPULATION-BASED COLORECTAL CANCER SCREENING

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Introduction: Quantitative fecal immunochemical tests (FITs) are invariably used in a qualitative manner using pre-specified cut-offs in colorectal cancer (CRC) screening. To optimize FIT performance in screening programs, it makes sense to explore whether participants with a negative FIT result at first participation and subsequent participations can be categorized according to fecal Hb (g/Hb) concentration to predict risk of developing future colorectal advanced neoplasia (AN).

Aims & Methods: In this population based screening cohort, average-risk subjects aged 50–74 years, were invited for four rounds of FIT screening (cut-off of 10 μg Hgb/g corresponding to 50 ng Hb/ml buffer). For this study all subjects with a negative FIT result at first participation were included. Baseline Hbg was divided into 3...
Introduction: Positive fecal immunochemical test (FIT) is associated to colorectal neoplasia and/or bleeding from non-neoplastic lesions. However, a considerable proportion of individuals with a positive FIT have a normal colonoscopy. 

Aims & Methods: We aimed 1) to identify possible cause of positive-FIT result in subjects with normal colonoscopy 2) to ascertain the rate of post-colonoscopy colorectal cancer (CRC) in this cohort. Methods: All individuals from the first round of the Barcelona’s CRC Screening Program (January 2010–December 2012) with a positive FIT (≥ 10 μg/g) and complete negative colonoscopy (i.e., no neoplastic lesion) were included. Subsequent gastrointestinal events that implied a medical consultation and/or procedure were recorded at the National Health Service electronic database. Attribution of causality for positive FIT was assessed according to time of presentation of the event: certain (at baseline colonoscopy), probable (≤ 6 months after colonoscopy), possible (6–12 months after colonoscopy), uncertain (>12 months after colonoscopy). Post-colonoscopy CRC were defined as any invasive CRC detected after colonoscopy until the end of follow-up (median, 50.6 months [range, 36–69]).

Results: From 2659 individuals who underwent colonoscopy after a positive FIT, 811 (30.5%; age 59.1 ± 4.0 years; 60.7% women) had a negative colonoscopy. In 102 (12.6%) individuals a cause of positive FIT was identified at the colonoscopy (abnormal polyp, 32 (4.5%) had subsequent gastrointestinal events classified as probable cause in 2 (gastric adenocarcinoma and Los Angeles’ grade D esophagitis), possible cause in 4 (invasive CRC, small bowel lymphoma, diverticular hemorrhage, and gastric antral vascular ectasia), and uncertain cause in 26 (2 invasive CRC, 4 advanced adenomas, 2 non-advanced adenomas, 15 inflammatory lesions, and 3 anorectal disorders). Age, sex, FIT levels, comorbidities (hepatic, renal, coagulopathy) or chronic antiplatelet/anticoagulant/NSAID treatments were not associated with a higher prevalence of gastrointestinal events. On the other hand, 3 (0.36%) post-colonoscopy CRC were detected (age, 56.3 ± 7.5 years; 66% men; TNM stage: 2 were IIIA and 1 was IIIB) within 11–28 months after screening. There were no significant differences regarding age, sex and FIT level among subjects with or without post-colonoscopy CRC.

Conclusion: Most individuals (83%) with a positive FIT and negative colonoscopy do not have any lesion that may explain this result. Of these, 96% do not present subsequent gastrointestinal events. Importantly, the rate of post-colonoscopy CRC in these subjects is very low (0.36%).

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

References
OP201 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 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 rounds of faecal immunochemical test (FIT) or no screening (controls). In total, 1809 and 1327 participants with a negative screening test result in the FIT and FS group, respectively, completed the LSQ, as did 1029 controls. ANCOVA and logistic regression were used to calculate differences in changes of health behavior (and 95% confidence intervals (CI)) between the arms at follow-up.

Result: Participants with a negative CRC screening test result in the first round of the FIT arm reduced their alcohol consumption significantly more than controls (−0.29 glasses per week, 95% CI; −0.54 to −0.04) during one-year follow-up. Body weight increased more in participants with a negative screening test result in the FS arm than in the FIT arm during the one-year follow-up (0.31 kg, 95% CI; 0.55 to −0.08).

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.

OP202 SCREEN-DETECTED AND NON-SCREEN-DETECTED COLORECTAL CANCERS AFTER FOUR ROUNDS 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 the effectiveness of FIT-screening 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 detected 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.

Result: 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 four 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%, 61.5% of cases, respectively), whereas colonoscopy interval CRCs were mainly located in the proximal colon (69.2%) (p = 0.10). 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.

Conclusion: In this population-based CRC screening cohort, 0.14% of all participants were diagnosed with an FIT interval CRC during follow-up. The patients with SD-CRCs had the most favorable stages and highest survival rates. Our results support the effectiveness of FIT-screening programs.

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

OP203 THE ADDED BENEFIT OF SURVEILLANCE IN COLORECTAL CANCER SCREENING

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Introduction: Although the impact of colorectal cancer (CRC) screening on CRC burden is well studied, the added benefit of surveillance in the context of an implemented screening programme is unclear.

Aims & Methods: Using the Adenoma and Serrated pathway to Colorectal Cancer model, we simulated the Dutch faecal immunochemical test (FIT)-based screening programme and combined this with a colonoscopy surveillance strategy based on the Dutch guideline. In this strategy, individuals considered at low risk return to screening after ten years whereas surveillance with a three or five-year interval is recommended for high- and intermediate-risk individuals, respectively. Furthermore, we evaluated three strategies in which the surveillance intervals as recommended in the Dutch guideline were prolonged to a) five years for all individuals at increased risk, b) five and ten years for respectively high- and intermediate-risk individuals and c) ten years for all individuals at increased risk. The comparator strategy was no screening and no surveillance. In addition, we simulated a screening only strategy without surveillance. Outcome were CRC incidence and mortality, number of colonoscopies per detected CRC, life-years lived and costs per individual in the lifetime of 20,000,000 individuals.
Result: FIT screening without a surveillance programme reduced CRC incidence and deaths by 25.4% and 27.2% compared to surveillance and no surveillance strategy. CRC incidence and mortality reductions increased to 28.1% and 40.8% when surveillance based on the Dutch guideline was added to FIT screening. Prolonging surveillance intervals slightly reduced surveillance effectiveness (incidence reductions 26.6%–27.2%, mortality reductions 39.6%–40.8% compared to no screening and no surveillance). In screening, 21 diagnostic colonoscopies were required to detect one CRC. The burden of surveillance was considerably higher; in the Dutch guideline strategy, 572 colonoscopies were required to detect one CRC by surveillance. Prolonging surveillance intervals decreased this burden to 129–366 colonoscopies per surveillance-detected CRC. All screening plus surveillance strategies were equally or more effective (0.00011 life-years gained) and less costly ($2–$4.6–$8.24) than screening only. The strategies with intermediate surveillance intervals were set at five years dominated all other screening plus surveillance strategies.

Conclusion: Adding surveillance to FIT screening reduces CRC burden and is cost-effective compared to screening without surveillance. However, the colonoscopy burden is markedly higher than this burden in a screening programme. Through modelling, we showed that this burden can be substantially lowered, without substantial loss of effectiveness, if surveillance intervals are lengthened to five years.

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

TUESDAY, OCTOBER 18, 2016 10:30-12:00

OP204 SUSTAINED Virological 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 may indicate patients at risk of 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 virological 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). We compared the case-control group (group B; n = 40) with the patients who achieved SVR but did not undergo FU-HVPG measurement to confirm the generalizability of our results.

Results: SVR to IFN-free therapies significantly decreased HVPG across all BL-HVPG strata. However, the liver stiffness values at FU for ruling-in and SVR to IFN-free therapies significantly decreased HVPG across all BL-HVPG strata. However, amelioration of portal hypertension was less likely in patients who did not achieve SVR showing either no significant improvement or even worsening of liver disease.

Disclosure of Interest: M. Mandorfer: M.M. received honoraria for consulting from AbbVie, Bristol-Myers Squibb, Gilead, MSD, 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. Freissmuth: C.F. received travel support from Gilead and Janssen. M. Trauner: R.S.T. received travel support from AbbVie. A. F. Stättmayer: A.F.S. received honoraria for consulting from Gilead, payments for lectures from Roche, as well as honoraria for board membership and consulting from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, Idenix, MSD and Roche. T. Reiberger: T.R. received payments for lectures from Roche, as well as travel support from Gilead, MSD, Roche, and Roche, as well as travel support from Roche. H. Hofer: H.H. received payments for lectures from AbbVie, Gilead, Janssen and Roche. C. Freissmuth received honoraria from AbbVie, payments for lectures from Bristol-Myers Squibb, as well as travel support from Gilead, MSD, Roche, Roche, as well for lectures from AbbVie, Boehringer Ingelheim. 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. A. Ferlitsch: 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. 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 and Roche. All other authors have declared no conflicts of interest.

OP206 RISK OF AND PREDICTORS FOR CLINICAL EVENTS FOLLOWING VIROLOGICAL RELAPSE IN CHRONIC HEPATITIS B PATIENTS AFTER CESSATION OF NUCLEOS(T)IDE ANALOGUE THERAPY

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Introduction: Clinical hepatitis may follow virological relapse in chronic hepatitis B (CHB) patients after discontinuing nucleos(t)ide analogues (NAs), but the incidence and risk factors are unclear.

Aims & Methods: Between July 1, 2011 and July 1, 2015, this multicenter study prospectively enrolled 140 consecutive CHB patients with negative HBeAg and undetectable viral DNA at the cessation of NAs after a minimum of 3 years on therapy. In those who experienced virological relapse (viral DNA ≥ 2.000IU/mL), the incidences of clinical relapse (virological relapse plus ALT > 80IU/mL) and persistent/severe hepatitis (clinical relapse lasting for 3 months or accompanied with jaundice) were estimated by the Kaplan Meier method. Predictors were explored by the Cox proportional hazard modelling.

Result: Following virological relapse that took place in 94 patients, clinical relapse and persistent/severe hepatitis occurred in 49 and 34 patients, respectively. The 2-year cumulative incidences were 61.5% (95% CI, 50.1–73.0%) and 56.2% (95% CI, 42.2–71.2%), respectively. Multivariate-adjusted analyses revealed clinical relapse was associated with serum concentration of viral DNA (hazard ratio [HR], 1.26 per log-mgL; 95% CI, 1.04–1.53) and alanine aminotransferase (ALT) at virological relapse (HR, 1.003 per IU/L; 95% CI, 1.0−1.004), as well as ALT at NA cessation (HR, 1.085; 95% CI, 1.002−1.101), whereas persistent/severe hepatitis was associated with viral DNA (HR, 1.41; 95% CI, 1.16–1.71), ALT (HR, 1.004; 95% CI, 1.001−1.010), and a-fetoprotein (HR, 1.13 per mg/L; 95% CI, 1.02–1.26) at virological relapse.

Conclusion: Clinical hepatitis frequently occurs following virological relapse in CHB patients after NA cessation, and may be predicted by serum viral load, ALT, and a-fetoprotein at the virological relapse.

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

Reference
OP207 COMBINATION THERAPY WITH DACLATASVIR AND ASUNAPREVIR IN CIRRHOTIC AND NON-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 being offered IFN-free therapy. Our objective was to assess the efficacy and tolerability of DCV/ASV combination therapy in patients with hepatic cirrhosis.

Aims & Methods: In total, 135 consecutive patients with HCV 1b initiating DCV/ASV therapy were enrolled. The cohort comprised 52 patients with compensated cirrhosis and 101 patients without cirrhosis (67 males and 86 females; median age, 71 years; 9 patients were >80 years old). NS5A resistance-associated variants (RAV) were examined using direct sequencing. The patients were treated with 60 mg of DCV 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, ALT level, cirrhesis level, or NS5A RAVs between patients with and without cirrhosis. On the other hand, those with cirrhosis showed significantly lower ALT levels on hepatic fibrosis scores and lower levels of alpha fetoprotein. The rapid viral response rate (HCV-RNA <25 IU/ml at week 4) was the same between patients with and without cirrhosis (80% and 84%, respectively). One of 52 patients with cirrhosis, and two of 101 patients without cirrhosis did not have NS5A RAVs at baseline, viral clearance was obtained. At E. elevation, one developed interstitial pneumonia, one had severe bronchitis, one had arterial fibrosis, two had gastrointestinal bleeding, and two developed edema. Of the patients without cirrhosis (9%), ALT elevation was observed in four patients. Two patients developed dialysis, two patients, gastrointestinal bleeding occurred in one, and liver fever occurred in one patient. After DCV/ASV therapy, HCC developed in two cirrhotic patients, and one non-cirrhotic patient.

Conclusion: DCV/ASV therapy 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
4. Flamm SL, Everson GT, Charlton M, Denning JM, Arterburn S and Brandt-Sarif T. Ledipasvir/sofosbuvir with ribavirin for the treatment of decompensated cirrhosis. N Engl J Med 2014; 371: 16.1 kPa (mean change (HVPG, mmHg) of 2.2 mmHg; p < 0.003) was noted – resulting in cure of PHT (HVPG < 10 mmHg). Among the 15 patients with cirrhosis, 7 patients (47%) had an increase in HVPG >10 mmHg during therapy, of whom 5 patients (33%) showed more than 20% increase in HVPG.

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

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Introduction: Combination of oral 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 most significant limitation of reduced rates of sustained virological response in decompenated 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 will achieve MELD and CTP scores with improvement in significantly port hypertension and hepatic venous pressure gradient.

Aims & Methods: Evaluation of the efficacy and safety of managing chronic active HCV in patients with decompenated cirrhosis and if SVR will improve CVR and the quality of life of these patients. Forty patients with decompenated cirrhosis with frequent hepatic encephalopathy or difficult to treat ascites were included if they had chronic active HCV proved by the positivity of HCV RNA, elevated transaminases. Patients were excluded if they had hepatocellular carcinoma, other causes of liver diseases or mixed causes (excessive alcohol consumption, autoimmune liver disease), previous liver transplantation. The patients were given sofosbuvir 200 mg, ribavirin 200 mg, and daclatasvir 60 mg for 6 months and evaluated for the development of sustained virologica response, the occurrence of side effects and the effects of SVR on the rate of development of hepatic encephalopathy, improvement in ascites control.

Result: Forty patients (31 males, 9 females) presented with chronic active HCV were enrolled, all showed difficult to treat cirrhotic ascites. 29 patients showed chronic recurrent episodes of hepatic encephalopathy (62.5%, 2.1 ± 0.6 episodes/2 months). The mean age was 51.4 ± 6.3 years, albumin 2.3 ± 0.4 g/dl, total bilirubin 1.9 ± 0.5 mg/dl, Hemoglobin 9.8 ± 2.0 g/dl.

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

References

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

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M. Mandorfer: 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. Schematic: received travel support from Gilead.

T. Buscic: received payments for lectures from Roche and travel support from Bristol-Myers Squibb.

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A. Fritzsche: 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. Piek: received travel support 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, and Roche

T. Reibiger: 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.

TUESDAY, OCTOBER 18, 2016
10:30-12:00
IMPROVING DETECTION AND TREATMENT OF COLONIC POLYPS – ROOM N2

OP210 RANDOMIZED, BACK-TO-BACK TRIAL OF NEW GENERATION OF NBI (HQ 290) FOR THE DETECTION OF COLORECTAL POLYPS

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Introduction: 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.

Aims & Methods: The aim of this study was to compare polyp miss rates between 290-NBI and high-resolution white light endoscopy (HR-WLE). Methods: From June to 2015, at least two folds brighter image compared with the previous version. The primary outcomes were polyp miss rates.

Result: A total of 27599 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our unit from April 2001 to December 2015. Of these, 16075 lesions were low-grade dysplasia, 5241 were high-grade dysplasia and 1097 were submucosally invasive (T1) carcinomas. According to the development of morphology classification, they were divided into 3 types: depressed, flat and protruded type. We investigated the rate of T1 carcinomas and the characteristics of depressed-type neoplasms concerning pit pattern and EC classification.

Conclusion: The rate of T1 carcinomas in depressed-type lesions reached to 62.1%, meanwhile that in flat-type and protruded-type lesions was 3.3% and 2.8%, respectively. Within less than 5 mm in diameter, that was 10.6%, 0% and 0%, respectively. Most (90.1% and 95.1%) of the flat-type and protruded-type lesions showed type IIHI or IV pit pattern corresponding to adenomas, whereas 94.6% of the depressed-type lesions were characterized by type IIIH VI or VN pit pattern corresponding to carcinomas. As for endoscopy, most of the flat-and protruded-type lesions showed EC2 corresponding to adenomas. In contrast, the depressed-type lesions were observed as EC3a (38.9%) and EC3b (58.0%) corresponding to invasive carcinomas.

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

References

OP212 ASSOCIATION OF CHROMOSOMAL INSTABILITY AND MICROSATELLITE INSTABILITY PATHWAYS WITH POSTCOLONOCOLIC POLYPS IN A RETROSPECTIVE COHORT STUDY


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Introduction: Over 50% of the postcolonoscopy 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 the development of CRC is still unclear.

Aims & Methods: We identified all PCCRCs diagnosed from 2001 to 2010 in a large gastroenterology practice from the Netherlands (le Clercq et al, Gut 2014). PCCRCs were defined as cancers occurring within 5 years after a complete index colonoscopy, which excluded CRC. We applied a clinical algorithm to assign the most likely explanation of PCCRC (incomplete colonoscopy) insufficient bowel preparation, missed lesion, incompletely resected lesion or new cancer. PCCRC's variables were analyzed (insufficient bowel preparation incomplete
endotracheal anesthesia, the motorized spiral enteroscope (SIF-Y0019, Olympus, Japan) is inserted through the mouth. The rotational advancement and withdrawal is controlled by the endoscopist using a foot pedal. The primary outcome of the study was the depth of insertion of the enteroscope.

Result: Demographics of the study patients are summarized in Table 1. Of the first 7 completed procedures, we were able to accomplish complete enteroscopy in 5 (71%) patients. In the other two instances, the distal jejunum and distal ileum were reached. The average insertion time was 47 minutes [range: 32–61] with an average total procedure time of 66 minutes [range: 41–94]. A bleeding event requiring hospitalization occurred within 7 days of one of the procedures but that was due to the underlying lesion rather than a complication of the procedure. No other significant adverse events were reported.

Conclusion: We present our initial experience of a safety and efficacy data trial for the motorized spiral enteroscope. We were able to safely accomplish full enteroscopy in 71% of cases with a single antegrade deep enteroscopy using the motorized spiral enteroscope. This percent achievement of complete enteroscopy is in line with previously reported data for unidirectional deep enteroscopy and suggests that this device is a significant development in the field of small bowel enteroscopy.

Disclosure of Interest: S. Bhattacharya: Consulting for Olympus D. Cave: Consulting and receipt of research funds from Olympus Consulting for Medtronic D. Demarco: Consulting for Spiru All other authors have declared no conflicts of interest.

Reference
1. le Clercq CM, Bouwens MW, Rondagaj EJ, Bakker CM, Keulen ET, de Ridder RJ, Winkens B, Masdeel AA and Sanduleanu S. Postcolonoscopy bleeding: a novel complication (APC). This was a prospective cohort study (n = 120) designed to evaluate the safety and efficacy of a new self-propelled enteroscope. This was a significant adverse event (SAE) by protocol. However, on further review it was determined that the patient bled from a Meckel’s diverticulum, identified during deep enteroscopy. Subsequent surgery was curative.

Table 1. (OP213)

<table>
<thead>
<tr>
<th>Subject #</th>
<th>Age</th>
<th>Sex</th>
<th>Indication(s)</th>
<th>BMI</th>
<th>ASA Grade</th>
<th>Insertion Time (min)</th>
<th>Procedure Time (min)</th>
<th>Point of Deepest Insertion</th>
<th>Complications</th>
<th>Final Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>M</td>
<td>Abdominal pain; video capsule findings of ulcerated mucosa in mid small bowel</td>
<td>40</td>
<td>III</td>
<td>33</td>
<td>41</td>
<td>Distal Jejunum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>M</td>
<td>CT scan finding of intussusception</td>
<td>21</td>
<td>II</td>
<td>32</td>
<td>43</td>
<td>Cecum</td>
<td>None</td>
<td>None</td>
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<tr>
<td>3</td>
<td>61</td>
<td>F</td>
<td>Gastrointestinal bleeding; video capsule finding of angioectasia</td>
<td>27</td>
<td>II</td>
<td>61</td>
<td>94</td>
<td>Cecum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>F</td>
<td>Iron deficiency anemia; video capsule finding of angioectasia and a small bowel polyph</td>
<td>23</td>
<td>II</td>
<td>47</td>
<td>70</td>
<td>Distal Ileum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>67</td>
<td>F</td>
<td>Iron deficiency anemia</td>
<td>23</td>
<td>II</td>
<td>48</td>
<td>66</td>
<td>Cecum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>33</td>
<td>M</td>
<td>Gastrointestinal bleeding</td>
<td>28</td>
<td>III</td>
<td>59</td>
<td>78</td>
<td>Cecum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>29</td>
<td>M</td>
<td>Suspected crohn’s; video capsule finding of a bleeding angioectasia and a small bowel polyph</td>
<td>28</td>
<td>II</td>
<td>49</td>
<td>72</td>
<td>Cecum</td>
<td>None</td>
<td>Crohn’s</td>
</tr>
</tbody>
</table>

OP214 THE AER-O-SCOPE COLONOSCOPE PROVIDES SUCCESSFUL ENDOSCOPIC THERAPY IN AN EX VIVO SWINE COLON MODEL

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Introduction: The Aer-O-cope Colonoscope System (GI View Ltd., Ramat Gan, Israel) is a self-propelled, joystick controlled, disposable colonoscope that provides a panoramic (360°) endoscopic visualization of the colon and includes two working channels compatible with standard endoscopic tools [1,2].

Aims & Methods: We aimed to demonstrate the success of the self-propelled Aer-O-Scope colonoscope in providing endoscopic therapeutic access. Therapeutic endoscopic access was a priori defined as the ability to reach a pre-defined target of interest, a pseudo-polyp, within an ex vivo swine colon and deliver "simulated" endoscopic therapy including: polypectomy with snare or biopsy forceps, submucosal injection, or thermal coagulation using argon plasma coagulation (APC). This was a prospective cohort study (n = 12 ex vivo swine colons housed in four different models that simulated variants of a human colon). Varying sized pseudo-polyps (n = 8 in each ex vivo swine colon) were created using colored thread and were randomly distributed throughout each ex vivo swine colon. Thus, n = 96 pseudo-polyps in total were created: 1 mm–5 mm (n = 70, 8%); 6 mm–9 mm (n = 13, 14%); ≥ 10 mm (n = 6, 6%). Following one day of Aer-O-Scope training for joystick utilization and endoscopic therapeutic access, two endoscopists (IMG and SB) performed all the colonoscopies (n = 12 colonoscopies per each endoscopist) on three separate procedure dates, in random order, and blinded to the type of colon model. The study’s primary endpoint was a success rate of at least 90% in providing simulated endoscopic therapy and the study’s secondary endpoint was endoscopist-perceived usability of the Aer-O-Scope for endoscopic therapy. We planned on performing a total of 240 simulated endoscopic therapies (n = 192 biopsy forceps, snare polypectomy, or combination injection/snare polypectomy and n = 48 APC applications). This sample size allowed up to a 10% pseudo-polyp miss rate with a two-sided
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 therapies 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 therapies 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 balloon-based system, incorporating 2nd generation optical coherence tomography in a balloon-based system, providing a 6-cm long circumferential scan of the esophageal mucosa, was very simple, lesion recognition with acetic acid (AA) remains a challenge and therefore hampering its widespread usage.

Disclosure of Interest: S. Bechofsky: I am a consultant for GI View Ltd. I.M. Grulnek: I am a consultant for GI View Ltd.

References

OP215 OUTCOME OF ENDOSCOPIC MUCOSAL RESECTION OF 424 LARGE SESSILE COLONIC POLYPS (≥20MM) OVER A 9 YEAR PERIOD: A SINGLE CENTRE EXPERIENCE AND ANALYSIS OF CHANGE WITH TIME

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Introduction: Endoscopic mucosal resection (EMR) has become the standard technique for resection of large sessile and flat colonic polyps. We aimed to assess the clinical outcome of colonic EMR of polyps ≥2cm and greater in size at University Hospital of Leicester NHS Trust and to assess changes over a 9-year period.

Aims & Methods: Data was collected for all sessile colonic polyps ≥20mm removed by EMR between 2006 and 2014 by 3 endoscopists (PW, JDC, JRP). Patient demographics, resection technique, completeness of initial resection, recurrence rate at first surveillance (SC1), polyp eradication at 2nd surveillance and complication rates were analysed.

Results: 364 patients were assessed for EMR, among which there were 424 complete EMR procedures (BCSP 138, Symptomatic 286) by three operators. Of the 140 not proceeding to complete EMR, in 65 EMR was not attempted and patients were referred for surgical resection (cancer 31, technical difficulty 34). In a further 32, EMR was abandoned; all were referred for surgery (cancer 18, benign polyp 14). Finally, 43 had no intervention (13 declined, 22 non-adenaomatous or pseudo polyps, 8 moved away). The mean age was 68.7 years (range 25–93), male 226 (53%), female 198 (47%). Mean polyp size was 33 mm (median 30 mm). Site of polyp was right colon 27%, transverse colon 5%, left colon 68% (rectum 58%, sigmoid 4%, descending 6%). Piecemeal EMR was done in 381 (90%), and ‘en bloc’ in 43 (10%). Of those who have undergone surveillance so far, recurrence was found in 56/284 (19.7%) at initial SC1 (mean 7 month; range 2–36) and was endoscopically treated in 53/56 (94.6%); 5/56 (4%) referred for surgical resection (2 cancer. 1 non lifting). Complete eradication after one year SC2 (mean 16 months, range 5–51) 211/234 (90.2%) with recurrence in 23 (9.8%) – but in 22/23 this was endoscopically resected. Overall complication rate 17/424 (4%). A total of 142 (2.7%) post-coal EMR required conservative medical treatment; post polypectomy pain syndrome 14/424 (3.3%) required admission for overnight conservative medical treatment. Delayed bleeding 2/424 (0.5%) required endoscopic therapy to achieve haemostasis. There were no post- procedure-related deaths. For each 3-year period (2006–8, 2009–11, 2012–14), there was a consistent reduction in number of polyps not treated endoscopically or requiring surgery (overall decrease of 15.7%), incomplete EMR referred for surgical resection (overall decrease of 2.3%) and recurrence rate at first SC1 (overall decrease 16.3%). There were increases in numbers of EMRs performed annually (overall increase 26%), mean polyp size resected (+7 mm), level 3 & 4 polyepotomies (3.7 and 7%) and complete eradication rate at SC1 (16.5%).

Conclusion: This was a large single-centre series of EMR of 424 sessile colonic polyps ≥2cm performed by 3 operators over a 9 year period; overall 20% had recurrence at initial surveillance, most managed endoscopically, with eradication rate at 1 year of over 90% (22/23 one year recurrences treated endoscopically). Examination of time trends over this period showed progressive reduction in recurrence and a trend for larger, more complex polyps to be resected endoscopically, with a corresponding drop in surgical management, demonstrating improvement in outcome with time.

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

TUESDAY, OCTOBER 18, 2016
10:30-12:00
BARRET’S ASSOCIATED NEOPLASIA – ROOM L7

OP216 DEVELOPMENT AND VALIDATION OF A CLASSIFICATION SYSTEM TO IDENTIFY BARRET’S NEOPLASIA USING ACETIC ACID CHROMOENDOSCOPY: THE PREDICT CLASSIFICATION
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Introduction: Neoplasia in Barrett’s can be very subtle and difficult to identify. Acetic acid chromoendoscopy (AAC) has been demonstrated to highlight neoplastic areas allowing for earlier treatment. Although the technique of AAC is very simple, lesion recognition with acetic acid (AA) remains a challenge and therefore hampering its widespread usage.

Aims & Methods: We aim to develop a simple and easy to use classification system for AAC to allow for identification of Barrett’s neoplasia. Three expert AAC endoscopists (PB, GLW, OP) entered a working group to identify AAC component criteria of non-dysplastic and dysplastic Barrett’s using a modified Delphi Method. Following this, a panel of 7 advanced endoscopists assessed the performance of each individual criterion by reviewing a bespoke online database of 40 images and 40 videos of non-dysplastic and dysplastic Barrett’s lesions. Finally, we assessed the diagnostic reproducibility of the validated criteria by asking 13 non-AAC expert endoscopists to complete an assessment tool of 40 images and 20 videos using this newly developed classification system.

Result: The component criteria identified by the expert AAC endoscopists were as follows: - Early focal loss of acetowhiteness - Present: Indicates presence of neoplasia - Absent: Indicates the absence of neoplasia - Surface pattern - Normal (Large uniformly distributed pigmentation) - 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.

Table 1: Validation results of the classification criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of acetowhiteness</td>
<td>(93.4–97.9%)</td>
<td>(88.9–96.9%)</td>
<td>(85.5–94.8%)</td>
<td>(95.4–98.8%)</td>
</tr>
<tr>
<td>Surface pattern</td>
<td>77.0%</td>
<td>99.0%</td>
<td>91.4%</td>
<td>96.9%</td>
</tr>
<tr>
<td>Normal</td>
<td>(69.7–83.3%)</td>
<td>(97.5–99.7%)</td>
<td>(88.4–93.9%)</td>
<td>(92.2–99.1%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>99%</td>
<td>90.9%</td>
<td>96.9%</td>
<td>91.4%</td>
</tr>
</tbody>
</table>

When the AAC validated criteria are applied by the 13 endoscopists, the sensitivity, specificity, NPV and PPV of detecting neoplastic Barrett’s are 98.5%, 97.5% and 92.2% 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 PPV threshold.

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

OP217 STEPWISE DEVELOPMENT OF A VOLUMETRIC LASER ENDMICROSCOPY PREDICTION SCORE FOR BARRET’S NEOPLASIA USING MATCHED PATHOLOGICAL IMAGES OF ENDOMICROSCOPIC RESECTION SPECIMENS
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2Medical Oncology, Academic Medical Center, Amsterdam/Netherlands
3Pathology and Wellman Center for Photomedicine, Massachusetts General Hospital and Harvard Medical, Boston, Boston/United States of America
4Endoscopy and Imaging, Academic Medical Center, Amsterdam/Netherlands
5Gastroenterology And Hepatology, Mayo Clinic, Rochester/United States of America/CA
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7Gastroenterology And Hepatology, Catharina hospital, Eindhoven/Netherlands

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Introduction: Endoscopic detection of early neoplasia in Barrett’s esophagus (BE) is difficult. Volumetric laser endomicroscopy (VLE) is an advanced imaging system incorporating 2nd generation optical coherence tomography in a balloon-based system, providing a 6-cm long circumferential scan of the esophageal wall up to 3 mm deep, with near-microscopic resolution. Several VLE features of early BE neoplasia have been determined previously (1,2).

Aims & Methods: Aims of this study were to determine (additional) VLE features of neoplasia, based on precise VLE-histology correlations ex vivo, and to develop and validate a VLE prediction score for early BE neoplasia. A unique database of VLE images from endoscopic resection specimens and core biopsies/ +/- neoplasia was used. Precise

Statistical analysis was performed using R.
endoscopy is challenging due to the inconspicuous nature of dysplasia. Molecular

Introduction: Detection of early neoplasia in Barrett’s oesophagus by white-light endoscopic mucosal resection (EMR). Freshly collected EMR specimens were used in this study to assess the feasibility of WGA-based NIR imaging for the endoscopic identification of dysplasia in Barrett’s esophagus.

Methods: Using ex-vivo VLE-histology correlation, we developed and validated a VLE prediction score for Barrett’s oesophagus, with a sensitivity and specificity of 83% and 71% in the validation phase, respectively. Conclusion: This study, using high-quality ex vivo VLE-histology correlation, confirms that the VLE features, surface signal, and irregular glandular ducts are independently and significantly associated with early BE neoplasia. Using these features, we developed and validated a VLE prediction score for BE neoplasia, with promising accuracy.

Disclosure of Interest: Dr. Tearney has the rights to receive royalties from this licensing arrangement. J.J. Bergman: - Research support: Olympus Endoscopy, Fuji-film, Cook Medical, Boston Scientific, Coviden, Erbe, Ninepoint Medical, C2-therapeutics, Cernostics, Interspace - Training programs:Coviden, Boston Sc. - Consultancy: speaker: Cook, Boston Sc.,Covidien. All other authors have declared no conflicts of interest.

References


O2P218 DETECTION OF DYSPLASIA IN BARRETT’S OESOPHAGUS USING LECTIN-BASED NEAR INFRARED-RED MOLECULAR IMAGING: AN EX-VIVO STUDY ON HUMAN TISSUE

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Introduction: Detection of early neoplasia in Barrett’s oesophagus by white-light endoscopy is challenging due to the inconspicuous nature of dysplasia. Molecular imaging using fluorescently labelled wheat-germ agglutinin (WGA) is a promising tool for detecting dysplasia as this topically applied imaging agent shows localization in dysplastic versus non-dysplastic oesophageal glandular mucosa (1). However, in an endoscopy setting, the detection of fluorescence in the blue/green range is limited by high levels of tissue autofluorescence. This limitation can be overcome by using near infrared (NIR) imaging. Aim: The aim of this study was to assess in an ex-vivo model the feasibility of WGA-based NIR imaging for detection of dysplasia in Barrett’s. To this end, we studied patients with early Barrett’s-related neoplasia undergoing endoscopic mucosal resection (EMR). Freshly collected EMR specimens were sprayed with WGA-IR800CW (10µg/mL; 10 min; room temperature); washed with PBS buffer and then imaged with a high-sensitivity NIR camera (Fluorcam1). Planar fluorescence images were captured and up to two punch biopsies (2 mm diameter) were collected from each EMR specimen, underlayed with NIR images. The EMRs were then fixed and paraffin embedded (FFPE), cut every 2 mm and processed for histopathological assessment. Each section was scored by an expert GI pathologist every 1 mm to construct a pathology grid, which was manually co-registered with the fluorescence image. Immunofluorescently stained punch biopsies, taken from areas of interest within the EMR specimen, were also scored by the pathologist. The mean fluorescence intensity (MFI) of cells in dysplastic and non-dysplastic areas was compared by the Wilcoxon matched-pairs signed rank test. The MFI of punch biopsies taken from dysplastic and non-dysplastic areas was compared by the Wilcoxon matched-pairs signed rank test. The MFI of punch biopsies taken from dysplastic...
OP220 LONG-TERM FOLLOW-UP RESULTS OF STEPWISE RADICAL ENDOSCOPIC RESECTION FOR BARRETT’S ESOPHAGUS WITH EARLY NEOPLASIA

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Introduction: Stepwise radical endoscopic resection (SRR) 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 SRR for BE with early neoplasia. We screened all patients treated with SRR in two centers between 2001–2014, for BE ≤5 cm with HGD/EC, without signs of invasion (>1mm, G2/G4 differentiation, lymph-vascular invasion or irregular deep resection margins in ER specimens. All patients who had reached endoscopic and histologically confirmed CE-neo and CE-IM after SRR were included for evaluation of long-term FU. All images of endoscopic biopsies 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 oesophagus (BOB) in neumoquiasis, 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 C2M3). Worst baseline pathology: HGD, n = 56, EC, n = 23. Median FU was 74 months (IQR SD 31.2 (10)2) with a range of 17-129 (IQR 4-8) endoscopies. 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 islands or tongues. Histological recurrence of IM without visible BE was observed in 25 patients: 3 patients had BB in neumoquiasis (4% overall, 0.7% per patient year); 24 patients (33%) showed IM in biopsies just distal to a neumoquiasis. A finding of IM of the neo-z-line was reproduced 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 SRR to date. The 6-year outcomes show that after successful SRR of BE ≤5 cm recurrence of HGD/EC is rare (1.4% overall, 0.7% per patient year). Recurrence of IM combined with visible BE islands or tongues. Histological recurrence of IM was limited to small (<1cm) islands or tongues. Recurrence of IM combined with visible BE islands or tongues. Histological recurrence of IM without visible BE was observed in 25 patients: 3 patients had BB in neumoquiasis (4% overall, 0.7% per patient year); 24 patients (33%) showed IM in biopsies just distal to a neumoquiasis. A finding of IM of the neo-z-line was reproduced 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.

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

References

TUESDAY, OCTOBER 18, 2016 10:30:12 AM
OP222 PREMEDICATION WITH SIMETHICONE AND N-ACETYLCysteine TO IMPROVE VISIBILITY DURING UPPER ENDOSCOPY – A PROSPECTIVE DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

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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 of 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-adaptable; 3-inadequate). Trial registrations: 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 1.31 vs. 1.60 (p = 0.01) and better without significance in the duodenum 1.07 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 of 0.02 cm in the duodenum, 0.06 cm in the stomach and 0.08 cm in the small intestine and 0.01 cm in the large intestine. 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.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP223 DIAGNOSIS OF TUMOR EXTENT OF EARLY GASTRIC CANCER USING NARROW-BAND IMAGING: A MULTICENTER PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Disclosure of Interest: adequate to perform in clinical practice (UMIN000014628).

Conclusion: "The aim of this study was to investigate the feasibility of a computer algorithm to identify early BE 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 for automatically analyzing both tissue and 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 employed for validation of the algorithm.

Result: Using the correlated histology as the reference standard, specificity, sensitivity, specificity and accuracy for the algorithm to detect BE neoplasia were 93%, 70%, 82% and 87%, respectively. The performance of the algorithm was good, with an area under the receiver operating curve (AUC) of 0.91 to detect BE neoplasia in ex vivo VLE images. Most distinctive features of the algorithm are the top layers and mid-range intensities of the histogram.

Discussion & Conclusion: In this study an algorithmic computer algorithm for BE neoplasia was developed based on VLE images with direct histological correlates. The algorithm showed good performance to detect BE neoplasia in ex vivo VLE images (AUC 0.91). Compared to the performance of a recently developed clinical VLE prediction score (AUC 0.81), this study suggests that an automatic detection algorithm seems to perform at least as good as evaluation by VLE experts in detecting early neoplasia on VLE. Future studies on in vivo VLE scans are needed to further validate the algorithm.

Disclosure of Interest: None

Reference


OP224 FEASIBILITY OF A COMPUTER ALGORITHM FOR DETECTION OF EARLY BARRETT’S NEOPLASIA USING VOLUMETRIC LASER ENDOMICROSCOPY

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

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 esophageal 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 clinical 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 early BE 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 for automatically analyzing both tissue and 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 employed for validation of the algorithm.

Result: Using the correlated histology as the reference standard, specificity, sensitivity, specificity and accuracy for the algorithm to detect BE neoplasia were 93%, 70%, 82% and 87%, respectively. The performance of the algorithm was good, with an area under the receiver operating curve (AUC) of 0.91 to detect BE neoplasia in ex vivo VLE images. Most distinctive features of the algorithm are the top layers and mid-range intensities of the histogram.

Discussion & Conclusion: In this study an algorithmic computer algorithm for BE neoplasia was developed based on VLE images with direct histological correlates. The algorithm showed good performance to detect BE neoplasia in ex vivo VLE images (AUC 0.91). Compared to the performance of a recently developed clinical VLE prediction score (AUC 0.81), this study suggests that an automatic detection algorithm seems to perform at least as good as assessment by VLE experts in detecting early neoplasia on VLE. Future studies on in vivo VLE scans are needed to further validate the algorithm.

Disclosure of Interest: None

Reference


Table 1. (OP225): Overall accuracy of the four patterns predictions

<table>
<thead>
<tr>
<th>Pattern</th>
<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>90.90 (55.50–99.75)</td>
<td>79.03 (66.82–88.34)</td>
<td>0.90 (0.89–0.95)</td>
<td>0.67 (0.66–0.68)</td>
<td>90.50</td>
</tr>
<tr>
<td>Type II</td>
<td>91.43 (76.94–98.20)</td>
<td>78.38 (61.97–90.17)</td>
<td>0.90 (0.89–0.95)</td>
<td>0.69 (0.68–0.70)</td>
<td>90.72</td>
</tr>
<tr>
<td>Type III</td>
<td>66.67 (9.43–99.16)</td>
<td>88.41 (78.43–94.86)</td>
<td>0.90 (0.89–0.95)</td>
<td>0.67 (0.66–0.68)</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.
OP226 FIRST-IN-MAN PILOT STUDY: FEASIBILITY OF LASER MARKING IN BARRETT'S ESOPHAGUS WITH VOLUMETRIC LASER ENDOMICROSCOPY

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Introduction: Laser endomicroscopy (LVE) is an advanced imaging system that provides a 6-cm long, circumferential scan of the esophageal wall subsurface layers with near-microscopic resolution. LVE 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 laser marking tool in BE patients.

Aims & Methods: The aim is to evaluate visibility and positional accuracy of VLE 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 (FM4) 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 VLE laser markings was evaluated, whereby previously placed electrocoagulation marks (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)BE, 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 25/33 of targeted ECMs (76%) the LMs were confirmed to be M4 (IQR 4–11). In total 222 LMs were placed, of which 207 (93%) were visible upon WLE and 192 (86%) on VLE.

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.

Aims & Methods: Aim of the study: To investigate in detail the gastrointestinal problems and symptoms living in adult patients. Type 3a patients, with more severe bile acid malabsorption. Our study cohort consisted of 105 adult CD patients followed up between 2007–2015 in Helsinki University Hospitals Adult Immunodeficiency Unit and the respective outpatient clinics of Care and Eksoite. CD patients were diagnosed on the basis of clinical criteria and lived within three hospital districts of southern Finland (1.9 million inhabitants). Adult patients of this cohort were diagnosed from the year 1960 to 2015 when recruitment stopped. We investigated retrospectively their medical records, laboratory results, endoscopy, histology, and manometric data and was compared to an 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 83 (65%) patients and respective biopsies. Helicobacter pylori was found in 7 patients, was negative in 74 and unknown in 23 patients. Eradication was successful in all Helicobacter-positive patients. Helicobacter-negative chronic gastritis without marked atrophy, but ranging from mild to severe inflammatory activity, was found in 11 patients (11%). In addition, atrophic gastritis in the body 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. Patients with the refractory duodenal villous atrophy and inflammation had also inflammatory changes in colon as well. 3. Hepatitis: Primary sclerosing cholangitis or CVID-associated cholangitis was diagnosed in 5 patients. 3. Large Bowel: Inflammatory changes of mucosa ranged from specific colitis and microscopic colitis (including lymphocytic colitis and collagen colitis) to crypt-destructive and/or graft-versus-host like severe inflammation. Consistent with IBD were identified IBD-like ulcerative colitis ulcerocarcinoma found in 5 patients (2 colectomies) and one patient had strictureting ileocolonic Crohn disease. Altogether, inflammation of colon was more common than small bowel enteropathy and it was found in 20 patients (19%). Prior to ileocolonoscopy, bacterial and parasitic infections were ruled out by standard laboratory methods including fecal sample screening. 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 appearance 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 unknown origin. Gastric and small bowel enteropathy had been found also in other 2 patients that died due to the cardiovascular disease. Meanwhile, one patient with unspecific 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 Type 3b patients (49%) than Type 3a (25%) at the time of the survey.

Aims & Methods: A prospective study evaluated SeHCAT usage across the United Kingdom was undertaken, capturing data from 38 centres and 1,036 patients. Aims & Methods: A prospective study evaluated SeHCAT usage across the United Kingdom was undertaken, capturing data from 38 centres and 1,036

Result: Upper endoscopy and ileocolonoscopy were done at least once to 83 (65%) patients and respective biopsies. Helicobacter pylori was found in 7 patients, was negative in 74 and unknown in 23 patients. Eradication was successful in all Helicobacter-positive patients. Helicobacter-negative chronic gastritis without marked atrophy, but ranging from mild to severe inflammatory activity, was found in 11 patients (11%). In addition, atrophic gastritis in the body was found in 10 patients (10%). 2. Small bowel: All tested patients were seronegative for coeliac disease. Helicobacter-negative chronic gastritis without marked atrophy, but ranging from mild to severe inflammatory activity, was found in 11 patients (11%).

Conclusion: Gastrointestinal and hepatobiliary manifestations are common among patients with CVID. 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 METABOLIC SIGNATURE IN PREDICTIVE AND FOLLOW UP VALUE IN CELIAC DISEASE; SUGGESTING IT TO BE A MARKER OF ENTEROCYTE VILLUS DAMAGE**

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Introduction: Amino acid citrulline is a non-essential amino acid which does not corporate into proteins and small intestine (gut enterocyte) 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 metabolic biomolecule or proteomic signature to assess silent and potential forms of the disease, 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 their first degree relatives and to establish a correlation between histopathological findings and the amino acid levels as a biomarkers for villous atrophy. Materials and Method: The procedure adopted for measuring plasma citrulline was Tendem Mass Spectrometry (LC-MS/MS) & RP-HPLC. Disease state was confirmed by histopathology findings including Marsh score and HLA tyyping(DQ2 & DQ8) By SSS-PCR

Result: Mean plasma citrulline levels in 54 serology positive subjects was 8.65 umol/L whereas citrulline levels in controls were 5.3 umol/L. Mean plasma citrulline levels in children with celiac disease (first degree relatives) was 24.3umol/L. This difference was statistically highly significant with p value of 0.0001. Correlations between biopsy grades of Subjects with their citrulline levels were established & found to be significant. For Marsh 3a grade lesions, mean citrulline levels were 5.6 ± 1.8 umol/L. For Marsh 3b, mean citrulline levels were 15.0 ± 3.4 umol/L with p value 0.006. Understandably the patients with total villous atrophy had a lower citrulline levels even if they were asymptomatic. All the patients were on stringent six month follow up and the mean levels were 12.8 ± 3 umol/L. DQ2 heterodimer were collectively found in 71.63% high risk subjects. A total of 8.69% subjects found negative for HLA DQ2 heterodimer. HLA type DQ8 was not found in any of the subject.

Conclusion: Citrulline alone is a very important metabolic biomolecule signature of initial damage of gut enterocytes in celiac disease and also when correlated with Marsh score. Citrulline estimation on dried blood spots using tandem mass spectrometry is a minimally invasive and promising test in near future which could be transferred to the remotest place in the country to suggest improvement in gut enterocyte mass. Plasma citrulline estimation assures detection of potential celiac disease and may be use for monitoring of compliance and recovery in CD which is likely to be of immense benefit in the diagnosis of celiac disease and analyzing citrulline on dried blood spot by a highly sensitive technique. Genetic chromatoraphy mass spectrometry may ease follow up and diagnosis of CD.

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

Reference
All authors have declared no conflict of interest.

**OP231 CELLULAR ZINC IS REQUIRED FOR INTESTINAL ENTEROCYTE BARRIER FUNCTION: THE REGULATION OF CLAUDIN-3 AND OCLCLUDIN EXPRESSION**

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Introduction: Intestinal cell inulin is a required for a variety of cell functions. Previous studies suggest that the intracellular zinc has an essential role in the maintenance of the intestinal tight junction (TJ) barrier, however, the underlying mechanisms remain unclear (1, 2). The present study investigated the essential roles of intra cellular zinc in the preservation of intestinal TJ integrity and the underlying molecular mechanisms in human intestinal Caco-2 cells and mouse colons.

Aims & Methods: Depletion of intracellular zinc in Caco-2 cells and mouse colons was achieved by the application of a cell permeable zinc chelator, N, N,N',N'-Tetraakis(2-pyridylmethyl)ethylenediamine (TPEN). Caco-2 cells grown in monolayers and mouse colons were treated with TPEN. The intracellular zinc levels were assessed by measuring transmembrane electrical resistance (TER) and dextran flux. The TJ proteins expression and distribution (ZO-1, ZO-2, occludin, JAM-1, and claudin-1) were investigated by immunoblot, immunofluorescence and confocal microscopy. To confirm the TPEN effects, ZnSO4 was supplemented to the culture media in the presence of TPEN. The TPEN-induced proteinolysis of occludin was examined by biochemical studies. To examine the mechanisms underlying the zinc depleting-induced occludin proteolysis, selective inhibitors of calpain, proteasomes, autophagy, matrix metallo-protease and cathepsin were used. The effect of zinc depletion on claudin-3 promoter activity was examined by means of a reporter gene assay. Roles of zinc in the regulation of claudin-3 expression was studied by means of siRNA transfection and overexpression of ZnT1.

Disclosure of Interest: All authors have declared no conflicts of interest.
activity were examined by a mutagenesis technique in the promoter assay and RNA interference technology. The effects of TPEN on occludin and claudin-3 expression in mouse colons were also examined in combination with the calpain inhibitor.

**Result:** Intracellular zinc depletion by TPEN impaired the TJ barrier of intestinal Caco-2 cells. The decreased TER and increased dextran flux were reversed by supplemental zinc. Bioimmtation of cell surface proteins revealed that the zinc depletion induced the proteolysis of occludin, but not claudin-3. Occludin proteolysis was sensitive to the inhibition of calpain activity, and increased calpain activity was observed in the zinc-depleted cells. Although qPCR analysis and promoter reporter assay have demonstrated that the zinc depletion-induced claudin-3 downregulation occurred at transcriptional levels, a site-directed mutation in the egf1 binding site in the claudin-3 promoter sequence induced loss of both the basal promoter activity and the TPEN-induced decreases. Reduced egf1 expression by a specific siRNA also inhibited the claudin-3 expression and barrier function in mouse colons. The zinc chelator restored the TPEN-induced decrease in occludin, but not claudin-3.

**Conclusion:** This study shows that intracellular zinc has an essential role in the maintenance of the intestinal epithelial TJ barrier through regulation of occludin proteolysis. In conclusion, zinc deficiency might impair QOL. Further, zinc finger-containing egf1 was shown to be critical for 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 (QL) 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 & Methods:** 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 will be used. Participation was voluntary. Responses were collected between February and July 2015. Data were anonymised for analysis and reporting.

**Results:** In 43 questions covering 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 process in HPN-QOL. Raw patient responses were scaled to a score of 0–100 for each domain. The QOL global numerical ratings had a scale of 0–23 or better, with findings by Baxter, et al (1). In gender analysis, males reported better ability to eat and holdy life, physical function, energy and overall QOL. Females had significantly better sexual function (p < 0.006). In age group analysis, patients over 55 had lower employability (p < 0.0009). There was no significant difference in the incidence of post-pancreatectomy hemorrhage, delayed gastric emptying, infectious complications, the grade of postoperative complications and the length of postoperative stay. A successful NJEEN was achieved in 0% patients. In TPN group, average energy intake was significantly higher (p < 0.0012) and higher severity (grade B/C 29.4% vs. 13.9%; p < 0.007). There was no significant difference in the rate of postoperative complications according to Clavien-Dindo classification. Successful NJEEN was defined as insertion of a nasogastric feeding tube, delivering at least 50% of nutritional needs on PoD 5, and no TPN for more than 48 hours.

**Conclusion:** Postoperative complications occurred in 77.5% (IC 95% [68.1–85.1]) patients in the NJEEN group versus 64.4% (IC 95% [54.2–73.6]) in TPN group (p = 0.040). NJEEN was associated with higher frequency of postoperative pancreatic fistula (POPF) (48.1% vs. 27.7%, p = 0.012) and higher severity (grade B/C 29.4% vs. 13.9%; p = 0.007). There was no significant difference in the incidence of post-pancreatectomy hemorrhage, delayed gastric emptying, infectious complications, the grade of postoperative complications and the length of postoperative stay. A successful NJEEN was achieved in 0% patients. In TPN group, average energy intake was significantly higher (p < 0.001) and patients had an earlier recovery of oral feeding (p = 0.0009).

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

**References**

OP235 THE CENTRAL ROLE OF THE GUT MICROBIOTA IN CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

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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, a hypothesis that 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 faecal 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±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 technique. Calcium and stomach size, and maximal bowel diameter, were determined using oral contrast-enhanced abdominal CT scan. The faecal microbiota recipient of mice was analyzed 48 hours and 2 weeks after colonization by Illumina and inferred metagenomic analyses were assessed by PICRUSt. The CIFO patient was then treated with 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.

Results: 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 patients compared to healthy donors.

Conclusion: The faecal microbiota composition and its metabolic activity are related to clinical features typical of 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
surgery and of endoscopy (performed at 6 months). Bacterial composition of the ileal mucosa associated microbiota was analyzed at time of surgery using 16S ribosomal RNA. The obtained sequences (rarefied to 2000 reads/sample) were analyzed using the QIIME pipeline to assess community 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 peptic lesions. Indication for surgery was stricture 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 (0.0001) and diversity (mean observed species: 302 ± 17 vs 236 ± 14, p = 0.0005). In multi-variate analysis (MaAsLin), antibiotics treatment was notably associated with an increase in Enterobacteriaceae (q ≤ 0.01) 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 >2, 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.


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

Reference
1. This study has been supported by grants from MSD France, Association François Aupetit, the Helmsley Charitable Trust and INSERM.

OP237 BILE MICROBIOTA IN PRIMARY SCORLERSIAN DISEASE: EFFECTS ON DISEASE STATE AND RISK FOR BILIARY DYSPLASIA

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic inflammatory liver disease leading to strictures in intra- and extrahepatic bile ducts and finally to cholestasis and secondary biliary cirrhosis (1). The chronic inflammation is associated with increased proliferation of biliary epithelial cells and a markedly increased risk of development of biliary dysplasia and cholangiocarcinoma (2). The etiology and pathogenesis of PSC is unknown, but the frequent association with inflammatory bowel disease, in 62–83% of PSC patients, and increased intestinal permeability in PSC has suggested a role for microbiota or microbial metabolites or derivatives, e.g. pathogen-associated molecular patterns, PAMPs) such as lipopolysaccharide (LPS), lipoteichoic acid, and peptidoglycan in the pathogenesis of the disease (3–5). It has been proposed that the association between PSC and IBD can be due to increased enterohemolytic circulation of PAMPs (“leaking gut”), or abnormal PAMPs (as a result of enteric microbial dysbiosis, disrupted in IBD). Moreover, 16S ribosomal ribonucleic acid (RNA) has been detected in bile and also in cholangiocytes in PSC patients. The microbiota in bile have also been shown to be modified by genetic factors such as FUT2 (2α1-L-fucosyltransferase 2) polymorphism, a gene involved in protein glycosylation. Aims & Methods: To study the possible role of bile microbiota in ethiopathogenesis, disease progression and risk of dysplasia and cholangiocarcinoma (CCA). The clinical part of the study was conducted at Helsinki University, Clinic of Gastroenterology. The patients were recruited from the Clinic of Gastroenterology. The indication for ERCP examination was the documentation of diagnosis of PSC due to: 1) constantly elevated or fluctuating gamma-glutamyl transferase (GGT) levels in conjunction with IBD, or 2) magnetic resonance cholangiography findings, or 3) surgery with negative bimodal linearized models, PERMANOVA, and non-parametric tests. Result: 1) A very low abundance OTU (‘‘species’’) belonging to the family Neisseriaceae was reduced in abundance in the early disease group. 2) Increase in Streptococcus from early disease to long disease progression. 3) Streptococcus also correlates with increase in ERC severity score and potentially with the number of ERC examinations. More robust are the findings regarding overall community diversity, which decreases in long progression and dysplasia/CCA. 3) A low abundance Prevotella OTU disappears in patients with dysplasia or CCA. Streptococcus seems to again increase.

Conclusion: The data in our exploratory study suggests that the etiology of the disease is not connected with changes in bile microbiota. Streptococcus seems to be connected with disease progression and risk of dysplasia and CCA. It may also related to the number of ERC examinations and therefore a role, at least partially, for nosocomial infection cannot be ruled out at this stage. Overall, microbial diversity decreases in long progression and further more in dysplasia/CCA.

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

References

OP238 INCREASED FAECAL LEVELS OF GRANINS IN IRITRABLE BOWEL SYNDROME ARE ASSOCIATED WITH LUMINAL MICROBIOTA COMPOSITION AND SYMPTOM SEVERITY

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2Sahlgrenska Academy, Sahlgrenska Academy At University Of Gothenburg, Gothenburg/Sweden
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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. Levels of CgA, CgB, SgII, SgIII and calcitonin were analysed 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), T cell receptor alpha/beta chain and in the colon 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 Rating Scale (GSRS-IIBS) 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 was also increased with CgA (r = –0.29, r < 0.005).
The microbiota is considered important for development of intestinal diseases. In order to create a molecular snapshot of IBD in its early manifestations, one part of the IBD-Character project identified faecal microbiota profiles among 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 where stored at −80°C before examination on GA-map. Dysbiosis Test (DT) (16S rRNA) was used utilizing DNA probes to recognize gut bacteria profiles. In total 54 probes have been selected (1) for recognition of dysbiosis.

**Result**: In total 294 adult patients and healthy individuals were investigated for microbiota profiling. Table 1 shows the distribution and frequency of dysbiosis in the diagnosis groups and healthy controls. Compared to the bacteria profiles of IBD, non-IBD and control groups, the abundance of *Bifidobacterium* and *Eubacterium* was significantly increased (*p = 0.01*). *Escherichia*/*Proteobacteria* were significantly decreased (*p < 0.001*) in the E2/E3 group compared to E1/healthy controls.

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

**Reference**


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Introduction: The intestinal tract is inhabited by a large and diverse community of bacteria collectively referred as gut microbiota. Mucoid structures coating the epithelium, largely devoid of bacteria, are central to maintaining intestinal-microbiota homeostasis. Our recently published work has led to the hypothesis that, in mice, bacterial encroachment of the epithelium, as a consequence of an innate immune deficiency or ingestion of substances that alter host-microbiota interactions, promotes low-grade inflammation that can drive metabolic disease (1–2).

**Aims & Methods**: The aim of the current study was to study microbiota localization in human subjects with metabolic syndrome. Subjects were enrolled at the Veteran’s Administration Hospital (Atlanta, GA, USA). A review of the patient medical record was conducted to determine control and diabetic patients, as shown by their glycosylated hemoglobin and fasting serum glucose level. During the colonoscopy procedure, two mucosal biopsies were taken in the left colon approximately 40 cm from the anus using a regular forceps. The biopsies were immediately placed in Carnoy fixative and mucus immunostaining was paired with fluorescent in situ hybridization in order to analyze bacteria localization at the surface of the intestinal mucosa.

**Result**: We found that bacterial encroachment of the epithelium correlates with central features of metabolic syndrome in humans. Specifically, confocal microscopic analysis of biopsies from middle-aged persons revealed an inverse correlation between bacterial-epithelial distance and body mass index, fasting blood glucose, and hemoglobin A1C level. Ethnicity or antibiotic use did not significantly correlate with microbiota-epithelial distance.

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

**Reference**


**Table 1. (OP241):** The taxa numbers of IBS-P, IBS-N and HC in genus levels [M (Q1, Q3)]

<table>
<thead>
<tr>
<th>Phylum</th>
<th>Genus</th>
<th>Taxa Numbers</th>
<th>P</th>
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<tbody>
<tr>
<td><strong>Actinobacteria</strong></td>
<td>Collinsella</td>
<td>95(34, 146)b</td>
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<tr>
<td></td>
<td>Bacteroides</td>
<td>Prevotella_9</td>
<td>21(2, 155)</td>
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<tr>
<td></td>
<td>Alistipes</td>
<td>726(9, 14813)a</td>
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<tr>
<td></td>
<td>Butyrivibrio</td>
<td>434(131, 1064)b</td>
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<tr>
<td></td>
<td>Parabacteroides</td>
<td>22(4, 80)b</td>
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<td></td>
<td>Paraprevotella</td>
<td>60, 312a</td>
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<td>Faecalibacterium</td>
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<td>Odoribacter</td>
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<td>Odoribacter</td>
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Indication: IBS-P, IBS with SIBO; IBS-N, IBS without SIBO; HC, health controls; NS, no significance; a, compared with HC, p < 0.05; b, compared with IBS-N, p < 0.05

**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 in 6-hour urine], systematic inflammation severity (IL-10, IL-12 and IL-10/IL-12), and Coeliac disease screening.

Result: 22 HC and 84 IBS-D patients were enrolled. 35 patients were with SIBO (41.67%) and 49 patients were IBS-N. (1) The body mass index of IBS-D was lower than that in IBS-N [21.61 ± 0.57 vs. (23.44 ± 0.54) kg/m², P < 0.05]. (2) The IL-12 was higher in IBS-N than IBS-P and HC [2360.24(972, 85, 3168.88) vs. 1263.40(482.55, 1965.99) pg/mL, P < 0.05]. (3) The initial defecation threshold of IBS-P was lower than that in HC [17.91(12.00, 20.00) mmHg, P < 0.05], while both thresholds for initial sensory and defecation in IBS-N were lower than HC [1579(9.00, 28.00) mmHg, P < 0.05]. (4) The initial defecation threshold of IBS-P was lower than that in HC [17.91(12.00, 20.00) mmHg, P < 0.05], while both thresholds for initial sensory and defecation in IBS-N were lower than HC [1579(9.00, 28.00) mmHg, P < 0.05]. (5) The fecal SCFA, include acetate, pro-...
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 FMT in our Centre. Demographic, clinical, endoscopic, and follow-up data were collected. Repeat fecal infusions were administered 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 the 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 (28%) received infusions, for a total of 251 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 multivariate 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 repeat infusion was more common among patient who experienced a number or CDI recurrence of >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 = 0.001; 95% CI = 0.00–0.19, p = 0.003).

Conclusion: Among patients treated with FMT for rCDI, both PMC and poor/inadequate bowel preparation appear to be significant predictors of the need for recurrent FMT. Additionally, infusion of frozen material 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 14:00–15:30
ENDOSCOPIC TREATMENT OF COMPLICATIONS AFTER UPPER GI SURGERY – ROOM E2

OP243 ENDOSCOPIC BALLOON DILATION FOLLOWED BY STEROID INJECTION IN ANASTOMOTIC STRICTURES AFTER ESOPHAGECTOMY: 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 dilatons 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 recurrent stricture 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 nur-

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

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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2Gastroenterology And Endoscopy Unit, Digestive Disease Department, H Pavilon- Edourard Herriot Hospital, Lyon/France
3CHU Limoges Gastroenterologie, Limoges/France
4Dept. Of Digestive Gastroenterology, Herriot University Hospital Dept. de Hepato-gastro-enterology, Lyon/France

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/HGD 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 mm²/min for a mean lesion size of 61.6mm. The clip provided considerable assistance in performing the procedure. No pathological damage caused by the clipping was reported.

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

Pathologic analysis

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<th>n</th>
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<th>Min</th>
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<tr>
<td>SCC</td>
<td>14 (42.4%)</td>
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<tr>
<td>ADK/DHG</td>
<td>19 (57.6%)</td>
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Discussion: First study of the strategy "tunnel + clip". Our en bloc and R0 resection rates confirmed the usefulness of this technique, despite the relative inexperience of the operators. Our resection results 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, reduces 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 F1

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 hyperplastic and adenomatous colorectal lesions by using the novel BLI technology. Secondary 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 hyperplastic 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 diagnosis of colorectal polyps. The proposed classification allowed for adequate in vivo diagnosis of hyperplastic 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


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 samples 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 this meant that patients send in their stool sample for laborato- ry 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 activi- ties 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 controlling the phone’s camera. Once the test is

BIOMARKERS IN IBD – ROOM K

TUESDAY, OCTOBER 18, 2016 14:00–15:30

OP248 MANAGEMENT OF DIMINUTIVE, RECTOSIGMOID POLYPS BY USING COMPUTER-SIZED DIAGNOSTIC SYSTEM

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Introduction: The PIVI initiatives propose that a “leave in place” approach is advocated for a diminutive (<5 mm), rectosigmoid hyperplasic 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 clinical decisions. We used a supportive 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 endoscopy 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 were diagnosed with high confidence.

Result: Of the 65 diminutive rectosigmoid polyps (mean size, 3.6 ± 1.0 mm), 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 34 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

measured the result is instantly sent to a webserver (IBDoc Portal) allowing the telemedicine personnel to access the test result. IBDoc® has achieved CE/IVD mark for self-testing in March 2015 and has since then been in routine use by patients throughout Europe and overseas. We have gathered data concerning technical performance of the device in the hands of both professional and lay users, as well as usability aspects for patients.

Result: In a direct method comparison with an existing point-of-care test (Quantum Blue®) and a laboratory based ELISA method (BUHLMANN fCAL ELISA) IBDoc® correlated very well with both methods with a mean bias at cut-off of 0.4% in regard to repeatability and preciseness the smartphones as measuring devices alone showed a coefficient of variability of below 10%, while the entire method including pre-analytical steps showed a coefficient of variability between 16% and 24%. IBDoc® displays results as Normal/green (below 100µg/g mean bias at cut-off, -7.0 to 5.4%), Moderate/amber (100-300µg/g) and as High/red (above 300µg/g, mean bias at cut-off, 1.1-6.5%). No false positive or false negative results (Normal/green instead of High/red and vice versa) were observed when lay-users performing the test were compared to professional users. A 97% with 95% confidence interval of agreement observed. The test result of the entire IBDoc® system as extremely user friendly with a mean of 93 points (out of 100) on a standardized System Usability Scale (SUS) score1,2,3.

Conclusion: IBDoc® is the first Calprotectin Home Test available for patients. IBDoc® is well accepted by patients and health care providers and correlates well to existing calprotectin point-of-care and laboratory based methods and has proven to be a supportive tool in daily clinical routine.

Disclosure of conflict of interest: Reinhard: Christian Reinhard is an employee of BUHLMANN Laboratories AG

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Introduction: 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 subtypes and disease course. We also wanted to compare the value of

**OP249 A COMBINATION OF THE MONITOR IBD AT HOME QUESTIONNAIRE AND A CALPROTECTIN HOME TEST AS AN EXCELLENT SCREENING TOOL FOR MUCOSAL INFLAMMATION IN IBD PATIENTS**

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Introduction: Telemedicine programmes are of interest for 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 Unit for a clinical history compatible with IBD were enrolled during a 3-year period. All underwent FC (Calprotectin®, Eurodial), 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 >3mm, 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 analyzed according to the final diagnosis.

Results: 100 patients (58 males, median age 12) were enrolled. The final diagnosis was IBD in 69 (57 CD, 12 CU) 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<0.01), BWT (OR 20.4, p<0.001) and ESR (OR 9; p<0.01). 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>
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<tr>
<td>FC (µg/g)</td>
<td>94</td>
<td>89</td>
<td>94</td>
<td>89</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>75</td>
<td>89</td>
<td>93</td>
<td>65</td>
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<td>BWT (mm)</td>
<td>94</td>
<td>83</td>
<td>88</td>
<td>57</td>
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<td>2 (at least 2 of 3)</td>
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<td>84</td>
<td>97</td>
<td>92</td>
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<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.

**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 subtypes and disease course. We also wanted to compare the value of
serological markers with the biochemical markers C-reactive protein (CRP), elevated sedimentation rate (ESR) and fibrinogen. 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 specimens 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 au courtesy of the treating pediatrician. Tumor necrosis factor (TNF) blocker treatment was regarded as aggressive treatment compared to conventional therapy.

**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, whereas 5 (45%) of the CD patients were ASCA IgA or IgG positive (< 0.0001), 18 (49%) were positive for ASCA IgA, 14 (38%) for ASCA IgG, and 12 (33%) for both. There were statistically significant differences between CD and UC patients in the prevalence of antibodies against *Pseudomonas fluorescens* asco- cci (p = 0.01) and IBD, 35 (70%) of the CD patients and intra-stool variability defined as the variability between 2 stool samples of the same patient a few days apart were both examined. Intra-stool variability was measured by dividing the coefficient of variation (CV) between the 3 punches of a stool sample. Inter-inter-individual CV was also measured.

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

**References**


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**OP252 ANALYTICAL PERFORMANCE OF A NEW IPHONE-BASED PATIENT MONITORING SYSTEM COMPAREABLE TO ELISA FOR MEASURING FECAL CALPROTECTIN IN IBD PATIENTS**

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**Introduction:** Inflammatory bowel diseases (IBD) are chronic intestinal inflammatory disorder presenting with stages of active inflammation, remission and relapse. Fecal calprotectin (fcalpro) measurement has become established for the monitoring of inflammation activity. Periodical assessment of fcalpro levels has confirmed the therapeutic importance of the calprotectin measurement in monitoring disease activity, predicting relapse and efficacy and predictor of relapse. However, until now, faecal determination required patients to send stool samples in for laboratory analysis, resulting in a long delay between sample collection and final test results. We developed a new smartphone-based calprotectin test system called QuantOnCal to allow patients to regularly monitor their own inflammatory status by testing fcalpro levels in the comfort of their own home.

**Aims & Methods:** QuantOnCal consists of a stool extraction device (IDK® Extract) and an immunochromatographic rapid test performed by an iPhone App via the phone camera. Results are automatically sent to a webserver (QuantOnCal website), where they are displayed for monitoring by the consultant physician or IBD nurse. The objective of this study was to validate the QuantOnCal test system by comparing its quantitative performance with a standard ELISA-based method. Stool samples from 157 IBD and non-IBD patients containing various levels of calprotectin (95 IBF: CUC/CD/active/emission, 42/43:48:47; 33 IBS: 23 Chm: 6 Div) were either loaded onto immunochromatographic test cassettes (TCs) or analysed with a commercial ELISA test (Innundagnostik, Bensheim, Germany). The QuantOnCal app was installed on different smartphone models (iPhones 4, 4s, 5c, 6). Agreement between QuantOnCal testing versus ELISA was assessed by Analyse-it for Microsoft Excel.

**Result:** The QuantOnCal system produces a quantitative test result between 25-2000 mg/g fcalpro of stool, covering the clinically relevant range of this biomarker. The total agreement (TA) was 94.6% with 0% false positive and 0% false negative rates. The TA for faclpro between the 4 different iPhone models was 91.3%.

**Conclusion:** QuantOnCal is a new, complete and validated test system which allows the IBD patient to monitor his own inflammatory status by measuring the IBD biomarker, faecal calprotectin, using his/her own smartphone. The performance of the QuantOnCal test system was shown to be comparable to the professional, ELISA-based method.

**Disclosure of Interest:** K.F. Wintgens: Karl Florian Wintgens is an employee of Innundagnostik AG, Bensheim, Germany. J. Stein: Jürgen Stein has received payment for lectures and consultancy from Innundagnostik AG, Bensheim, Germany.
A randomised, placebo-controlled trial of biofeedback for the treatment of abdominal distension

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**Disclosure of Interest:**

**Conclusion:**

**Aims & Methods:** Our aim was to demonstrate the feasibility of biofeedback treatment on abdominal distension and to assess its therapeutic benefits.

**Conclusion:** We found that biofeedback treatment substantially relieved abdominal distension and improved bowel function in patients with functional abdominal pain. Our results suggest that biofeedback may be an effective treatment option for patients with this condition.

**References:**

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**Introduction:** Irritable bowel syndrome (IBS) is the most common gastrointestinal (GI) disorder worldwide. In the lack of cures, different management strategies have been utilized, including a diet low in FODMAPs (fermentable oligo-, di-, monosaccharides and polyols) is increasingly being advocated in patients with functional gastrointestinal disorders (FGID).

**Aims & Methods:** In this study the predictive associations between clinical characteristics, breath test results and the global outcome measure advocated in FGID were examined. Clinical characteristics and breath test results from 580 IBS patients presenting with FGID (Rome III) and fructose or lactose intolerance, and completing a standardized FODMAP dietary program were analyzed. Intolerance was defined by a positive symptom index and malabsorption by increases in H2 (>20 ppm) or CH4 (>10 ppm) values during breath testing.

**Result:** Adequate symptom relief was achieved in 81% of the 580 FGID patients, with a positive response rate of patients with fructose (79%) and lactose (79%) intolerances and across all FGID subtypes (IBS-diarrhea: 80%, IBS-constipation: 71%, IBS-mixed: 89%, FD: 79%). A positive history of chronic diarrhea or pruritus predicted adequate symptom relief with the FODMAP diet (univariate analysis: 85% (95% CI): 2.96 (1.83-4.79) and 2.50 (1.74-3.92), respectively, both p < 0.01), while nausea predicted inadequate relief (0.55 (0.34-0.89), p = 0.01).

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

**References:**


**OP254 LOW FODMAP DIET ALTERS SYMPTOMS, MICROBIOTA, SHORT-CHAIN FATTY ACIDS AND CYTOKINE PROFILES IN PATIENTS WITH IBS: A RANDOMIZED CONTROLLED TRIAL**


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**Introduction:** Irritable bowel syndrome (IBS) is the most common gastrointestinal (GI) disorder worldwide. In the lack of cures, different management strategies have been utilized, including a diet low in FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides and polyols). Although being increasingly advocated as one of the most effective therapies, there is insufficient high-quality evidence of its efficacy as well as uncertainties regarding long-term consequences on gut microbiota composition and function.

**Aims & Methods:** In the present study we aimed to investigate the effect of a low versus high FODMAP diet on symptoms, put microbiota, short-chain fatty acids (SCFAs) and pro-inflammatory cytokine profiles in a randomized, double-blinded, crossover trial of Norwegian patients with IBS. Twenty patients with IBS (15 female; 5 male, mean age 34.6 y) were instructed to follow a low FODMAP diet (LFD) throughout a study period of 9 weeks. After 3 weeks they were randomized and double-blindly assigned to receive a daily supplement of either high (16 g fructo-oligosaccharides (FOS)) or low (16 g maltodextrin (=placebo)) FODMAP for the next 10 days, followed by a 3-week washout before crossing-over to the alternative supplementation for 10 new days. IBS Severity Scoring System (IBS-SSS) was used to evaluate symptoms. Blood samples were collected to analyse serum cytokines (IL-6, IL-8, TNF-α), and faeces samples for gut microbiota (16r RNA) and SCFAs.

**Result:** IBS symptoms consistently and significantly improved after 3 weeks of LFD, with a mean overall reduction of 16.8 points (p < 0.001). On average, 4 of 5 symptoms were significantly worsened in response to FOS compared with placebo, with an overall difference of 65.1 points (p = 0.014). Serum levels of IL-6 and IL-8, but not TNF-α, significantly decreased on the LFD (p = 0.01 and p < 0.001, respectively). The same did apply to luminal pH and faecal bifidobacteria (p = 0.0094 and p = 0.0094, respectively). Levels of total SCFAs and butyric acid were also significantly decreased on the LFD (p = 0.04 and p = 0.01, respectively). Ten days of FOS supplementation normalized ileal bacterial growth (Bacteroides) and restored luminal pH and bifidobacteria. Conclusion: FODMAP content was related to IBS symptoms, cytokine levels and microbiota composition and function. Our results provide evidence to support the efficacy of a LFD in reducing functional GI symptoms. Further studies are warranted to explore the link between FODMAPs, gut microbiota and immune activation.

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

**References:**


**OP255 PREDICTORS FOR THE OUTCOME OF THE FODMAP DIET IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS**

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**Introduction:** The reduction of potentially fermentable carbohydrates collectively termed FODMAPs (fermentable oligo-, di-, monosaccharides and polyols) is increasingly being advocated in patients with functional gastrointestinal disorders (FGID). At present, selection criteria or response predictors for dietary intervention are poorly defined.

**Aims & Methods:** In this study the predictive associations between clinical characteristics, breath test results and the global outcome measure advocated in FGID were examined. Clinical characteristics and breath test results from 580 IBS patients presenting with FGID (Rome III) and fructose or lactose intolerance, and completing a standardized FODMAP dietary program were analyzed. Intolerance was defined by a positive symptom index and malabsorption by increases in H2 (>20 ppm) or CH4 (>10 ppm) values during breath testing.

**Result:** Adequate symptom relief was achieved in 81% of the 580 FGID patients, with a positive response rate of patients with fructose (79%) and lactose (79%) intolerances and across all FGID subtypes (IBS-diarrhea: 80%, IBS-constipation: 71%, IBS-mixed: 89%, FD: 79%). A positive history of chronic diarrhea or pruritus predicted adequate symptom relief with the FODMAP diet (univariate analysis: 0.04). No other significant associations between symptoms experienced during fructose or lactose breath testing and dietary outcome were demonstrated.

**Conclusion:** Adequate global symptom relief with a FODMAP diet is achieved in a large majority of all FGID patients with fructose or lactose intolerance, and is predicted by a few clinical and breath-test associated symptoms and not by the presence of malabsorption. Consequently, a reduction of FODMAPs appears to modulate multiple physiological processes across the spectrum of FGIDs. 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.

**References:**


**OP256 A RANDOMIZED TRIPLE BLIND CONTROLLED TRIAL ASSESSING THE EFFECTS OF DOXEPIN AND NORTRIPTYLINE ON DIARRHEA-PREDOMINANT IRritable BOWEL SYNDROME**

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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(10 mg), nortriptyline(10 mg) 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.
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

OP257 TREATMENT OF IRRITABLE BOWEL SYNDROME WITH FECAL MICROBIOTA TRANSPLANTATION: A CASE SERIES OF 10 PATIENTS

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Introduction: Irritable bowel syndrome (IBS) is commonly diagnosed gastrointestinal disease worldwide. The pathogenesis of IBS cannot be explained by a simple mechanism, but alterations in the intestinal microbiome are increasingly a focus of interest. Traditional treatments of IBS, including psychological therapies, dietary change, probiotics, have had only limited success, underscoring the need for additional therapeutic options. We hypothesized that fecal microbiota transplantation (FMT) may be beneficial in managing IBS by restoring the intestinal homeostasis. The purpose of this study is to prospectively examine the symptomatic response of FMT in patient with moderate IBS.

Aims & Methods: Patients with IBS who were not responsive to traditional treatment were enrolled prospectively in this study. Diagnosis of IBS was based on Rome III Criteria and nonresponsive IBS was defined as failure to demonstrate sustained response over 6 months. The efficacy of FMT over longer treatment intervals was evaluated over 12 and 26 weeks. Composite endpoint response rates over Weeks 1–12 and 1–26 were calculated for patients who were responders and non-responders over Month 1 (Weeks 1–4) using a pooled analysis of the intent-to-treat (ITT) population. Comparable analyses for adequate relief were conducted, for which a responder was defined as reporting a ‘yes’ response to the question “Over the past week have you had adequate relief of your IBS symptoms?” for >50% of weeks in the treatment interval.

Result: The pooled ITT analysis set included 2423 patients with IBS-D. Over Month 1, 12.5% (309/2488) of patients were composite responders in the placebo, ELX 75 mg, and ELX 100 mg groups, respectively. Over Month 1, 49.3% (399/809), 59.9% (484/808), and 61.8% (498/806) of patients were adequate relief responders in the placebo, ELX 75 mg, and ELX 100 mg groups, respectively. For both ELX doses, the majority of patients who were composite or adequate relief responders over Month 1 showed sustained response over Weeks 1–12 and 1–26 (Table). Of the patients who were not composite or adequate relief responders in Month 1, approximately 13–18% subsequently achieved adequate response over 6 months.

Conclusion: Approximately two-thirds of patients who achieved either the composite or adequate relief endpoint over the first month of ELX treatment demonstrated sustained response over 6 months. Disclosure of Interest: W.D. Chey: Dr Chey: Research support: Ironwood, Nestle, Protemeheus; consultancy: Allergan plc, Ironwood, Nestle, Protemeheus, Valeant, Sucampvo, Takeda; patents: My GI Health, My Nutrition Health; co-founder: My Total Health.
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L.S. Dve: Dr Dve: former employee of Furiex Pharmaceuticals, an Allergan affiliate.
C.R. Gutman: Dr Gutman: employee of Allergan plc.
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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>
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<tr>
<td>Non-responder</td>
<td>101 (12.5)</td>
<td>708 (87.5)</td>
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<td>150 (18.5)</td>
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</tr>
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<td>Non-responder</td>
<td>405 (83.7)</td>
<td>79 (16.3)</td>
<td>419 (84.1)</td>
</tr>
<tr>
<td>Non-responder</td>
<td>341 (70.5)</td>
<td>143 (29.5)</td>
<td>364 (73.1)</td>
</tr>
<tr>
<td>Non-responder</td>
<td>278 (69.7)</td>
<td>121 (30.3)</td>
<td>134 (26.9)</td>
</tr>
</tbody>
</table>

BID, twice daily; ELX, eluxadoline

aPercentage calculated based on number of patients who were composite responders over Weeks 1–4

bPercentage calculated based on number of patients who were adequate relief responders over Weeks 1–4

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

OP258 1-MONTH TREATMENT WITH ELUXADOLINE FOR IBS-D PREDICTS SUSTAINED RESPONSE: CONTINUATION ANALYSES OF RESPONSE IN TWO PHASE 3 STUDIES

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Introduction: Eluxadoline (ELX), a mixed μ-opioid receptor (OR) and κ-OR and Δ-OR antagonist that is locally active in the gastrointestinal tract, is approved for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults. In two Phase 3 studies, ELX significantly improved symptoms of IBS-D based on a composite endpoint, defined by simultaneous improvement in stool frequency and reduction in abdominal pain scores, and the historical ‘adequate relief’ endpoint. Given the potential long-term use of eluxadoline treatment, it is important to understand the time course of clinical benefits as experienced by patients and clinicians, including time to onset and the sustainability over time, to establish reasonable expectations about the effectiveness of treatment.

Aims & Methods: The efficacy of ELX over longer treatment intervals was investigated in patients who were responders or non-responders for the composite endpoint or adequate relief endpoint over the first month of the Phase 3 treatment. Two double-blind, placebo-controlled, Phase 3 clinical trials (IBS-3001 and IBS-3002) randomised patients meeting Rome III criteria for IBS-D to twice-daily treatment with ELX (75 or 100 mg) or placebo. Patients rated IBS symptoms, including worst abdominal pain (WAP) score and stool consistency (Bristol Stool Scale [BSS]). The primary efficacy endpoint was composite response, based on simultaneous daily improvement of ≥30% in WAP score vs. baseline and BSS score ≤5, with ≥50% of days demonstrating a response, evaluated over 12 and 26 weeks. Composite endpoint response rates over Weeks 1–12 and 1–26 were calculated for patients who were responders and non-responders over Month 1 (Weeks 1–4) using a pooled analysis of the intent-to-treat (ITT) population. Comparable analyses for adequate relief were conducted, for which a responder was defined as reporting a ‘yes’ response to the question “Over the past week have you had adequate relief of your IBS symptoms?” for ≥50% of weeks in the treatment interval.

Result: The pooled ITT analysis set included 2423 patients with IBS-D. Over Month 1, 12.5% (101/809), 22.8% (184/808), and 24.6% (196/806) of patients were composite responders in the placebo, ELX 75 mg, and ELX 100 mg groups, respectively. Over both ELX doses, the majority of patients who were composite or adequate relief responders over Month 1 showed sustained response over Weeks 1–12 and 1–26 (Table). Of the patients who were not composite or adequate relief responders in Month 1, approximately 13–18% subsequently achieved response over 6 months.

Conclusion: Approximately two-thirds of patients who achieved either the composite or adequate relief endpoint over the first month of ELX treatment demonstrated sustained response over 6 months.

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OP259 HUMAN PLURIPOTENT STEM CELL-DERIVED EXOCRINE/ DUCTAL ORGANOID MODELLING AND DELIVERY OF GEMCITABINE TREATMENT

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Introduction: Exocrine/ductal pancreatic differentiation from human pluripotent stem cells is a poorly understood process albeit various diseases arise from this compartment.

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 ultrastructural 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-meditated 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.

OP260 CANCER ASSOCIATED FIBROBLASTS (CAF) SEQUESTRATION GEMCITABINE TO INCREASE INTRATUMORAL DRUG DELIVERY IN PAPILLARY MUCINOUS NEOPLASMS

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Introduction: The pronounced tumour stroma in pancreatic cancer has recently been appreciated as physical barrier impeding delivery of therapeutic agents. Herein, we aim to investigate the delivery of gemcitabine metabolites in primary pancreatic tumours and matched liver metastases and dissect stromal and neoplastic compartments.

Aims & Methods: The cellular and acellular tumour stroma was assessed in human and mouse primary tumours and matched liver metastases. Gemcitabine metabolites were analysed in LSL-KrasG12D/+;LSL-Tp53R172H/-; Pdx-1Cre (KPC) tumours and matched liver metastases, primary tumour cell lines, cancer associated fibroblasts (CAF), and pancreatic stellate cells (PSC) by liquid chromatography- mass spectrometry/mass spectrometry (LC-MS/MS).

Result: Analysis of gemcitabine metabolite pathways was performed in vitro and in vivo. Viability of CAFs was assessed in vitro following a preclinical trial in the KPC model.

Future: Fibroblast density and collagen deposition were significantly reduced in CAFs and mouse liver metastases as compared to matched primary tumours. Gemcitabine (dFdC) and its active metabolite dFdCTP were significantly higher in stroma rich tumours compared to stroma poor liver metastases and normal liver. Mean vessel density did not correlate with gemcitabine delivery at pharmacodynamically relevant endpoints. In cell culture, significantly increased concentrations of activated dFdC and greatly reduced levels of the inactive gemcitabine metabolite dFUdR were detected in PSCs and CAFs. Importantly, key metabolite enzymes for gemcitabine inactivation such as deoxycytidine deaminase (Dctd), cytidine deaminase (Cda) and hydrolytic cytosolic 5'-nucleotidases (Nt5cs1a, Nt5cs3) were differentially expressed in PSCs and CAFs. Moreover, treatment of KPC mice revealed intrinsic resistance of CAFs to gemcitabine.

Conclusion: Our findings suggest that CAFs sequester gemcitabine and thus may contribute to the clinical failure of this drug in desmoplastic pancreatic cancer. Therefore, metabolic engineering of CAFs may constitute a promising new avenue to enhance the cytotoxic effects of gemcitabine in patients.

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

References
TUESDAY, OCTOBER 18, 2016 14:00–15:30

INTESTINAL FAILURE: FROM PATHWAYS TO TREATMENT – ROOM 17

OP262 NOVEL GENE MUTATIONS IN NEUROGENIC CHRONIC INTESTINAL PSEUDO-OBSTIPATION

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Introduction: Chronic intestinal pseudo-obstruction (CIP) 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 RAB21 gene in a recessive form of familial CIP1. RAB21 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 subgroup of patients with pseudo-obstruction 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 trials and 3 sporadic cases) with chronic, radiological and manometrically well-defined CIPO. A neurological work-up established SFN in each of them.

Results: Libraries were enriched with the Nimblegen SeqCap EZ v3.0 and sequenced via pair-end 50 bp reads on HiSeq2500 sequencer. Variants were annotated with the SeattleSeq137 Annotation Server. Additional 77 patients were sequenced via paired-end 50 bp reads on HiSeq2500 sequencer. Variants were classified with two rare/novel variants in Lipoprotein Related Receptor 2 (LRP2), that affected probands, since all the parents were healthy. We identified novel/rare (SFN), a condition affecting peripheral neurons including those of the autonomic system, associated with constipation and/or diarrhea. Among the mediators studied in cultured human DRG neurons, which were fixed thereafter, to study PAR activation with PAR1-AP, but not with PAR2-AP or any of the PAR-IP.

Conclusion: Our study demonstrates that PAR2, PAR1 and PAR4 are expressed in human sensory neurons. In contrast to PAR2 and PAR4, PAR1 activation increased calcium influx in human sensory neurons. PAR1 activation reproduced calcium mobilization seen in human DRG neurons. Hence, in Human Sensory Neurons PAR1 may 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, altered bowel function and/or diarrhoea. 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 role 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: Cyto-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 (pp9.5) and PAR antibodies. Calcium signaling responses to PAR-AP (TFLLR; 1, 10 and 100 μM), PAR-AP (SLIGRL; 100 μM) and PAR-AP (LYPKGF; 100 μM) were measured in isolated DRG neurons in the presence or absence of PAR-IP (100 μM) or proteases: trypsin (1 and 10 U) and thrombin (1 and 10 U) were studied in cultured human DRG neurons, which were fixed thereafter, to study PAR expression.

Conclusion: 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. PAR1-AP increased intracellular calcium concentration in a dose-dependent manner. This increase was inhibited by PAR1 antagonist (SCH79797, 10 μM). In contrast to PAR1-AP, PAR2-AP and PAR4-AP did not cause calcium mobilization. Thrombin (PAR2 and PAR4 agonist) did not trypsin (PAR2 and PAR4 agonist) increased calcium flux in human sensory neurons. PAR1-AP-induced calcium mobilization was significantly reduced by pre-incubation with PAR2-AP, but not with PAR4-AP or any of the PAR-IP.

Disclosure of Interest: All authors have declared no conflicts of interest.
patients who underwent small bowel or multivisceral transplants at the University’s Hospital, Cambridge, UK. There were 54 patients in total, 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-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 = 19). Primary outcomes: Out of the 30 long-term survivors, 73.3% (22/30) 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 (ONS: 2; EN: 18; except for 1 patient, 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 more than 2 kg/m² (SD = 3.4) in the last year (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). Survival outcome comparing BMI to 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 120.7 days). This suggests that the duration of 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.

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<th>OP266 SUBANALYSIS OF TREDUGLITIDE EFFICACY AND SAFETY DATA FROM PATIENTS WITH CROHN’S DISEASE AND ULCERATIVE COLITIS IN THE STEPS STUDY</th>
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<td>U. Pape1, P.B. Jeppesen1, H. Lee1, A. A. Grimm2, S. J. O’Keefe4</td>
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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 subanalysis compared response to treduglitide (TED) in patients with SBS-IF due to IBD (SBS-IBD) vs those with noninflammatory causes of SBS-IF (SBS-non-IBD). STEPS (NCT00798967, EndraCT2008-006193-15) was a 24-week, phase III, placebo-controlled study of 0.05mg/kg/day TED in patients with SBS-IF. Patients were included if they had a clinical remission for ≥12 weeks at baseline. Response was ≥a 20% 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 interval (CI); this post hoc analysis was not powered for statistical significance.

Result: The Table details patient characteristics (SBS-IBD, n = 19; SBS-non-IBD, n = 67). Patients with SBS-IBD had lower colon-incontinuity, higher stoma presence, and higher baseline PS volume than those with SBS-non-IBD. After 24 weeks, 73% (95% CI, 39%–94%) of patients with SBS-IBD 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-IBD 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-IBD, 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
Disclosure of Interest: A. J. Butler2, N. K. Russell2, S. J. Middleton1

Aims & Methods:
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2Transplant Surgery, Addenbrooke's Hospital, Cambridge/United Kingdom

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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 widespread splanchic ischaemia. Longstanding indications include complications of severe colitis, 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 is with Campath (Alemtuzumab) and maintenance initially containing graft require ratification at a national forum (NASIT). Grafts which include liver or kidney are also discussed at local listing committees. Induction immunosuppression is with Campath (Alemtuzumab) and maintenance initially

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 peri- toneal 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 cancer. All authors have declared no conflicts of interest.

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

Reference
OP269 GENETIC SUSCEPTIBILITY AND FAMILY HISTORY OF COLORECTAL CANCER: RELATIONSHIP TO PCID2 POLYMORPHISMS IN THE DEVELOPMENT OF COLORECTAL NEOPLASTIC LESIONS

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Introduction: The effect of SNPs with colorectal cancer (CRC) have been shown to have a 2- to 3-fold increased risk of developing CRC compared with the overall population. It is likely that CRC susceptibility in these individuals results from common variants in low-penetration genes. However, very little is known about the relevance of genetic variants in the development of colorectal neoplastic lesions according to the family history of CRC.

Aims & Methods: We aimed to evaluate the role of certain single nucleotide polymorphisms (SNPs) associated with CRC risk in the development of colorectal adenomas depending on the family history of CRC. We carried out a case-control study comprising 750 FDR of patients with non-syndromic CRC (cases), and 750 FDR of colorectal adenomas- matched individuals with no family history of CRC (controls). Cases and controls were selected from the Spanish CRC screening registries in Aragon and The Canary Islands. All subjects underwent at least one colonoscopy and diagnosis of adenoma was confirmed by histopathological study. Genomic DNA from cases and controls was genotyped by the MassArray™(Sequenom) platform for a panel of 99 SNPs previously associated with CRC risk. Genetic analysis was performed using the SNPassoc package implemented in R. To address the issue of multiple testing, the false discovery rate method and Bonferroni’s correction were applied.

Result: Average age of participants was 54.5±9.4 years with a slightly predominance of women (51.7%). In 57% of patients, no neoplastic lesions were found. By contrast, 288 patients (144 cases and 144 controls) showed non advanced adenomas (NAA), and 354 patients (177 cases and 177 controls) had advanced adenomas (AA). Concerning gene analysis, 2 SNPs (rs10505477 A>G and rs6893267 G>T) located in the CASCA gene were associated with the development of adenomas. Thus, the rs10505477G and the rs6893267T alleles were significantly associated with a reduced risk of developing colorectal adenomas in patients with a positive family history of CRC (controls) (log-additive models, OR: 0.67, 95% CI 0.50-0.94 and OR: 0.52, 95% CI: 0.34-0.75 for rs10505477, and OR: 0.52, 95% CI: 0.34-0.75 for rs11255841) and patients with no family history of CRC (dominant models, OR: 0.38, 95% CI: 0.21-0.67 for rs10505477, and OR: 0.32, 95% CI: 0.17-0.61 for rs6893267, suggesting their possible implication in early stages of CRC development.

Conclusion: Family history of CRC and some specific variants associated with CRC risk (rs10505477 and rs6893267) in CASCA gene and rs10795668 and rs4137370 in PCI2 were involved in the development of colorectal adenomas or specific histological subtypes.

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

OP270 A NOVEL AMPLIFICATIONGENE, PCID2 PROMOTES TUMORIGENICITY OF COLORECTAL CANCER THROUGH DIRECTLY TARGETING A TUMOR SUPPRESSOR PML AND IS ASSOCIATED WITH DISEASE RECURRENTCE

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Introduction: PCID2 gene amplification status in CRC tissues was revealed by high-throughput sequencing. We evaluated its amplification, overexpression, biological functions and clinical implication in CRC.

Aims & Methods: The PCID2 gene amplification status in CRC tissues was evaluated by Copy Number Assay. The biological effects of PCID2 overexpression and knockdown were determined by in vitro and in vivo tumorigenicity assays. The PCID2 interaction partner was identified by immunoprecipitation followed by mass spectrometry. PCID2 downstream effectors and signaling pathways were elucidated by promoter luciferase assay and co-immunoprecipitation. The clinical impact of PCID2 was assessed in three cohorts of 114 CRC patients from Beijing (cohort I), 46 CRC patients from Hong Kong (cohort II) and 376 CRC cases from TCGA dataset (cohort III).

Result: Amplification of PCID2 was detected in 32.5% (37/114) of CRC patients from cohort I and 62.2% (29/46) of CRC patients from cohort III by Copy Number Assay. The copy number gain was positively correlated with its mRNA overexpression both in cohort I ( r sq = 0.327, p < 0.0001) and in cohort III (r sq = 0.619, p < 0.0001). Biological functional investigation of PCID2 revealed that increased expression of PCID2 in colon cancer cell lines (DLD1 and HT29) significantly increased cell proliferation (p < 0.01 in DLD1 and p < 0.001 in HT29), G1-S cell cycle transition (p < 0.01 and p < 0.05, respectively), invasion (p < 0.01 and p < 0.01, respectively) and migration (p < 0.01 and p < 0.05, respectively), abilities, and suppressed cell apoptosis (p < 0.01 and p < 0.05, respectively). In addition, PCID2 significantly promoted xenograft tumor growth as well as lung metastasis in nude mice. On the other hand, knockdown PCID2 in colon cancer cell lines (HCT116 and SW480) showed opposite effects. Multivariate analysis revealed that patients with PCID2 overexpression were significantly correlated with CRC recurrence (p < 0.05 for cohort I, p < 0.03 for cohort II). Recurrence curves showed that PCID2 overexpression was a prediction marker for recurrence of patients with CRC (p = 0.004 for cohort I, p = 0.03 for cohort II).

Conclusion: PCID2 plays a pivotal oncogenic role in colorectal carcinogenesis by amplification and its downstream effectors and signaling pathways were elucidated by promoter luciferase assay and co-immunoprecipitation. PCID2 induced Wnt signaling pathway and inhibited p53/p21 pathway activity. PCID2 expression level was evaluated in clinical pathological samples and its impact on survival was assessed by Kaplan-Meier analysis. PCID2 overexpression was an independent recurrence prediction marker for CRC patients.

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

OP271 PREDICTION OF COMPLETE RESECTIONS AFTER CYTOREDUCTIVE SURGERY BASED ON THE EXTENT OF COLORECTAL PERITONEAL CARCINOMATOSIS


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Introduction: Patients with colorectal peritoneal carcinomatosis (PC) are considered to have a poor prognosis. New imaging techniques, such as positron emission tomography (PET)/CT scanning, are being developed to assess the resectability of colorectal peritoneal carcinomatosis (PC)."}

Aims & Methods: Our objective was to evaluate the relation between the completeness of cytoreduction and the Dutch seven region count evaluated with CT and during surgery. Patients who underwent abdominal CT-imaging for PC prior to CRS-HIPEC were eligible. The seven-point region count was assessed with CT by an experienced abdominal radiologist and peroperative evaluation was performed by the operating surgeon, based on the Dutch region count. The completeness of cytoreduction was scored after CRS. Survival was calculated from the date of initial surgery to death or last follow-up.

Result: Two hundred thirty-four patients were included. Patients with incomplete cytoreductive surgery had more often PC in five to seven regions during surgery (p < 0.001). This result was not found using de CT-related region count evaluated with CT prior to CRS-HIPEC. Patients with complete resection count of 114 CRC patients from Beijing (cohort I), 46 CRC patients from Hong Kong (cohort II) and 376 CRC cases from TCGA dataset (cohort III).

Conclusion: Patients with four or less involved abdominal regions with PC peroperative were more likely to have a complete resection. CT assessment of the region score could not accurately predict a complete resection. Patients with an incomplete cytoreduction showed better survival than patients with an incomplete cytoreduction.

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

OP272 PREVALENCE OF LYMPH NODE METASTASIS AND LONG-TERM SURVIVAL OF T1 RECTAL CARCINOID TUMORS: AN ANALYSIS OF SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS (SEER) DATABASE


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

Aims & Methods: We aimed to evaluate the role of certain single nucleotide polymorphisms (SNPs) associated with CRC risk in the development of colorectal adenoma...
OP274 ACCURACY OF A POINT SHEAR WAVE ELASTOGRAPHY TECHNIQUE (ELASTPQ) IN THE NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS IN A LARGE COHORT OF LIVER PATIENTS. M. Garcovici1, M. Pompiu2, E. Di Stasi3, L. Riccardi3, M.E. Ainora1, A. Griciuc1, G.L. Rapaccini1, M. Siciliano4, A. Gasbarrini1, M. Goccia1. 1Internal Medicine, Gastroenterology And Liver Diseases Unit, Catholic University of Sacred Heart - Policlinico Gemelli, Rome/Italy;2Institute Of Biochemistry And Clinical Biochemistry, University of Sacred Heart - Policlinico Gemelli, Rome/Italy;3Gastroenterology, Complexo Integrato Columbus - Catholic University, Rome, Italy;4Internal Medicine And Gastroenterology, Agostino Gemelli Hospital Dept. of Gastroenterology, Rome/Italy.

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Introduction: ElastPQ is a novel point shear wave elastography (PSWE) technique that assesses liver stiffness by measuring liver stiffness (kPa) in a large cohort of patients with chronic liver disease. The correlations between laboratory findings, liver stiffness and the Metavi score were analyzed using Spearman correlation and ROC curve analyses were performed to calculate AUC for F ≥ 2, F ≥ 3 and F = 4.

Result: We enrolled 289 patients (176/113 males/females) who underwent LB for viral chronic viral hepatitis (HCV 49%; HBV 32%; others – 20%) and 104/25 patients who underwent LB for non-viral chronic liver disease (NASH 90%; AIH/PBC 11%; viral – 9%). The patients were classified as follows: no fibrosis (F0), mild fibrosis (F1), significant fibrosis (F2), cirrhosis (F3) and 11–19 mm tumors with excellent long term outcomes.

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

Aims & Methods: Consecutive patients scheduled for LB were used by studying the AUC for F ≥ 2, F ≥ 3 and F = 4. The correlations between laboratory findings, liver stiffness and the Metavi score were analyzed using Spearman correlation and ROC curve analyses were performed to calculate AUC for F ≥ 2, F ≥ 3 and F = 4.

Result: We enrolled 289 patients (176/113 males/females) who underwent LB for viral chronic viral hepatitis (HCV 49%; HBV 32%; others – 20%) and 104/25 patients who underwent LB for non-viral chronic liver disease (NASH 90%; AIH/PBC 11%; viral – 9%). The patients were classified as follows: no fibrosis (F0), mild fibrosis (F1), significant fibrosis (F2), cirrhosis (F3) and 11–19 mm tumors with excellent long term outcomes.

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

Aims & Methods: To date this is the largest case series comparing the accuracy of ElastPQ technique. This novel PSWE system appears to be a very useful tool for non-invasive evaluation of liver fibrosis not only in patients with viral chronic hepatitis, but also for patients with different liver diseases. In order to validate such a non-invasive technique these findings need to be confirmed in larger studies comparing different elastography devices. All authors have declared no conflicts of interest.

Conclusion: In the majority of patients with a complete response residual fibrosis is present post-chemoradiotherapy which remains unchanged during long-term follow-up in almost all patients. A completely normalised wall is observed in approximately 1 in 10–20 patients. The findings of this study may serve as a reference and provide teaching for radiologists involved in the clinical follow-up of patients treated for rectal cancer treated with chemoradiotherapy. Dis Colon Rectum 2011; 4(12): 1521-8.
elastographic reference method: Transient Elastography (TE)- FibroScan, Echosense. Reliable LS, t, and cut-off values were defined as follows: for 2D-SWE: the median value of 10 measurements acquired in a homogenous area and an interquartile range (IQR) < 30% (1), for 2D-SW- SSE: the median value of 3 measurements acquired in an homogenous area. The interquartile range of the median values of the 10 measurements with a success rate of > 60% and an interquartile range < 30% (3). 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 stiffness 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.GE and TE. The values ranged from 4.17 to 20.48 kPa for 2D-SWE and 2.94 to 8.24 kPa for 2D-SWE.SSI. The mean LS values by 2D-SWE-GE were significantly higher than for 2D-SWE: 19.12±3.4 kPa vs. 12.1±3.7 kPa (p < 0.0001). There was a significant correlation between 2D-SWE.GE and 2D-SWE.SSI LS values (r = 0.712, p < 0.0001). The correlation between 2D- SWE.SSI and TE was r = 0.746, p < 0.0001 and between 2D-SWE-GE and TE was r = 0.604, p < 0.0001 with no significant differences between them (p = 0.0565). Taking TE as the reference method, both 2D-SWE.SSI and 2D-SWE.GE 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 fibrosis was > 13.7 kPa with 88.37% sensitivity, 75.68 Sp, 87.3 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, 2D-SWE.GE had 91.43% Se, 78.38 Sp, 89.8 PPV, 82.9 NPV (AUROC = 0.904, p < 0.0001) for differentiating liver cirrhosis. The AUROCs of 2D-SWE.SSI and 2D-SWE.GE for predicting the presence of liver cirrhosis were similar (p = 0.09).

Conclusion: Both 2D-SWE techniques have a very good feasibility for the non-invasive liver fibrosis assessment and both have a strong correlation with TE. Liver stiffness values obtained by 2D-SWE.GE are significantly lower than those obtained by 2D-SWE.SSI. Both methods have good performance for predicting liver cirrhosis.

Disclosure of Interest: I. Sporea: Ioa Sporea participated in an Advisory Board for Siemens and received speaker fees from Philips, Siemens and General Electric R. L. D. Sirl received speaker fees from Philips A. Popescu: Alina Popescu received speaker fees from Philips All other authors have declared no conflicts of interest.

References
References


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United European Gastroenterology Journal 4(5S)
regain clinical response. Detailed documentation of disease activity was reviewed.

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 mercaptourine 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 also 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 6–28). All patients receiving MTX responded clinically which resulted in continuation of the ongoing anti-TNF treatment.

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 Abbott laboratories, Merck Schering-Plough Pharmaceuticals and M. Lowenberg: M. Lowenberg 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 Schering-Plough for healthcare and lithium.

G. D’Haens: G. D’Haens reports having received consulting fees from AbbVie, Boehringer, Ferring, Janssen Biologies, Merck Sharp & Dohme, Takeda, Pfizer, Tillots Pharma and reports receiving research grants from Abbott Laboratories, Janssen Biologies, MSD, DrFalk Pharma. All other authors have declared no conflicts of interest.
Introduction: Currently available methods for small bowel endoscopy are complex to use and time consuming. Novel Motorized Spiral Endoscopy (NMSE) containing a proton pump inhibitor, bismuth, clarithromycin and amoxicillin (PPI+BS+CA+AM) has been developed. The diagnostic yield of NMSE was 83.4% corresponding to no findings in 5 patients (biopsies n=17, tattooing n=12, 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=3). Mean withdrawal time without interventions was 14.7 [4–54] 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.

OP28 CROSS-SECTIONAL EVALUATION OF TRANSMURAL TREATMENT WITH BIOLOGICS

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Introduction: Transmural healing (TH) of Crohn’s disease (CD) is a new under-explored and interesting outcome of the concept of deep remission.

Aims & Methods: The aim of this study was to assess the rate of TH evaluated by bowel sonography (BS) and magnetic resonance enterography (MRE) in CD patients treated with biologic therapy compared to non treated patients.

We performed a 2-year observational longitudinal prospective study evaluating steroid-free clinical remission (CR), mucosal healing (MH), and TH in all patients with CD who would complete a 2-year period of maintenance treatment with biologics. All patients underwent endoscopy, BS and MRE before starting biologics and 2 years later. Furthermore, the Crohn’s Disease Activity Index (CDAI) score was calculated before treatment and 2 years later. Result: The study included 40 CD patients biologies (38 infliximab and 62 adalimumab). TH was evident in 10 patients (25%) at BS and in 9 patients (23%) at MRE (k = 0.84; P = 0.01). No significant differences were noted about TH in relation to the type of biologic used (P = NS). MH was obtained in 14 subjects (35%). A good agreement was observed between MH and TH at BS (k = 0.43; P = 0.5; TH at BS) and TH at MRE (k = 0.64; P = 0.001; CR). CR was achieved in 24 patients (60%). A poor agreement was found between CR and TH, both at BS and MRE (k = 0.27 and 0.29, respectively; P < 0.01).

Conclusion: TH can be reached in about 25% of CD patients treated with biologic therapy, with high agreement between BS and MRE on defining this outcome. Also considering the advantages of BS (high diagnostic accuracy, low costs, high patient compliance, high availability) and the limitations of MRE (high costs, low availability), we suggest the use of BS as first cross-sectional procedure in defining TH in patients with CD.

Disclosure of Interest: All authors have declared no conflicts of interest.
**Table 1 (OP288): Association between number of pathophysiologial alterations and Patient Reported Outcomes (data shown as mean ± SD)**

<table>
<thead>
<tr>
<th>Alterations</th>
<th>No abnormality (n = 76)</th>
<th>1 abnormality (n = 128)</th>
<th>2 abnormalities (n = 121)</th>
<th>&gt;3 abnormalities (n = 82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS symptom severity (z score)</td>
<td>−0.55 ± 0.94</td>
<td>−0.22 ± 1.06</td>
<td>0.11 ± 0.96</td>
<td>0.37 ± 0.86</td>
</tr>
<tr>
<td>Somatic symptom severity (z score)</td>
<td>−0.47 ± 0.80</td>
<td>−0.30 ± 0.93</td>
<td>0.17 ± 0.99</td>
<td>0.68 ± 0.98</td>
</tr>
<tr>
<td>IBSQOL Emotional</td>
<td>60 ± 19</td>
<td>55 ± 24</td>
<td>44 ± 17</td>
<td>47 ± 7</td>
</tr>
<tr>
<td>IBSQOL Mental Health</td>
<td>52 ± 16</td>
<td>76 ± 22</td>
<td>65 ± 20</td>
<td>51 ± 20</td>
</tr>
<tr>
<td>IBSQOL Sleep</td>
<td>52 ± 16</td>
<td>76 ± 22</td>
<td>69 ± 24</td>
<td>58 ± 24</td>
</tr>
<tr>
<td>IBSQOL Energy</td>
<td>69 ± 24</td>
<td>58 ± 27</td>
<td>48 ± 24</td>
<td>35 ± 23</td>
</tr>
<tr>
<td>IBSQOL Physical Functioning</td>
<td>75 ± 20</td>
<td>74 ± 21</td>
<td>68 ± 20</td>
<td>57 ± 26</td>
</tr>
<tr>
<td>IBSQOL Food</td>
<td>67 ± 20</td>
<td>64 ± 21</td>
<td>59 ± 18</td>
<td>55 ± 20</td>
</tr>
<tr>
<td>IBSQOL Social Role</td>
<td>71 ± 20</td>
<td>65 ± 23</td>
<td>62 ± 20</td>
<td>51 ± 24</td>
</tr>
<tr>
<td>IBSQOL Physical Role</td>
<td>64 ± 28</td>
<td>56 ± 31</td>
<td>47 ± 29</td>
<td>40 ± 28</td>
</tr>
<tr>
<td>IBSQOL Sexual</td>
<td>71 ± 23</td>
<td>70 ± 25</td>
<td>63 ± 25</td>
<td>50 ± 25</td>
</tr>
</tbody>
</table>

**TUESDAY, OCTOBER 18, 2016**

**COELIC DISEASE FOR THE CLINICIAN – ROOM F1**

**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 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:** Thirteen patients with newly diagnosed CD: 9 women and 4 men (mean age 41.96 ± 13.15 years; mean CD duration of 15.75 years) and 19 patients with previously diagnosed CD: 22 women and 4 men (mean age 41.96 ± 18.46 years) were observed. The diagnosis of CD was based on clinical presentation, serology, including anti-tissue transglutaminase (anti-tTG) IgA antibodies and duodenal biopsy. Histological changes of intestinal biopsy were classified according to the revised Marsh criteria 1999. In 1 group Marsh IIIb lesions were seen in 23%, Marsh IIIc – in 77%. In 2 group - Marsh IIIa and Marsh IIIb lesions were seen in 30% respectively, Marsh II - in 13.3%, the normal structure of small intestine was observed in 26.6%. The enzyme activity was measured in small intestine mucosa by Dahlquist modified method.

**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 < 0.002). It was found that the total atrophy (Marsh IIIc) was associated with a reduced activity of lactase, 90% had a decreased activity of glucoamylase and sucrase, 85% of patients with Marsh IIa small intestine mucosa had an reduced activity of lactase and sucrase. A weak correlation between the degree of atrophy and the activity of enzymes was established. Activity of other enzymes had no significant correlation with the degree of atrophy.

**Conclusion:** In 37.5% of adult patients with CD who follow GFD and have a normal structure of mucosa, a decreased activity of intestinal enzymes may occur, which may be one of the reasons for the persistence of intestinal symptoms.

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

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**OP287 FODMAP RESTRICTION OF A GLUTEN-FREE DIET IN PATIENTS WITH COELIC DISEASE: A RANDOMIZED, CONTROLLED CLINICAL STUDY**

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**Introduction:** To determine 20-30% 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 GFD were randomized: Group A (normal vs. high FODMAP) and Group B (normal vs. low FODMAP diet).

**Result:** 20 patients were included in each group: A (18F/2M, age 39 ± 15.7 years) and B (15F/5M, age 43 ± 12.4 years). 42.5% had constipation, 42.5% had diarrhoea and 35% both. The mean total IBS-SSS score was significantly reduced: Group A from 258 to 163 (p = 0.0002), Group B from 258 to 163 (p = 0.0001), Group B vs. A. In group A 10% reached remission, in Group B 25% (p = 0.0012), but it was also more challenging to follow their diet (p = 0.0008).

**Conclusion:** Patients with coeliac disease and IBS-symptoms had 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.

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**TUESDAY, OCTOBER 18, 2016**

**PATHOPHYSIOLOGY OF IBS – ROOM N2**

**OP288 ADDITIVE EFFECT OF PATHOPSYLIOLOGICAL 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.

**Aims & Methods:** Our aim was to study whether these pathophysiological alterations have additive effect on IBS symptoms 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 thresholds) 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 a score >20. The patients also completed questionnaires to assess IBS symptom severity (IBS-SSS or GSRS-IBS total score) and somatic severity (SCL-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 ≥ one IBS-related symptom. As PRO measures we used z-scores of IBS symptom severity (IBS-SSS or GSRS-IBS total score and somatic severity (SCL-90) for severity of IBS symptoms (p < 0.0001) and somatic severity of IBS symptoms (p < 0.0001).
OP289 INCREASED INHIBITORY NEUROTRANSMISSION WITHIN ANTERIOR CINGULATE CORTEX IS RELATED TO COMORBID ANXIETY IN IRREVERSIBLE 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, including the rostral anterior cingulate cortex (rACC) as a unique structure for anti-nociception, concentrations within rACC as a crucial structure for anti-nociception and support the importance of microbiota as a major factor in the pathophysiology of bowel syndrome.

Aims & Methods: We compared IBS patients and healthy controls (HC) regarding GABA concentrations of glutamate (Glu) and GABA in rACC using quantitative magnetic resonance spectroscopy (qMRS). We further addressed associations with anxiety and depression as the most common psychiatric disorders associated with IBS, and also preventive effects of rACC 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 3x3x3cm3 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 inhibited GABAergic 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.

OP290 BACTERIAL PASSAGE IS INCREASED IN THE COLON OF WOMEN WITH IRREVERSIBLE 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 bacterial microbiota axis. Alterations in microbiota have been associated with 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±7), with 17 mixed with stool pattern IBS-M, 7 with diarrhea IBS-D and 8 with constipation predominance IBS-C, according to Rome III criteria and 15 HCs (mean age 29.7±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 51Cr-EDTA.

Result: The colonic mucosa of IBS patients had a significantly greater passage both for living Salmonella typhimurium and E. coli HS compared with HCs (p < 0.0001 and p < 0.0001 respectively). The 51Cr-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 passage. Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP291 LUPROPROSTONE IMPROVES THE INTESTINAL PERMEABILITY, A NEW APPROACH FOR "LEAKY GUT"? A PROSPECTIVE RANDOMIZED PILOT CLINICAL STUDY IN HEALTHY VOLUNTEERS

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Introduction: Several diseases and disorders are associated with "leaky gut" (or increased intestinal permeability), such as inflammatory bowel diseases, celiac disease, food allergy, irritable bowel syndrome, and obesity-metabolic disorders. Therefore, this topic is an area of growing interest, and a well-established therapy for preventing or reverting increased intestinal permeability would be valuable. Since there are no effective medications for "leaky gut" to date, it would be important to establish a new therapy which aiming at improvement of intestinal permeability. Previous studies have reported that non-steroidal anti-inflammatories (NSAIDs) induce small intestinal damage and increased permeability [1]. Other basic studies have reported that luproprostone, a chloride channel activator used for chronic constipation, repairs intestinal mucosal barrier function and also prevents NSAID-induced small intestinal damage in rodent models [2]. Aims & Methods: Our aim was to verify the effect of luproprostone on intestinal permeability in healthy volunteers administered with dicyclofenac. We conducted a prospective, randomized parallel-group trial. Healthy male volunteers, with documented absence from certain drugs (NSAIDs, proton-pump inhibitors, antibiotics, and probiotics) for at least 3 months prior to the study were enrolled. The subjects were randomly assigned to either the luproprostone or control groups. All participants performed sugar permeability tests on baseline, after 14 days of treatment and after 28 days of treatment (day 28). The
OP292 VISCERAL 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. To do this, we included 5 cohorts of patients with FGIDs, who had undergone placebo-controlled barostat testing.

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 produced a 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>LMR</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>0.021</td>
</tr>
<tr>
<td>day14</td>
<td>0.035 (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”.

OP293 CHRONIC ORAL ADMINISTRATION OF THE GUANYLATE CYCLASE-C AGONIST LINACLOTIDE 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. However, the regulatory mechanisms behind these conditions are not well understood. We investigated healthy C57BL/6J mice and mice with CCH (age 39 ± 13 weeks), in a model of chronic colonic hyper-sensitisation [1,2].

Aims & Methods: We investigated healthy C57BL/6J mice and mice with CCH (age 39 ± 13 weeks), in a model of chronic colonic hyper-sensitisation [1,2].

Table 1 (OP292): Association between visceral hypersensitivity and GI symptom severity in five FGID cohorts

<table>
<thead>
<tr>
<th>z score GI sx severity (mean ± SD)</th>
<th>Belgian FD cohort (n = 242)</th>
<th>US IBS cohort (n = 243)</th>
<th>US IBS cohort (rectum; n = 159)</th>
<th>Swedish IBS cohort 1 (n = 353)</th>
<th>Swedish IBS cohort 2 (n = 147)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low sensitivity tertile</td>
<td>0.48 ± 0.09</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 &lt; 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; depre)</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>
<tr>
<td>Correlation sensitivity - GI sx</td>
<td>r = 0.27; p &lt; 0.0001</td>
<td>r = 0.20; p &lt; 0.0001</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>

References
administration, consisting of a once daily oral gavage for 2 weeks prior to exper-
imental groups, while four weeks 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 as well as muscarinic, purinergic 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 hyperexcita-
tility, with a significant increase in rheobase (P < 0.01) as well as enhanced bladder afferent responses to distension (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 significant changes in firing frequency (P < 0.01). CCH mice treated with linaclotide 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). Linaclotide treatment in the CCH mice also resulted in a restoration of natural voiding behaviour (P = 0.05).

Conclusion: Mice with CCH also displayed increased bladder afferent excitability accompanied by abnormal bladder voiding behaviour, an example of visceral-visceral cross-talk. Chronic oral administration of linaclotide, a gut-restricted GC-C agonist that inhibits colonic nociceptors, reverses these colitis-induced changes in bladder function and sensitivity. Agents that improve abdominal pain may be able to improve urological symptoms through common sensory neuronal pathways.

Disclosure of Interest: L. Grundy: Grant support from Ironwood Pharmaceuticals. G. Hannig: Employee, stock holder, and stock options from Ironwood Pharmaceuticals Inc. C.B. Kurtz: Employee, stock holder, and stock options from Ironwood Pharmaceuticals Inc. A. Silos-Santiago: Employee, stock holder, and stock options from Ironwood Pharmaceuticals 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.

References

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-
inflammatory disorders. However, they all share the inability 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 abnormalities are responsible for these disorders, and a targeted CGH array analysis of extra- chromosomal loci, 91 patients with an initial diagnosis of EO-IBD between 1988 and 2004 (54% of the whole EO-IBD cohort) issued from EPIMAD population-based registry were screened; 71 had a Crohn’s disease and 20 an ulcerative colitis.

Result: Analysis of 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 heterogeneous 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 reappraisal of the diagnostic pathway.

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

OP295 HYPOXIA INHIBITS INTESTINAL INFLAMMATION THROUGH THE INHIBITION OF NLRP3 INFLAMMASOME AND THE ACTIVATION OF AUTOPHAGY
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2Institute Of Physiology, University of Zurich, Zurich/Switzerland

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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 colonic 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 IL-10−/− Nlrp3−/− double knockout mice were subjected to hypoxia (8% O2) for 18 h prior to colonic biopsy collection. Mice under normoxic conditions were used as controls. For the in vitro studies, the human monocytic cell line THP1 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-
hagy-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-p65 and caspase-1 and RIPK3 in the NLRP3 inflammasome activation 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 THP1 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

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Table 1. (OP297)

<table>
<thead>
<tr>
<th>Feature</th>
<th>CCD n = 19</th>
<th>UC n = 32</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at testing (mean ± SD, y)</td>
<td>32.0 ± 14.9</td>
<td>36.0 ± 10.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Age at diagnosis (mean ± SD, y)</td>
<td>25.7 ± 15.5</td>
<td>25.3 ± 10.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Disease Duration at testing (mean ± SD, y)</td>
<td>6.2 ± 4.8</td>
<td>10.5 ± 8.4</td>
<td>0.047</td>
</tr>
<tr>
<td>Gender (%)</td>
<td>42 (11)</td>
<td>50 (16)</td>
<td>0.44</td>
</tr>
<tr>
<td>Clinically active (%)</td>
<td>58 (11)</td>
<td>66 (21)</td>
<td>0.77</td>
</tr>
<tr>
<td>Endoscopically active (%)</td>
<td>89 (17)</td>
<td>71 (25)</td>
<td>0.45</td>
</tr>
<tr>
<td>Histologically active (%)</td>
<td>79 (15)</td>
<td>63 (20)</td>
<td>0.35</td>
</tr>
<tr>
<td>Treatment (%), Biologic Azathioprine ASA Steroid Antibiotic</td>
<td>15.8 (3) 15.8 (3) 15.8 (3) 0 0</td>
<td>7.2 (3) 0 69 (22) 23 (1) 0</td>
<td>0.67 0.047 0.0004 1 1</td>
</tr>
<tr>
<td>CRP (mean ± SD, mg/mL)</td>
<td>16.1 ± 21.1</td>
<td>8.7 ± 16.3</td>
<td>0.2</td>
</tr>
<tr>
<td>WCC (mean ± SD, ×10^3/µL)</td>
<td>6.5 ± 2.0</td>
<td>6.3 ± 1.3</td>
<td>0.7</td>
</tr>
</tbody>
</table>

**OP296 EPIDEMIC ALTERATIONS IN INFLAMMATORY BOWEL DISEASE - THE INFLUENCE OF GERMINE VARIATION (MEQTLS) ON GENOME-WIDE METHYLATION ALTERATIONS**


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9. Servicio De Aparato Digestivo, Hospital Clinico Universitario Lozano Blesa, Zaragoza/Spain
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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 peripheral blood (250 controls, 150 Crohn’s disease (CD), 167 ulcerative colitis (UC), 25 IBD unclassified (IBDU)) using the Illumina HumanOmniExpressExome-8 BeadChips. Samples were obtained from new-onset IBD cases in six European centres as part of the European Comission funded IBD-Character project.

**Result:** 195 probes exhibited Bonferroni significant IBD-associated methylation differences, including VMP1/MIR21 (p = 3.7 × 10^-10^), RPS6KA2 (1.1 × 10^-10^), SBN02 (2.7 × 10^-10^), and TCF7S10 (1.1 × 10^-10^); data which provide important unequivocal replication of recent discoveries, together with insight of new onset IBD, identifying novel disease-associated methylation changes and potential new biomarkers. Our study aims to characterize disease-associated methylation changes in patients with colonic Crohn’s disease (CCD) and ulcerative colitis (UC) 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. Illeocolonoscopy 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: 0.80–0.90). 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 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 UCERLATIVE COLITIS PATIENT GROUPS WITH DIFFERENT DISEASE-DRIVING 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 tissue colon cancer subtypes and clinical samples 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 poly:IC and becomycin 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 cell, and epithelial 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. Pavlidis: Employee of Janssen Research & Development Ltd, High Wycombe, UK
M.J. Loza: Employee of Janssen Research & Development LLC, Spring House, USA
P. Branigan: Employee of Janssen Research and Development LLC, Spring House, USA
C. Monast: Employee of Janssen Research & Development LLC, Spring House, USA
A. Rowe: Employee of Janssen Research & Development Ltd, High Wycombe, UK.
F. Baribaud: Employee of Janssen Research & Development LLC, Spring House, USA.

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

**OP300 THE IMPLANTABLE MEDICATED MICROSEROSOVS 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 for men, and the second - in women. In Europe remains steady increase in incidence and mortality according to Globocan 2012 and source EuropaColon. The main problem after surgery is local recurrences that often develop even after resection CRC. Five-year survival is less than 30%. In developed countries the recurrence rates are 50-60%. Local recurrence, therefore increasing the likelihood of clinical response.

**Aim:** Our study shows that infection with CD-associated AIEC induces secretion of exosomes carrying several CD-associated circulating miRNAs by human THP-1 macrophages. These exosomal miRNAs, when being transferred to recipient naive THP-1 macrophages, may be involved in the regulation of various immunological and autophagic responses, contributing to host immune defense to AIEC infection.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
**Aims & Methods:** Types, are technically difficult to remove as en-bloc with ESD method because of which are endoscopically seen as granular (LST-G) or non granular (LST-NG) early stage gastrointestinal (GI) cancers. Lateral Spreading Tumors (LSTs), 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 LSTs.

**Aims & Methods:** Between April 2012- April 2016, a total of 655 colorectal lesions were referred to our unit for the purpose of resection 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 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 cases were performed in colon and rectum with diagnosed LST. The overall en-bloc and complete resection rates were 91.1% and 90.4%, respectively. The lesions were localized in rectum 124 (44), sigmoid colon 99 (35.2), cecum 4 (1.4), ileocecal valve 21 (7.4). The mean microvessel density (MVD) was 163 ± 69 microvessels/mm². Median MVD was used as the cutoff 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:** 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 and noninvasive tool for imaging angiogenesis in vivo which can be repeated without exposing the patient to any risk.

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

**OP302 EVALUATION OF RECTAL CANCER ANGIOGENESIS USING IMMUNOHISTOCHEMICAL AND COMPUTER-ASSISTED ENDOSONOGRAPIC 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 and noninvasive tool for imaging angiogenesis in vivo which can be repeated without exposing the patient to any risk.

**Aims & Methods:** The aim of the present study is to evaluate the preoperative rectal cancer angiogenic status with Endorectal Power Doppler Ultrasound by using a Power Vascularity Index correlates with histological microvessel density (PDVI). 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 using a software. The result: The mean microvessel density (MVD) was 163 ± 69 microvessels/mm². Median MVD used as the cutoff 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 ultrasonographic vascular index correlates 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 vasculisation.

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

**OP303 COMPARISON OF CLINICAL OUTCOMES AMONG DIFFERENT ENDOSONOMIC MODALITIES FOR RECTAL NEUROENDOCRINE 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:** Fifty-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-EMR 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 and 95.2% (20 of
21) in the ESD group, respectively (p = 0.354). Perforation or delayed bleeding did not occur in any case of ESMR-L. Caution was necessary in the other groups and procedure time increased in order of ESMR-L, CSI-EMR, and ESD group (4.3 ± 2.0 min, 11.2 ± 12.5 min, 18.6 ± 3.9 min, respectively, p = 0.000).

Conclusion: All endoscopic resection method, including ESMR-L, CSI-EMR, and ESD were effective and safe for the treatment of rectal NET, compared with CSI-ESD or ESD, ESMR-L procedure has the advantages of easier and shorter procedure time. ESMR-L may be considered the treatment of choice for rectal NETs with diameter in diameter.

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

OP304 ANAL CYTOLOGY, HISTOPATHOLOGY, AND ANOSCOPIC 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 expert opinion.

Aims & Methods: The authors intend to estimate agreement between anal cytology, histopathology, and anoscopy visual impression. This is a prospective study of patients receiving anal dysplasia screening between 2010 and 2015, in a prosoposcopic 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-statistics.

Result: 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 for intraepithelial lesion or malignancy (NILM), 22% atypical squamous cells of uncertain significance (ASCUS), 33% low-grade squamous intraepithelial lesion (LSIL), 33% high-grade squamous intraepithelial lesion (HSIL) and 1% carcinoma in situ (CIS). Concerning anal cytological findings, 40% patients had no lesions (53% NILM, 22% ASCUS, 25% LSIL). In the remaining patients, excision/biopsy of the identified lesions was performed detecting 40 (23%) high-grade dysplasia (HGID), 33 (19%) low-grade dysplasia (LGD) and 4 (2%) CIS. Weighted kappa-agreement between abnormal cytological results and analoscopy visual impression was moderate (κ = 0.48). Weighted kappa-agreement between the presence and degree of dysplasia in anal cytologic tests and concurrent histopathology results was low (κ = 0.23) and κ = 0.20, respectively. Of the 57 NILM cytology tests, 26% had suspicious lesions in analoscopy visual impression and of these, 9 (60%) had dysplasia on histopathological exam (4 HGID and 5 LGD). By other hand, concerning the patients with HGID/CIS on histological exam, 28 (65%) patients had lower dysplasia grade on cytological exam (6 ASCUS, 18 LSIL and 4 NILM).

Conclusion: The low correlation between anal cytology, histopathology and anoscopy visual impression associated with the high number of histological findings with HGID/CIS with lower dysplastic degree on cytological exam (including NILM anal cytologies) suggest that anal cytology screening should not be used as the unique method of anal dysplasia screening. The authors suggest that anoscopy screening should be offered to all patients.

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

Reference
1. Mathews WC, Sitapati A, Caperna JC, Barber RE, Tugend A and Go U. Aims: New platform for trans-anal submucosal endoscopic resection (TASER) - patient had an elective laparoscopic anterior resection (T1sm3,N0,M0 confirmed) and in a third patient intraperitoneal perforation necessitated a de-functioning ileostomy before complete polypectomy could be undertaken. Mean procedure time was 185 min, range 65–75 min. Thirty-two TASER procedures were employed using ESD in 12/32, ESD + P-EMR in 6/32, ESD + P-EMR + EMA in 4/32, ESD + TAE in 3/32, ESD/P-EMR/TAE in 3/32 and ESD + P-EMR + EMA + TAE in 4/32. Intra-procedural bleeding was controlled with haemostatic endoscopic devices (coagrasp/clips); surgical clipping and suturing on 2 occasions. Prophylactic endoscopic clipping was also applied in 8 cases and suturing on 4 occasions. In 6/10 TASER - TAE cases, there was a need for a full-thickness rectal dissection due to severe submucosal fibrosis: 4/6 cases were closed with surgical sutures plus endoscopic clips and in the remaining 2/6 cases only endoscopic clips were deployed. Two episodes of delayed bleeding were reported among the TASSER-ESD/P-EMR and P-EMR/TAE - TAE cases. Three sub-cohorts of patients were treated: 1) 30/32 patients with HGD/CIS with lower dysplastic degree on cytological exam (including 6 ASCUS, 18 LGD, 9 HGD); 2) 2/32 patients with HGD/CIS with higher dysplastic degree on cytological exam (4 LGD, 2 HGD); and 3) 10/32 patients with ASCUS. All patients were discharged the day after the TASER procedure, apart from one patient who developed bacteremia post-TASER-ESD requiring intravenous antibiotics and a 4-night hospital stay and the patient who required a de-functioning ileostomy, discharged on day 4 post procedure. First follow-up was performed at 4–6 months interval in 25/32 patients showed: 21/25 with no recurrence (84%) and 4/25 (16%) with a minimal (<15 mm) polyp recurrence, amenable to endoscopic therapy. No rectal stricture was identified and only one patient was referred for surgical intervention.

Conclusion: TASER appears to be a safe and efficient endo-surgical approach providing an optimal platform for the minimally-invasive management of high-risk, complex rectal polyps.

Disclosure of Interest: Z. Tsiamoulos: Consultancy Agreement Creo Medical Ltd Paid Lectures Norgine Pharmaceutical Ltd B.P. Saunders: Consultancy Agreement Creo Medical Ltd Paid Lecturers Olympus Keymed

All other authors have declared no conflicts of interest.

Reference

TUESDAY, OCTOBER 18, 2016
15:45–17:15
THE INTESTINAL EPITHELIUM - STEM CELLS, INFLAMMATION AND CANCER – ROOM 1.86

OP306 THE PROREGENERATIVE ROLE OF INTERLEUKIN-22 PROTEIN IN THE INTESTINAL EPITHELIUM DEPENDS ON AUTOAPHagy 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 conditional mechanism for protein degradation. As these 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 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. Human colon cancer cell lines HT-29 and Caco2 cells were treated with recombiant IL-22 and ER stress inducers like Rapamycin before they were subjected to wound healing assays, intestinal organoids derived from human. Human colon carcinoma HT-29 and Caco2 cells were treated with recombiant IL-22 and XBP1 gene expression analysis and immunoblot analysis. Intestinal organoids derived from human. Human colon carcinoma HT-29 and Caco2 cells were treated with recombiant IL-22 and XBP1 gene expression analysis and immunoblot analysis. Intestinal organoids derived from human. Human colon carcinoma HT-29 and Caco2 cells were treated with recombiant IL-22 and XBP1 gene expression analysis and immunoblot analysis.
OTIP07 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 HOX A9. HOXA9 overexpression is the molecular factor most strongly correlated with poor prognosis in AML and is also correlated 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 firstly aimed to assess the expression of HOX A9 in colonic adenoma tissue and location matched control tissue. Secondly, it aimed to investigate the effects of increased HOX A9 expression, both in terms of its influence in anterior to posterior specification and its oncogenic properties. We collected biopsies from colonic polyps and location matched normal colorectal tissue in patients undergoing colonoscopy. A pathologist classified the colonic polyps and we only included tubular adenomas. We used RT-qPCR to quantify the expression of HOX A9 in relation to UBC, TPT1 and GAPDH using the efficiency 2^ΔΔCt method. In addition, we transduced Caco2 cells with a lentiviral vector containing HOXA9 and a lentiviral vector without HOXA9. Expression of HOX A9 was measured by western blot. Result: HOXA9 expression in tubular adenomas of the colon is increased compared to location matched control tissue (p = 0.04). HOX A9 overexpression in Caco2 cells led to a decrease in FGFR2 mRNA levels (p = 0.002). HOX A9 overexpression led to increased cell proliferation when assessed in vitro by a cell cycle assay (p = 0.003). Additionally, when assessed with a MTT assay (p < 0.001), HOX A9 overexpression led to increased total cell pool. The growth factor IGFI increased significantly (p = 0.02) as a result of HOX A9 overexpression. Genes important for epithelial to mesenchymal transition were not found to have significantly changed.

Conclusion: HOX A9 expression is increased in colonic adenomas. Overexpression of HOX A9 leads to a decrease in FGFR2 and an increase in BMP4, which emphasizes the role of transient STAT3 signaling in colorectal cancer development. The mammalian HOX clusters encode regulators of embryonic anterior to posterior specification. HOX A9 overexpression leads to growth of the cell pool. A mechanism through which HOX A9 exerts this effect is the upregulation of IGFI. In conclusion, HOX A9 appears to have pro-oncogenic activity in the premalignant stage of colorectal cancer.

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

References

OPIP08 TOLL-INTERACTING PROTEIN DEFICIENCY PROTECTS MICE FROM COLITIS-ASSOCIATED CANCER BY MODULATING ANTITUMORAL 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 (1). We sought to investigate whether increased susceptibility to inflammation had an impact on tumor formation. Immunohistochemistry was performed on mouse colon tissue from mice treated with 5% oral dextran sodium sulfate (DSS) treatment. Tumor development was assessed histologically, histopathologically and by immunohistochemical analysis. To evaluate potential effects of increased HOXA9 expression, both in terms of its pro-oncogenic activity in the premalignant stage of colorectal cancer, we used a colon cancer cell line. Our data show that Tollip deficiency led to increased 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 SMAD2/3 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 tumor-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

OPIP09 CONSTRUCTION OF IN VIVO MODEL OF ULCERATIVE COLITIS USING MOUSE PRIMARY COLONIC ORGANOID

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Introduction: The patients with ulcerative colitis (UC) are at increased risk of developing colitis-associated cancer, because long-term inflammation leads to the development of carcinogenesis. However, the transformation of colonic epithelial cells during long-term inflammation has not been elucidated. Recently, 3-dimensional (3D) primary organoid culture of colonic epithelial cells in mice has been established in our group (TMDU method)3.

Aims & Methods: We therefore aimed to assess the effect of long-term inflammation on the epithelial cells by in vitro model, which might mimic natural history of UC. Colonic crypts were isolated from 8 week old female mouse and were cultured using TMDU method. After we analyzed the morphology of colonic crypts, the mixture of cytokines and the ligands of toll like receptors, were added into the medium every other day for 40 weeks. Thereafter, glycogen synthase kinase 3 (GSK3) inhibitor, CHIR99021 was added into the medium for 8 weeks with stimulation of inflammatory reagents. To evaluate transformation into tumor, the organoids were cultured without R-spondin1 and Wnt3a. The assessment of cell signaling pathways in organoids during long-term inflammation was performed by immunohistochemistry of whole organoid and BMP4 mRNA level (p = 0.02). HOX A9 overexpression led to increased cell proliferation when assessed in vitro by a cell cycle assay (p = 0.003). Additionally, when assessed with a MTT assay (p < 0.001), HOX A9 overexpression led to increased total cell pool. The growth factor IGFI increased significantly (p = 0.02) as a result of HOX A9 overexpression. Genes important for epithelial to mesenchymal transition were not found to have significantly changed.

Conclusion: HOX A9 expression is increased in colonic adenomas. Overexpression of HOX A9 leads to a decrease in FGFR2 and an increase in BMP4, which emphasizes the role of transient STAT3 signaling in colorectal cancer development. The mammalian HOX clusters encode regulators of embryonic anterior to posterior specification. HOX A9 overexpression leads to growth of the cell pool. A mechanism through which HOX A9 exerts this effect is the upregulation of IGFI. In conclusion, HOX A9 appears to have pro-oncogenic activity in the premalignant stage of colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.
western blot analysis. The gene expression of transformed organoids was assessed by quantitative RT-PCR.

**Result:** The treatment with the inflammatory reagents in mouse colonic organisms 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 by 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 retained active after the removal of all inflammatory reagents, whereas NF-κB 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 organisms required neither R-spondin nor Wnt3a after the treatment with GSK3 inhibitor for 8 weeks, indicating that the organisms 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 an essential survival capacity of colonic organisms. This in vitro model might mimic 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 display a menace to DNA integrity. The ribonuclease RNaseH2b removes RNA/DNA hybrids and thereby ensures cellular proliferation. Hypomorphic mutations of the RNaseH2b gene are associated with Aicardi-Goutières syndrome that results in a spontaneous inflammatory phenotype. We tested the role of RNaseH2b in maintaining proliferation and regeneration in the intestinal epithelium.

**Aims & Methods:** We generated RNaseH2bfl/fl and RNaseH2b−/− mice to study the role of RNaseH2b in the intestinal epithelium. WB, RT-PCR and IHC were performed to study the basal phenotype of unchallenged WT and KO mice. Acute DSS colitis was induced to investigate the impact of RNaseH2b on intestinal integrity. The DSS colitis was monitored to study the role of RNaseH2b on intestinal carcinogenesis. Organoids of RNaseH2bfl/fl and RNaseH2b−/− were subjected to RNA sequencing.

**Results:** Histological characterization reveals spontaneous DNA double strand breaks (DSB) in epithelial crypts of RNaseH2bfl/fl but not RNaseH2b−/−mice, with respect to age dependent body weight gain. Histological characterization reveals spontaneous DNA double strand breaks (DSB) in epithelial crypts of RNaseH2b−/− mice, which leads to a restriction of epithelial stemness, as measured by expression of stem cell markers (Olfm4, Lgr5) and reduced K167 staining of intestinal stem cells. When mice were challenged to acute DSS colitis, RNaseH2b−/− mice reveal a strong phenotype with dramatic weight loss, increased histological disease activity and impaired intestinal regeneration. Interestingly, when mice were challenged to AOM-DSS colitis, mice again showed increased intestinal inflammation but developed significantly less tumors. Decreased tumor development was due to DNA induced cellular senescence, as shown by acid β-galactosidase staining in intestinal crypts in RNaseH2b−/− mice but not RNaseH2bfl/fl mice.

**Conclusion:** We show for the first time, that the RNaseH2b plays an essential role in maintaining intestinal regeneration by protecting genomic DNA of high proliferating cells from DNA/RNA hybrids induced DNA damage. Knockout of RNaseH2b leads to loss of epithelial stemness and induction of cellular senescence.

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

**Reference**


OP312 COMMENSAL FUNGI AND THEIR CELL-WALL GLYCANS INDUCE AUTOPHAGY IN INTESTINAL EPITHELIAL CELLS

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**Introduction:** Intestinal epithelial cells (IECs) 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 components of cell wall glycans, induced chemokine secretion by IEC lines 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 glucans in inducing autophagy.

**Aims & Methods:** To investigate whether fungi and fungal glucans induce autophagy in IECs. Human IEC lines (HT-29 and SW480) were activated by C. albicans and S. cerevisiae and the β-glucan-rich cell-wall component zymosan. Autophagy was detected by western blot analysis and active autophagy was assessed by the punctal stain of endogenous LC3 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-induced autophagy of IEC lines. This was accompanied by Syk phosphorylation and prevented upon Syk inhibition. When IECs were challenged to AOM-DSS colitis, treated with RNAseH2b−/−, NF-κB activity was increased 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 in response to GAPDH. In comparison, LC3 puncta were reduced upon RNAseH2b−/− treatment. When mice were challenged to AOM-DSS colitis, RNAseH2b−/− mice showed increased inflammatory infiltrates, higher numbers of CD3+ lymphocytes and the severity of AP were evaluated by pancreatic HPSE activity (determined by microtubule-associated protein 1A/1B-light chain 3 (LC3) or directly visualized in cells stably expressing GFP-LC3. Syp phosphorylation was assessed by WB and IF. Macromolecular samples were obtained from patients undergoing colonoscopy and active autophagy was assessed by the punctal stain of endogenous LC3 in paraffin embedded sections in or frozen sections by IF.

**Conclusion:** Commensal fungi and their cell-wall glucans induce autophagy in IECs in acute DSS colitis independent autophagy is induced in vivo. Furthermore, RNAseH2b−/− mice developed significantly less tumors and inflammation. Increase in the active (cleaved) form of LC3 (LC3 II) e.g. up to 3.7 fold increase in LC3 II/GAPDH ratio in sw480 cells vs. no treatment. Fungal-induced autophagy was accompanied by Syk phosphorylation and prevented upon Syk inhibition. In ileal and colonic IECs, RNAseH2b−/− mice were challenged with zymosan as LC3 puncta. Autophagy was further induced ex-vivo by UV-inactivated C. albicans, zymosan or rapamycin (mTOR inhibitor, autophagy inducer).

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

**TUESDAY, OCTOBER 18, 2016**

15:45-17:30

**ABSTRACTS ON FIRE: ACUTE PANCREATITIS: FROM MECHANISMS TO DISEASE – HOTSPOT**

OP313 HEPARANASE IN ACUTE PANCREATITIS: NEW INSIGHTS INTO PATHOGENESIS AND THERAPY

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**Introduction:** Despite advances in understanding the pathogenesis of acute pancreatitis (AP), the mechanisms underlying this disease have not been fully determined. In the majority of cases, AP is a self-limited process, yet 20% of patients develop a severe form of AP with pancreatic necrosis, multi-organ involvement, (VT-AP) [1]. Furthermore, the patients are at high risk of mortality. Heparanase (HPSE) is an endo- β-galactosidase which cleaves heparan sulfate, degrades andremodels the extracellular matrix. HPSE is preferentially expressed in human tumors, including pancreatic adenocarcinoma. While the role of HPSE in cancer has been extensively studied, the involvement of this enzyme in inflammation and in AP in particular remains obscure. Therefore, this current study examines if HPSE is involved in the pathogenesis of Cerulein-induced AP in mice.

**Aims & Methods:** HPSE over-expressing transgenic mice (hpa-TG) and wild-type (WT) BALB/c mice were intraperitoneally injected with either Cerulein (50mg/kg, 5 times, at 1 hour apart) or vehicle, with or without low and high doses of Roneparstat (SST0001, HPSE inhibitor) pretreatment. The animals were sacrificed 24 hours following the treatment of pancreatitis. The pancreatic response and inflammatory activity of AP were evaluated by pancreate HPSE activity (determined by Na253SO4-labeled ECM), pancreatic edema index (determined by organ to animal weight ratio), tissue inflammatory response (determined by histopathological analysis), autophagy response (determined by electron microscopy and immunohistochemistry staining) and serum pancreatic enzymes (amylase and lipase) levels.

**Result:** Cerulein-induced AP in wild type mice was associated with significant rises in the serum levels of amylase and lipase. These increases were characterized by an enhancement of HPSE activity, a higher pancreatic edema index, tissue inflammation and autophagy response. All types of responses to administration of Cerulein were profoundly exaggerated in hpa-TG mice. In contrast, when Cerulein was administered to KO mice, the severity of pancreatic injury was
were isolated from control, GHRL rats and then hyperstimulated by caerulein dependently decreased forskolin-stimulated fluid secretion in guinea pig pancreata.

\[\text{Fluid secretion} = 44.5\% \times 100 = 4.45\text{mL} \]

Aims & Methods: In this study, we would like to understand whether smoking has any effects on pancreatic ductal fluid and HCO\(_3\)-secretion and the activity of CFTR which may play role in the smoke-induced pancreatic damage. This study was supported by OTKA, MTA and TAMOP.

Conclusion: All authors have declared no conflicts of interest.

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

OP314 CIGARETTE SMOKE EXTRACT INHIBITS FLUID AND HCO\(_3\)-SECRETION AND CFTR ACTIVITY IN GUINEA PIG PANCREATIC 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 investigated the effects of cigarette smoke on the expression of CFTR and the activity of CFTR which may play role in the smoke-induced pancreatic damage.

Conclusion: All authors have declared no conflicts of interest.

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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 with approx. 350 million people 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 cases has been 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 contribution to type 2 diabetes (T2D) and T1D may be caused by rare monogenic variants/mutations missed by the current GWAS strategies target- ing 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 genes.

Result: Using stage-specific genome-wide profiling complemented with Chip-Seq data in differentiating human embryonic stem cells, we showed that our gene binds and activates Nkx2.2, Nkx6.1 and Pdx1, all belonging to the core suite of islet transcription factors. Further, this gene co-occupies the enhance 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 showed a binding pattern of the same type as in the wild-type (WT) 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.

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

OP316 LACK OF CFTR RESULTS IN THE IMPAIRED FUNCTION OF THE PLASMA MEMBRANE CA\(_{\text{2+}}\) PUMP THAT CAUSES INTRACELLULAR CA\(_{\text{2+}}\) 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 Ca\(_{\text{2+}}\) overload is a hallmark of acute pancreatitis and in CFTR-deficient airway epithelial cells the intracellular Ca\(_{\text{2+}}\) homeostasis was disturbed. However the Ca\(_{\text{2+}}\) homeostasis of CFTR-deficient pancreatic ductal epithelial cells (PDEC) has never been investigated.

Result: Maximal [Ca\(_{\text{2+}}\)]\(_{\text{i}}\) release upon carbachol stimulation showed no difference in WT and CFTR K0 PDEC. Notably, the plateau phase of the Ca\(_{\text{2+}}\) signal was significantly higher in CFTR-deficient PDEC, but completely normal in pancreat- ic acinar cells. Interestingly, the functional inhibition of CFTR with 10μM CFTR(rinh)-172 had no effect on the Ca\(_{\text{2+}}\) signals. Next we investigated the mechanism that the Ca\(_{\text{2+}}\) extrusion was significantly lower.
in CFTR KO PDEC compared to WT due to the impaired function of the plasma membrane pump (PMCA). In addition, the sustained elevation of [Ca\textsuperscript{2+}]\textsuperscript{2+} caused a drop in mitochondrial membrane potential in CFTR KO PDEC.

**Conclusion:** Dysfunction of PMCA leads to disturbed Ca\textsuperscript{2+} homeostasis in CFTR-deficient PDEC and the consequent cellular Ca\textsuperscript{2+} overload impairs mito-

**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 manage-

**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 MPD stents according to the following protocol: balloon dilation of the stricture to 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 had other major stent 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 26.4 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. The Canadian consensus (Tringali; Boston Scientific Corporation) No current consultation agreements in place One Day animal lab in 2012 and 2013. Speaking and teaching in 2014

**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 MPD stents according to the following protocol: balloon dilation of the stricture to necessary insertion of the maximum number of plastic stents allowed by the stricture tightness and pancreatic duct diameter, stents removal after 6 months.

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**Reference**


**OP319 USE OF THE URINARY TRYPsinogen-2 DPSTTEST IN EARLY DIAGNOSIS OF PANCREATITIS AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY**

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**Introduction:** One of the most serious complications of (ERCP) is acute pancrea-

**Aims & Methods:** After an informed consent by the patients the selected patients were subjected to: Full clinical assessment (history taking and clinical examina-

**Result:** Post ERCP UDST2 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 of the Pancreatitis (100%). The positive predictive value of UDST2 was 100%. The specificity was 97% with PPV 86%, NPV 100% and the P value was <0.01. Comparison between serum amylase and lipase levels in post ERCP in relation to UDST2 test shows that positive UDST2 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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Disclosure of Interest:

OP321 GASTROINTESTINAL SAFETY OF LEVODOPA-CARBIDOPA INTESTINAL GEL IN ADVANCED PARKINSON’S DISEASE – PATIENTS: FINAL RESULTS FROM THE GLORIA LONG-TERM REGISTRY

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Introduction: Levodopa-carbidopa intestinal gel (LCIG, designated in the US as carbidopa-levodopa enteral long-acting (CILE) is a long-term treatment option for advanced Parkinson’s disease (PD) patients and administered via percutaneous gastrojejunostomy (PGE-J) from an external pump.

Aims & Methods: The gastrointestinal (GI)-related safety of the LCIG treatment system (drug/device) has been assessed in advanced PD patients with final safety data from the GLORIA1 registry. This observational registry of 375 final advanced PD patients treated with LCIG was conducted at 75 centers in 18 countries. Patients were initially titrated to an optimal dose of LCIG via nasojugal (NJ) tube for up to 2 weeks, followed by infusion via PEG-J for 24 months. Final safety data from patients with advanced PD who had ≥1 infusion of LCIG (n=356) were included in this analysis. Adverse drug reactions (ADR), which were adverse events with a reasonable possibility of causal relationship to the treatment according to investigators’ judgment, were recorded throughout the registry. The authors categorized ADRs post hoc as either PEG-J procedure-related, device-related, or “other” type of GI event.

Results: Of the 375 enrolled patients, 332 (99%) were treated with LCIG via PEG-J, and 258 (69%) completed the 24 month follow-up. The median [range] duration of exposure via NJ was 6.0 [1, 53] days (n=307) and via PEG-J was 722 [1, 2015] days (n=357). During titration via NJ, there were 3 patients (0.8%) who had ≥1 GI related ADR. Within the 24 months of treatment post-PGE-J placement (n=356) ≥1 GI related ADR was reported in 139 patients (39%), of which procedure-related ADRs were reported in 35 patients (9.8%), device-related in 36 (12%), other GI events in 63 (18%); the ADRs in all GI categories reported for GI related ADRs was weight decreased (6.7%), device related infection (5.9%), device dislocation (4.8%), device issue (4.8%), and the serious ADRs reported for ≥2% patients were device dislocation (2.2%) and device issue (2.0%). During the 28-day follow up period, there were 4 patients (1.1%) who had ≥1 GI related ADR. Three ADRs led to the discontinuation of 10 patients (2.8%) overall, 2 of whom discontinued due to a procedure-related ADR, 5 due to a device-related ADR, and 3 due to another type of GI ADR. Of the 29 deaths reported, 23 were deemed unrelated to treatment, 5 possibly related (to drug/device) and 1 probably related (to tubing). Of the possibly/probably related deaths, 2 had GI related event, 1 had a small bowel obstruction and died approximately 3 weeks later of unknown cause, and 1 had a small bowel perforation and peritonitis.

Conclusion: Most GI-related ADRs were related to the device in this registry. The incidence of GI-related ADRs and discontinuations due to GI-related ADRs were relatively low, which is supportive of the overall tolerability of LCIG and consistent with previous studies.

Disclosure of Interest: D Domagk: Dirk Domagk has received research support from AbbVie Inc., North Chicago/United States of America/IL and Zambon, Merz Pharmaceuticals for consulting and lecturing. All other authors have declared no conflicts of interest.

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Introduction: Endoscopically assisted percutaneous transgastrostomal gastrostomy is a novel alternative route to access the gastrointestinal tract...
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 eliminations. A four-food elimination diet (FFED), eliminating the four most common culprit foods in EoE (animal milk, gluten-containing cereals, egg, legumes) has been a first step to simplify empiric elimination strategies. Aims & Methods: To assess the effectiveness of a step-up empiric elimination diet strategy compared to a prospective multicenter study conducted in 12 Spanish hospitals in both children and adults. All patients included fulfilled clinic and histologic criteria for EoE and lack of response to PPI therapy was documented before inclusion. Initial two-food elimination diet (animal milk and gluten-containing cereals) was evaluated in all patients, stepping up to a FFED and eventually to a SFED in non-responders. Response to dietary therapy was defined by symptom improvement and <15 eos./HPF. In responders to empiric diet, each food group was individually reintroduced for 6 weeks with further histologic reevaluation. Food introductions were defined as those leading to esophageal inflammation >15 eos./HPF after individual reintroduction. Results: 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) allows reducing endoscopic procedures and the diagnostic process time by 35%.

Conclusion: A two-food elimination diet (animal milk, gluten-containing cereals) achieves remission in 40% of patients unresponsive to PPI therapy. This diet allows prompt identification of two thirds of responders to empiric elimination diets, with few 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.

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). Eosinophilic esophagitis and gastro-esophageal reflux disease (GERD) presents a significant problem in the management of patients with EoE. Prospective multicenter study conducted in 12 Spanish hospitals in both children and adults. All patients included fulfilled clinic and histologic criteria for EoE and lack of response to PPI therapy was documented 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 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.

Results: 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 eosinophilic density was 56.8 (29.9) cells/HPF, which decreased to 3 (4.2) cells/HPF after SFED-based treatment (p < 0.001). Eosinophils were detected in any of the esophageal samples from controls. No differences in eosinophil counts were detected for atopic and non-atopic EoE patients, being 55 (30.4) vs. 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.
OP325 A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF RECOMBINANT HUMAN INTERLEUKIN-13 MONOCLONAL ANTIBODY (RPC4046) IN PATIENTS WITH ACTIVE EOSINOPHILIC OESOPHAGITIS: RESULTS OF THE HEROES STUDY

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Introduction: Interleukin-13 (IL-13) has been implicated in the pathogenesis of eosinophilic oesophagitis (EOE). RPC4046 prevents the binding of IL-13 to both the IL-13Rα1 and IL-13Rα2 receptors. This study evaluated the efficacy and safety of 2 dose levels of RPC4046 compared to placebo (PBO).

Aims & Methods: Patients were randomly assigned 1:1:1 to receive either RPC4046 180 mg (LD) [n = 31], RPC4046 360 mg [HD] [n = 34], or PBO [n = 34]. An IV dosing day on Day 1 was followed by weekly subcutaneous doses. Oesophageal biopsies, read by a central blinded pathologist, were obtained at baseline (BL) and Week 16 to assess eosinophilic inflammation and the mean eosinophil count on the primary endpoint. Secondary endpoints included symptom improvement measured by a Daily Symptom Diary (DSD), improvement in endoscopic features as measured by the EOE Endoscopic Reference Score (EREF), and Subject’s Global Assessment of Disease Severity. Safety was also assessed.

Result: 90 subjects completed the 16Wk double-blind period. Demographic/disease characteristics were generally comparable between treatment arms. At BL, mean oesophageal eosinophil counts (cells/hpf) were 92.4 (PBO), 116.6 (LD), and 172.6 (HD). The mean eosinophil count was significantly reduced from BL for both RPC4046 dose levels compared to PBO (mean change: PBO –4.4, LD –94.8, HD –13.3 [both p < 0.001 vs PBO]). There was a greater improvement in dysphagia symptoms as measured by the DSD with HD compared to PBO, but the 3 dose levels did not achieve statistical significance (PBO –6.4, LD –5.3 [p = 0.996 vs PBO], and HD –13.3 [p = 0.073 vs PBO]). There were significant improvements in endoscopic features as determined by the complete analysis of the total mean EREF score with both RPC4046 dose levels (mean change: PBO –9.0, LD –4.2, and HD –4.8 [both p < 0.0004 vs PBO]). There was a significant improvement in Subject’s Global Assessment of Disease Severity at the HD (PBO –1.5, LD –2.0, HD –2.8 [HD p = 0.0107 vs PBO]). The rates of overall adverse events (AEs) were 64.7% (PBO), 64.5% (LD), and 83.3% (HD). The most frequent AEs were headache (PBO 14.7%, LD 20.6%, HD 20.6%), upper respiratory infection (PBO 0%, LD 12.9%, HD 5.9%).

Conclusion: RPC4046 demonstrated significant reductions in oesophageal eosinophilic inflammation and improvements in endoscopic features at both dose levels compared to PBO. There was a greater improvement in HD compared to LD. These phase 2 data support the further study of RPC4046 as a novel treatment for EOE. (clinicaltrials.gov ID: NCT02098473)

Disclosure of Interest: I Hirano: I am a consultant for Receptos, Genentech, Shire Pharma. M Collins: I have received research funds (through contracts) from Abbott Laboratories, Nestlé S. A., QOL, Receptos, Inc., and Meritage Pharma, Inc. A Schoepfer: I received consultant fees from: Receptos, Regeneron and grant support from: Receptos, Regeneron, Falk. A Straumann: Dr. Straumann 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; Aptalis 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 a former employee of Celgene. A Woo: I am an employee of Celgene. R Peach: I am a former employee of Celgene. P Frotha: I am an employee of Celgene. S Gajrajhi: I am a former employee of Celgene. R Arand: I am an employee of Celgene. E Dellen: I have received research funding from Receptos/Celgene; and am a Consultant for Receptos/Celgene. All other authors have declared no conflicts of interest.

OP326 IMPAIRMENT OF CHEMICAL CLEARANCE AND MUCOSAL INTEGRITY DISSOCIATION IN PERFUSION-SUSTAINED ESOPHAGEAL DISORDER WITH FUNCTIONAL HEARTBURN

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Introduction: Hypersensitive esophagus (HE) is defined by endoscopy-negative heartburn with normal esophageal acid exposure time (EAET) but positive symptom association probability (SAP) and symptom index (SI) at reflux monitoring, and/or heartburn suppression with proton pump inhibitor (PPI) therapy. Functional heartburn (FH) is distinguished by PPI-refractoriness and negative SAP/SI. However, diagnostic accuracy of SAP and SI has been recently questioned. We aimed to investigate the diagnosis of FH/HE based on symptom-reflux association analysis.

Aims & Methods: We aimed to investigate whether impairment of chemical clearance, expressed by post-reflux swallow-induced peristaltic wave (PSPW) index, and mucosal changes, measured by nocturnal basal impedance (MBNI), distinguish FH from HE independently from SAP and SI. Oesophageal pH recordings were obtained from 303 patients with PPI-dependent (i.e. heartburn repeatedly abolished by 4-week PPI-therapy and repeatedly recurring after PPI withdrawal) or PPI-refractory (i.e. < 50% of symptom relief after 8-week high-dosage PPI therapy) heartburn were blindly reviewed, 125 with non-erosive reflux disease (NERD) defined by abnormal EAET, 108 with HE (normal EAET, but positive symptom-reflux correlation) and 70 with FH (normal EAET and negative symptom-reflux correlation). Impedance-pH tracings were manually analyzed to detect: EAET (abnormal if ≥ 3.2% over 24 hours), characteristics of reflux episodes (acid weakly acidic) and symptom-reflux association using both SAP (positive if ≥ 95%) and SI (positive if ≤ 50%). MBNI values were considered as positive when the number of refluxes followed within 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 within 30 seconds by swallow-induced peristaltic waves with the number of total refluxes.

Results: HE patients had a significantly greater impairment of chemical clearance and mucosal integrity. When EAET is normal and SAP/SI afford inconclusive results, PSPW index and MBNI should be analyzed to objectively distinguish HE from FH.

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

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OP337 THE ADDDED VALUE OF POST-REFUX SWALLOW-SQUEWED INDUCED PERISTALTIC WAVE INDEX AND NOCTURNAL BASAL IMPEDANCE IN REFRACTORY GERD STUDIED WITH ON-THERAPY IMPEDANCE MONITORING.

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Introduction: On-therapy impedance-pH monitoring in proton pump inhibitor (PPI)-refractory reflux disease (GERD) yielded conflicting results. Recently, novel impedance parameters assessing esophageal chemical clearance and mucosal integrity, namely the post-reflux swallow-induced peristaltic wave (PSPW) index and the mean nocturnal basal impedance (MBNI), showed a significant diagnostic yield of impedance-pH monitoring in
investigating PPI-refractory patients studied off-therapy, further improving the meaningful improvement of symptoms.

**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 relieved after swallowing high-dose PPI therapy) were blindly reviewed. All tracings were manually analyzed to detect: acid exposure time (AET; abnormal if ≥3.2% 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 reflux episodes following washouts by swallow counts. AET has been shown to be a better parameter than CP for distinguishing SAP between acid and weakly acidic reflux.

**Results:** Median AET index and MNBI were significantly lower in 39 RRE (16%; 1145 Ohms) than in 41 HRE (25%; 1741 Ohms) at baseline. Seventy-one% (45/63) patients at 6 month and 75% (27/36) patients at 12 months were completely off PPI. Data on 24 h esophageal pH at 6 m showed a positive symptomatic and mucosal healing after baseline and follow-up high-dose PPI therapy were blinded reviews. All tracings were manually analyzed to detect: acid exposure time (AET; abnormal if ≥3.2% 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 reflux episodes following washouts by swallow counts. AET has been shown to be a better parameter than CP for distinguishing SAP between acid and weakly acidic reflux.

**Conclusion:** On-therapy impedance-pH monitoring, improved chemical clearance and mucosal integrity characterize PPI-refractory typical GERD. PSPW index and MNBI efficiently distinguish PPI-refractory NERD from FH and CP index for selecting surgical candidates.

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

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**OP328 PRELIMINARY RESULTS OF A PROSPECTIVE MULTI-CENTER REGISTRY OF LOWER ESOPHAGEAL SPHINCTER STIMULATION FOR GERD: THE LESS-GERD REGISTRY**

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**Aims & Methods:** The EndoStim® LES Stimulation System (The Hague, The Netherlands) was demonstrated in clinical trials. Demographics, adverse events, GERD symptoms recorded in daily diaries, physiological data (esophageal pH / manometry) are collected with LES-ES in clinical practice at baseline and at routine follow-ups for 5-year. Lesions, adverse events, and patient-reported outcomes were recorded. GERD-HRQL score on LES-ES at baseline and at routine follow-ups at 6, 12, 24 months were calculated. Data on 24 h esophageal pH at 6 m showed a positive symptomatic and mucosal healing after baseline and follow-up high-dose PPI therapy were blinded reviews. All tracings were manually analyzed to detect: acid exposure time (AET; abnormal if ≥3.2% 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 reflux episodes following washouts by swallow counts. AET has been shown to be a better parameter than CP for distinguishing SAP between acid and weakly acidic reflux.

**Results:** Median AET index and MNBI were significantly lower in 39 RRE (16%; 1145 Ohms) than in 41 HRE (25%; 1741 Ohms) at baseline. Seventy-one% (45/63) patients at 6 month and 75% (27/36) patients at 12 months were completely off PPI. Data on 24 h esophageal pH at 6 m showed a non-statistically significant improvement. Safety data was adjudicated by an independent DSMB. Four serious adverse events in the study population were non-serious including a patient with atrial fibrillation and a patient with hepatic failure with a white thrombus in a portal vein which decreased to 8% (4/50) at 6 months (p = 0.001). 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 = 11.983, p = 0.042).

**Conclusion:** On-therapy impedance-pH monitoring, improved chemical clearance and mucosal integrity characterize PPI-refractory typical GERD. PSPW index and MNBI efficiently distinguish PPI-refractory NERD from FH and CP index for selecting surgical candidates.

**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 determined but majority of detected cancers were asymptomatic and resectable. Surveillance also detects early stage PanNETs and HPCs. 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 ENSODUCOSCOPY IMAGING OF CHROMATIC PANCREATITIS IN THE PAPYRACEOUS PARENCHYMA IN PATIENTS WITH INTRADUCTAL PAPILLARY-MUCINOUS NEOPLASMS (IPMNs)

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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 ultrasonography 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 pathological 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% (17/40) vs. 3.4% (1/29), p = 0.0002). In addition, patients with EUS-CP findings had higher grades of pancreatic atrophy and inflammation 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 ENDOMIGSCOPY (nCLE) FOR THE DIAGNOSIS OF SOLITARY PANCREATIC CYSTS: A PROSPECTIVE MULTICENTER STUDY

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Introduction: Diagnosis of solitary pancreatic cysts is clinically challenging due to the malignant potential of several cyst subtypes. nCLE is emerging as a powerful tool for the diagnosis of cystic pancreatic lesions (CPL). nCLE was inconclusive in 27 cases. The 90 proven final diagnoses 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 lymphangioleiomyomatosis and 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>Classification</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA</td>
<td>88</td>
<td>87</td>
<td>57</td>
<td>100</td>
</tr>
<tr>
<td>ML</td>
<td>84</td>
<td>88</td>
<td>100</td>
<td>97</td>
</tr>
<tr>
<td>IPMN</td>
<td>88</td>
<td>87</td>
<td>57</td>
<td>100</td>
</tr>
<tr>
<td>MCN</td>
<td>98</td>
<td>97</td>
<td>96</td>
<td>97</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; 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.

L. Palazzo: Dr. Palazzo reports non financial support from Mauna Kea Technologies; grants from Mauna Kea Technologies during the conduct of the study; 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. Caillol reports non financial support from Mauna Kea Technologies; grants from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work.

M. Palazzo: Dr. Palazzo reports non financial support from Mauna Kea Technologies during the conduct of the study.

F. Maire: Dr. Maire reports non financial support from Mauna Kea Technologies; grants from Mauna Kea Technologies during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work.

A.I. Lemaistre: Dr. Lemaistre reports personal fees from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies during the conduct of the study.

M. Giovannini: Dr. Giovannini reports non financial support from Mauna Kea Technologies; grants from Mauna Kea Technologies during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work.

Disclosures:

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.
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 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.

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**OP333 MULTIMODALITY TREATMENT OF LOCALLY ADVANCED PANCREATIC CANCER, INCLUDING FOLFIRINOX CHEMOTHERAPY, SURGICAL EXPLORATION AND IRREVERSIBLE ELECTROPORATION: PROSPECTIVE SERIES OF 132 CONSECUTIVE PATIENTS**

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²Radiology, Academic Medical Center, Amsterdam/Netherlands
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⁴Medical Oncology, Academic Medical Center, Amsterdam/Netherlands
⁵Gastroenterology, Academic Medical Center, Amsterdam/Netherlands
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⁸Medical Oncology, Academic Medical Center, Amsterdam/ Amsterdam/ Netherlands

**Introduction:** Novel treatment options in locally advanced pancreatic cancer (LAPC), including FOLFIRINOX and irreversible electroporation (IRE) have shown promising survival-outcomes. 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, 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 (1/14 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.

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*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.
OP334 ORAL ADMINISTRATION OF THE GUT-RESTRICTED GUANYLATE CYCLASE-C AGONIST, LINACLOTIDE, REDUCES ENDOMETRIOSIS-INDUCED VAGINAL HYPERALGESIA

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2Visceral Pain Group, University of Adelaide, Adelaide/Australia

Introduction: Linacotide, 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 linacotide activates GC-C expressed on intestinal epithelial cells, resulting in the production and release of cyclic GMP (cGMP), which accelerates gastrointestinal transit and inhibits visceral nociceptor activity. In addition, alterations in the cyclic GC-C/cGMP signaling pathway are associated with several chronic diseases, including inflammatory bowel disease, irritable bowel syndrome, endometriosis, and endometriosis-induced chronic pain. Hence, this study was designed to assess the impact of linacotide on the GC-C/cGMP signaling pathway in endometriosis-induced chronic pelvic pain.

Objectives and Methods: GC-C mRNA expression was determined by qRT-PCR. Painful tissues were obtained from rats treated with a model of endometriosis, and GC-C mRNA expression was assessed. The effect of linacotide on plasma extravasation was also evaluated.

Results: GC-C mRNA expression was reduced in endometriosis tissues compared to control tissues. Chronic oral dosing of linacotide reduced plasma extravasation and altered key components of the GC-C/cGMP signaling pathway.

Conclusion: Oral administration of linacotide significantly reduced visceral pain in an animal model of endometriosis-induced chronic pelvic pain. These findings suggest 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 neurophysiological mechanisms.

Disclosure of Interest: P. Ge: Employee, stock holder and stock options from Ironwood Pharmaceuticals.

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.

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Disclosure of Interest: P. Ge is an employee of Ironwood Pharmaceuticals. C. B. Kurtz is an employee of Ironwood Pharmaceuticals. G. Hannig is an employee, stockholder, and stock option holder of Ironwood Pharmaceuticals.

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 GUANYLATE CYCLASE-C AGONIST, LINACLOTIDE, REDUCES ENDOMETRIOSIS-INDUCED VAGINAL HYPERALGESIA

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Introduction: Linacotide, a guanylate cyclase-C (GC-C) agonist, is an FDA-approved drug for the treatment of Irritable Bowel Syndrome with Constipation (IBS-C) and Chronic Idiopathic Constipation (CIC). Linacotide reverses colonic mechanical hypersensitivity in chronic colonic hyperresponsive mice, and reduces noxious signaling in vivo to the spinal cord. Painful Bladder Syndrome/Interstitial Cystitis and Overactive Bladder are common comorbidities of IBS-C. Chronic oral administration of linacotide in a mouse model of bladder overactivity reverses colitis-induced changes in bladder function and nociception in the C57BL/6 mouse. Linacotide contains visco-serosurgical activity. We hypothesized that linacotide may be able to similarly reduce visceral pain in other chronic pelvic pain conditions.

Objectives and Methods: GC-C expression was determined by qRT-PCR. Painful tissues were obtained from rats treated with a model of endometriosis, and GC-C mRNA expression was assessed. The effect of linacotide on plasma extravasation was also evaluated.

Results: GC-C expression was significantly reduced in endometriosis tissues compared to control tissues. Chronic oral dosing of linacotide reduced plasma extravasation and altered key components of the GC-C/cGMP signaling pathway.

Conclusion: Oral administration of linacotide significantly reduced visceral pain in an animal model of endometriosis-induced chronic pelvic pain. These findings suggest 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 neurophysiological mechanisms.

Disclosure of Interest: P. Ge: Employee, stock holder and stock options from Ironwood Pharmaceuticals.

C. B. Kurtz: Employee, stock holder and stock options from Ironwood Pharmaceuticals.

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Disclosure of Interest: P. Ge is an employee of Ironwood Pharmaceuticals. C. B. Kurtz is an employee of Ironwood Pharmaceuticals. G. Hannig is an employee, stockholder, and stock option holder of Ironwood Pharmaceuticals.
OP337 PATIENTS’ PERCEPTIONS OF CONSTIPATION DIFFER STRIKINGLY FROM THOSE OF GASTROENTEROLOGY 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 (GP) 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, 934 without), 365 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). The symptom most frequently reported as important for diagnosing constipation by the general population was straining (40-43%), whereas for GPs it was hard stools (66%).

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</th>
<th>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>41% &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Hard stool</td>
<td>26%</td>
<td>32%</td>
<td>57%</td>
<td>66% &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Straining</td>
<td>43%</td>
<td>40%</td>
<td>53%</td>
<td>61% &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Sense of incomplete evacuation</td>
<td>15%</td>
<td>24%</td>
<td>21%</td>
<td>13% &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Manual disimpaction</td>
<td>14%</td>
<td>15%</td>
<td>32%</td>
<td>34% &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Non-Rome III symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long time on toilet without stool</td>
<td>42%</td>
<td>29%</td>
<td>33%</td>
<td>23% &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Laxative use</td>
<td>37%</td>
<td>33%</td>
<td>56%</td>
<td>40% &lt; 0.001</td>
<td></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.

OP388 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 µ-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 NCT01963518 and NCT01993940).

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 = 0.0020, Study 2: naldemedine 53.5%; placebo 33.6%, P = 0.001). Naldemedine treatment also showed a greater increase, 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 Principal Investigator for the Clinical Trials, and a consultant for Shionogi J. Wild: I) was a Principal Investigator on Compose1 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 report 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 clinic nurse, we suggested three screening questions. We also gave
providers and nurses a modified Fecal Incontinence Severity Inventory (FISI) to help them decide whether FI was severe enough to warrant referral to a specialist, and instructions on how to refer to the GI Medicine Clinic.

All patients attending the GMC during 4 two-week periods were considered subjects. After an initial two-week baseline, all patients were exposed to the screening methods in the same sequence for two weeks each: GI symptom checklist, provider screening, and nurse screening. Three types of outcome data were collected: (1) A limited review of electronic medical records of all patients seen during these 4 two-week periods was used to identify the number of new FI diagnoses during these 4 periods. (2) Following the last screening intervention, all 11 clinic providers rated the effort required by each intervention and indicated whether they believed the benefit outweighed the burden. (3) Telephone interviews were conducted 2–4 weeks after the index clinic visit to determine what proportion of patients had been screened during their clinic visit. A-p value of <.10 accepted as significant in this small pilot study.

Result: 1034 unique patients were seen during the 4 two-week periods: 60 had a diagnosis of FI somewhere in their medical record, and 24 had a diagnosis of FI at the index visit of this study, including 6 new FI diagnoses. Three of the 6 new diagnoses occurred during the GI checklist intervention and 3 during provider screening (<.10). None occurred during nurse screening. The GI symptom checklist was rated the least burdensome by the 11 providers (p = .09). Five out of six 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: 33/88 (37.5%) confirmed they were screened by their doctor or nurse, 55.7% said no, and 8.8% said they did not know or declined to answer.

Conclusion: Systematically encouraging gastrointestinal medicine providers to screen for FI significantly increased the number of patients receiving a new diagnosis of FI compared to baseline (p = .004). Women were more likely to be screened compared to men (p = .05). The most commonly reported strategies were the use of pads (111/182, 61%), fiber or drugs for constipation (30/182, 16%), and avoiding sex (14/182, 7.7%). Avoidance strategies reported to be most effective were antidiarrheal medications (15/182, 8%), and incontinence pads (14/182, 7.7%). Individuals who had consulted a physician, compared to those who had not consulted, were more likely to use antidiarrheal and incontinence pads (21/182, 13%). Coping strategies reported to be most effective by the largest proportion of subject is taking anti-diarrheal medication. Consultation with a physician was negatively associated with coping strategies was unrelated to sex, age, race/ethnicity, or education. The status (3.32 for non-consulters vs. 4.28 for consulters, p = .001). The most commonly reported strategies were the use of pads (111/182, 61%), fiber or drugs for constipation (30/182, 16%), and avoiding sex (14/182, 7.7%). Avoidance strategies reported to be most effective were antidiarrheal medications (15/182, 8%), and incontinence pads (14/182, 7.7%). Individuals who had consulted a physician, compared to those who had not consulted, were more likely to use antidiarrheal and incontinence pads (21/182, 13%). Coping strategies reported to be most effective by the largest proportion of subject is taking anti-diarrheal medication. Consultation with a physician was negatively associated with coping strategies was unrelated to sex, age, race/ethnicity, or education. The status (3.32 for non-consulters vs. 4.28 for consulters, p = .001).

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Disclosure of Interest:
results in better management of intraprocedural and early complications.

Conclusion: (stenosis) occurred in the EMR group. No mortality reported during the study.

HER, p 0.001) and 2 cases needed surgery. Three cases of late complications
occurred after 15 days). Results were expressed as medians, and compared
procedural, early complications (occurring within 15 days) and late complica-
tions (occurring after 15 days).

Aims & Methods: In a single tertiary center, we cross-examined our database of
diagnostic 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 adenomatous 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 complica-
tions (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%
adrenocarcinomas, 34% HGD, and 60% LGD. No significant differences were
observed in terms of age, sex, location of lesions or length of hospitalization.
There were no significant differences in the procedure time (108 min. ESD/HER,
79 min EMR), intraoperative complications (46% ESD/HER, 23% EMR)
and early complications (23% ESD/HER, 9% EMR). Intra-procedural complica-
tions occurred in 46% of ESD/HER vs 23% in EMR (p = 0.015), including
haemorrhage (25.6%, EMR 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 (Haemorrhage, 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 intra-procedural 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 intra-procedural and early complications.

Disclosure of Interest: All authors have declared no conflicts of interest.
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 high-pressure waterjet EREBIE® 2 system to lift mucosa. We hypothesized that this waterjet could make submucosal dissection safer and studied this in porcine esophagus.

**Aims & Methods:** Water pressures of 30–70 bar were tested to determine the lack of serosa. HybridKnife® ESD using DualKnife® (C-ESD). Each of 3 virtual esophageal lesions in 2 pigs were resected 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 water pressure resulted in the best balance between dissection speed and view-disturbing water backflow. The dissection speeds for 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 immediately in porcine esophagus.

**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.
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

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2</td>
<td>50%</td>
<td>98.5%</td>
<td>75%</td>
<td>95.7%</td>
<td>94.5%</td>
<td>0.57</td>
</tr>
<tr>
<td>T1</td>
<td>41.7%</td>
<td>88.5%</td>
<td>41.7%</td>
<td>88.5%</td>
<td>80.8%</td>
<td>0.30</td>
</tr>
<tr>
<td>T3</td>
<td>35.8%</td>
<td>86.5%</td>
<td>50%</td>
<td>80%</td>
<td>74%</td>
<td>0.27</td>
</tr>
<tr>
<td>T4</td>
<td>77.3%</td>
<td>61%</td>
<td>61.5%</td>
<td>77.3%</td>
<td>68%</td>
<td>0.37</td>
</tr>
<tr>
<td>T4a</td>
<td>76.2%</td>
<td>65.5%</td>
<td>61.5%</td>
<td>75%</td>
<td>70%</td>
<td>0.40</td>
</tr>
<tr>
<td>T1-T2/T3-T4</td>
<td>87.3%</td>
<td>50%</td>
<td>84.2%</td>
<td>56.3%</td>
<td>78.1%</td>
<td>0.39</td>
</tr>
<tr>
<td>N0</td>
<td>73.9%</td>
<td>78.9%</td>
<td>81%</td>
<td>71.4%</td>
<td>76.2%</td>
<td>0.52</td>
</tr>
<tr>
<td>N1</td>
<td>50%</td>
<td>83.3%</td>
<td>33.3%</td>
<td>90.3%</td>
<td>78.6%</td>
<td>0.28</td>
</tr>
<tr>
<td>N2</td>
<td>55.6%</td>
<td>81.8%</td>
<td>45.5%</td>
<td>87%</td>
<td>76.2%</td>
<td>0.35</td>
</tr>
<tr>
<td>N3</td>
<td>97.4%</td>
<td>90.2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N+/N−</td>
<td>78.9%</td>
<td>73.9%</td>
<td>71.4%</td>
<td>81%</td>
<td>76.2%</td>
<td>0.52</td>
</tr>
<tr>
<td>PET N+/N−</td>
<td>50%</td>
<td>90.9%</td>
<td>81.8%</td>
<td>69%</td>
<td>72.5%</td>
<td>0.42</td>
</tr>
</tbody>
</table>

**Conclusion:** Our results, obtained from a real 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**

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**OP348 SORBITIN DEFICIENCY REDUCES DUCTURAL REACTION, HEPATOCYTE APOPTOSIS AND LIVER FIBROSIS IN CHOLESTATIC-INDUCED LIVER INJURY**

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**Introduction:** Sorbitin, 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. Sorbitin 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 secretion. Cholestatic injury was induced in wild type (WT) and Sorbitin−/− 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 Ly6G (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 amitrptyline administration. IL-6 effects was neutralized by administration of an anti-HL-6 antibody to WT mice before BDL. Sorbitin−/− mice displayed strongly attenuated liver fibrosis following BDL and CCl4 treatment, accompanied by an attenuated in vitro activation phenotype of Sorbitin−/− HSC culture. Sorbitin−/− hepatic aSMase activity was in line with reduced hepatocyte apoptosis following BDL and CCl4 injury and reduced susceptibility of hepatocytes from Sorbitin−/− 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, Sorbitin−/− 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. Short-term 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:** Sorbitin 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.

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**OP349 ACTIVATION OF NECROPTOSIS IN HUMAN AND EXPERIMENTAL CHOLESTASIS**

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**Introduction:** Targeting necroptosis, a programmed necrotic cell death pathway regulated by receptor-interacting protein 3 (RIP3), is being considered as a potential therapeutic option for the treatment of inflammation-driven liver diseases. Still, the role...
of necrosis in the pathogenesis of cholestatic liver injury has been poorly established.

**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 cholestatic liver injury. Initial flow cytometry and immunohistochemistry of RIP3 and its target phosphorylated-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 surgeries for 3 and 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.

**Results:** 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 necrosmere 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 was 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 results suggest a significant activity increase in 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 PBC 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 HMSP-ICT/0018/2011, SFRH/BD/91119/2012, SFRH/BD/88212/2012 and SFRH/BD/104160/2014, FCT, Portugal).

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

**References:**
OP352 IMPROVING METABOLIC PARAMETERS IN NAFLD BY TARGETING NUCLEAR RECEPTORS

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Disclosure of Interest: Therapies for NAFLD. (Supported by PTDC/BIM-MEC/0873/2012, SFRH/BD/53468/2010)

Aims & Methods: Steatohepatitis is a hallmark of non-alcoholic fatty liver disease (NAFLD) and the gene encoding protein tyrosine phosphatase non-receptor type 22 (PTPN22) is frequently mutated in autoimmune disorders. Recently, PTPN22 was shown to participate in disease pathogenesis and, as such, constitute potential therapeutic targets. In this work, we aimed to elucidate the role of the miR-21/PPARγ/C11 pathway in liver and muscle tissues of murine NASH models and ascertain the therapeutic potential of miR-21 abrogation alone or in combination with obeticholic acid (OCA).

Results: Wild-type (WT) and miR-21 KO mice were fed with chow (n = 10) or methionine and choline-deficient (MCD; n = 10) diets for 2 and 8 weeks. Alternatively, mice were fed either chow (n = 12) or fast food diet (FF; n = 12) for 25 weeks. Six animals from each group had their diet supplemented with OCA 10 mg/kg/day (Intercept Pharmaceuticals, Inc.). Human liver biopsies were obtained from morbid obese NAFLD patients (n = 28). Liver/muscle samples were processed for histological analysis and assessment of miR-21, pro-inflammatory/pro-fibrogenic cytokines, PPARγ and metabolic relevant genes, by qRT-PCR and immunoblotting. A Tg Aβ mouse model was performed to evaluate modulation of lipid regulated genes. ROS levels were analysed through the use of 2′,7′-dichlorodihydrofluorescein diacetate.

Conclusion: In conclusion, activation of PPARγ as a result of miR-21 abrogation, together with FXR activation by OCA, significantly improves metabolic parameters in NASH, highlighting the therapeutic potential of multi-targeting therapies for NAFLD. (Supported by PTDC/BIM-MEC/0873/2012, SFRH/BD/88212/2012, FCT, Portugal).

Disclosure of Interest: All authors have declared no conflicts of interest.
OP355 DIRECT INHIBITION OF HMBG1 BY NEUTRALIZING ANTIBODY AMELIORATES EXPERIMENTAL COLITIS IN MICE VIA MODULATION OF MACROPHAGES’ PLASTICITY
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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. While there is growing awareness of a relationship 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 CAMS with active ulcerative colitis, and colitic CgA-deficient mice demonstrated a significant decrease of colitis associated to a modulation of macrophage phenotype. As CgA is a prohormone, herein, we assessed the functional role of a specific CgA-derived peptides (Chromogranin (CHR); hCg-A47-66) in the regulation of acute colitis and the functional plasticity of murine macrophages.

Aims & Methods: Colitis was induced in C57BL/6 mice (7–8 weeks old) by administrating dextran sulfate sodium (DSS 3%) in drinking water for 5 days. Mice were treated with CHR (2.5 mg/kg) for 3 days before the DSS induction started 1 day before induction of colitis and lasted for a total of 6 days. Disease activity index (DAI) was evaluated daily and mice were sacrificed on day 5 post-DSS induction to assess the extent of colitis. At sacrifice macroscopic scores were evaluated, then a 25-gm tissue sample of colonic mucosa tissue was collected for ELISA and colonic interleukin (IL)-1β, IL-6, TNF-α, MIP-1α, MIP-1β, and ARG-1 were assessed using ELISA and RT-qPCR. Native peritoneal macrophages were isolated from C57BL/6 mice treated with CHR (200 mg/ml) then exposed for 6 h at 37 °C to LPS (100 ng/ml) to promote CAM to OR and to IL-4/IL-13 (20 ng/ml) to promote AAMS. CAMs markers (IL-6, IL-1β, TNF-α, MIP-1α & MIP-β) and AAMS markers (ARG-1) were quantified by using ELISA and RT-qPCR.

Results: Preventive treatment with CHR significantly reduced the DAI onset and severity of colitis associated to rectal bleeding, stool consistency and weight loss. Macrophage plasticity scores, serum-CRP, colon IL-1β, L-L, TNF-α, MIP-1α, MIP-1β were significantly decreased while ARG-1 was significantly increased. In vitro, CHR-conditioned CAMS expressed significantly less IL-1β, IL-6, TNF-α, MIP-1α, MIP-1β but, surprisingly, more ARG-1 when compared to LPS control condition. Moreover, CHR-conditioned AAMS expressed significantly more ARG-1 when compared to IL-4/IL-13 control condition.

Conclusion: These findings suggest that CHR can modulate the severity of experimental colitis. CHR treatment can attenuate the severity of experimental colitis and the inflammatory process via the modulation of the functional plasticity of murine macrophages and their functions. Targeting CgA-derived peptides may lead to novel therapeutic strategies in ulcerative colitis.

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

OP356 NEW, PEPTIDE INHIBITOR OF DIPEPTIDYL PEPTIDASE IV, EMD-1 ATTENUATES COLITIS IN MICE VIA POST-TRANSCRIPTIONAL ADMINISTRATION
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Introduction: PETIR (PepTidease-Targeted ImmuNoregulation) is a novel therapeutic strategy which takes for the purpose restoration of the immune balance by limiting the activation of immune cells and induction of endogenous protective mechanisms, such as TGFβ and glucagon-like peptide-2 (GLP-2) through inhibition of DPP IV-dependent pathways. Experimental data indicate that PETIR results in suppression of cell proliferation and reduced synthesis of pro-inflammatory cytokines without affecting cellular viability.

Aims & Methods: The objective of this study was to test the anti-inflammatory activity of a novel DPP IV inhibitor EMD-1 in the mouse models of colitis. The inhibitory effect of EMD-1 on DPP IV was characterized in vitro using the activity of a novel DPP IV inhibitor EMD-1 in the mouse models of colitis. The inhibitory effect of EMD-1 on DPP IV was characterized in vitro using the activity of a novel DPP IV inhibitor EMD-1 in the mouse models of colitis. The inhibitory effect of EMD-1 on DPP IV was characterized in vitro using the activity of a novel DPP IV inhibitor EMD-1 in the mouse models of colitis.

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

OP357 CHROMOFUNGIN (CHR) AMELIORATES EXPERIMENTAL COLITIS IN MICE VIA MODULATION OF MACROPHAGES’ PLASTICITY
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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. While there is growing awareness of a relationship 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 CAMS with active ulcerative colitis, and colitic CgA-deficient mice demonstrated a significant decrease of colitis associated to a modulation of macrophage phenotype. As CgA is a prohormone, herein, we assessed the functional role of a specific CgA-derived peptides (Chromofungin (CHR); hCg-A47-66) in the regulation of acute colitis and the functional plasticity of murine macrophages.

Aims & Methods: Colitis was induced in C57BL/6 mice (7–8 weeks old) by administrating dextran sulfate sodium (DSS 3%) in drinking water for 5 days. Mice were treated with CHR (2.5 mg/kg) for 3 days before the DSS induction started 1 day before induction of colitis and lasted for a total of 6 days. Disease activity index (DAI) was evaluated daily and mice were sacrificed on day 5 post-DSS induction to assess the extent of colitis. At sacrifice macroscopic scores were evaluated, then a 25-gm tissue sample of colonic mucosa tissue was collected for ELISA and colonic interleukin (IL)-1β, IL-6, TNF-α, MIP-1α, MIP-1β, and ARG-1 were assessed using ELISA and RT-qPCR. Native peritoneal macrophages were isolated from C57BL/6 mice treated with CHR (200 mg/ml) then exposed for 6 h at 37 °C to LPS (100 ng/ml) to promote CAM to OR and to IL-4/IL-13 (20 ng/ml) to promote AAMS. CAMs markers (IL-6, IL-1β, TNF-α, MIP-1α & MIP-β) and AAMS markers (ARG-1) were quantified by using ELISA and RT-qPCR.

Results: Preventive treatment with CHR significantly reduced the DAI onset and severity of colitis associated to rectal bleeding, stool consistency and weight loss. Macrophage plasticity scores, serum-CRP, colon IL-1β, L-L, TNF-α, MIP-1α, MIP-1β were significantly decreased while ARG-1 was significantly increased. In vitro, CHR-conditioned CAMS expressed significantly less IL-1β, IL-6, TNF-α, MIP-1α, MIP-1β but, surprisingly, more ARG-1 when compared to LPS control condition. Moreover, CHR-conditioned AAMS expressed significantly more ARG-1 when compared to IL-4/IL-13 control condition.

Conclusion: These findings suggest that CHR can modulate the severity of experimental colitis. CHR treatment can attenuate the severity of experimental colitis and the inflammatory process via the modulation of the functional plasticity of murine macrophages and their functions. Targeting CgA-derived peptides may lead to novel therapeutic strategies in ulcerative colitis.

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

OP358 DEFICIENCY OF PH-SENSING RECEPTOR TDAG8 AMELIORATES T-CELL TRANSFER COLITIS
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Abstract: Macrophage plasticity affects the severity of inflammatory bowel disease (IBD) and plays a role in the development of colitis. We, therefore, investigated the role of the ph-sensing receptor TDAG8 (TDG8) in experimental colitis and evaluated the potential therapeutic effect of TDG8 deficiency. We found that TDG8 deficiency ameliorates colitis and reduces the severity of this disease. Our results suggest that TDG8 plays a role in the pathogenesis of IBD.

Aim: To investigate the role of TDG8 in the development of experimental colitis.

Methods: We used a T-cell transfer colitis model and generated T-cell transfer colitis in TDG8-deficient mice. Our results showed that TDG8 deficiency ameliorates colitis and reduces the severity of this disease.

Conclusion: TDG8 deficiency ameliorates colitis and reduces the severity of this disease. Our results suggest that TDG8 plays a role in the pathogenesis of IBD.

Disclosures: All authors have declared no conflicts of interest.
Introduction: The adaptive immune system plays a crucial role in the pathogenesis of inflammatory bowel disease (IBD). Colony stimulating factor (CSF) production in IBD is typically associated with a decrease in local pH. The proton-sensing receptor T-cell death associated gene 8 (TDAG8), also known as G-protein-coupled receptor 65 (GPR65), has been identified as a risk gene for IBD in recent genome wide association studies.

Aims & Methods: We investigated the role of TDAG8 in T cell-mediated pathogenesis in intestinal inflammation using a murine adaptive transfer colitis model. Naive T-cells (CD4+CD25L-), from WT and TDAG8-/- donor mice, were intravenously transferred. Injection of PBS was used in a control group. The results of colitis were evaluated by weight change, colonoscopy score, spleen weight, H&E staining, IHC and mRNA expression.

Results: Induction of colitis was observed after 3 weeks by weight loss, diarrhea and bloody stool. The WT group showed severe weight loss (p < 0.013), whereas the TDAG8-/- group displayed only a minor delay in weight gain. No significant differences were observed in colon length, spleen weight and colonoscopy score between PBS and the TDAG8-/- groups. H&E staining of distal and proximal parts of the colon showed severe inflammation and crypt damage in the WT mice, whereas regulation of mRNA expression of pro-inflammatory cytokines (INFγ, TNF, IL17A) was observed in the TDAG8-/- group in comparison with the WT group. No significant differences were observed in mRNA expression levels of FOXP3, RORγt and IL18.

Conclusion: Our data demonstrate that TDAG8-deficiency in T-cells ameliorates the development of colitis suggesting an important physiological role of this pH receptor.

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

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00 SURGERY MEETS ENDOSCOPY IN THE COLON – ROOM F1

OP359 TRANSLATIONAL ENDOSCOPIC MICROSURGERY VERSUS ENDOSCOPIC MUCOSAL RESECTION FOR LARGE RECTAL ADENOMAS (IFN-ALY)


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Introduction: Non-randomized studies suggest that endoscopic mucosal resection (EMR) is usually effective in removing large rectal adenomas as compared to endoscopic submucosal dissection (ESD).

Aims & Methods: For this randomised controlled non-inferiority trial, patients with rectal adenomas ≥3 cm, without malignant features, from 20 hospitals were included and randomised (1:1) to EMR or ESD, allowing endoscopic removal of residual adenoma at 3 months. Unexpected malignancies were excluded post randomisation. Primary outcomes were recurrence within 24 months and 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 mortality, quality of life, anorectal function and costs. This trial is registered in the Dutch Trial Registry (TRN1422).

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 0.89, 95% CI 0.64–1.24, p = 0.45). Major complications occurred in 1% (EMR) vs. 8% (TEM) (p = 0.046). Quality adjusted life years were similar in both groups. Although EMR patients scored more favourably on disease specific quality of life questionnaires, mean scores were similar and continued improvement after adenoma resection regardless of treatment. EMR was approximately $3000 cheaper and therefore more cost-effective.

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.

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00 UPPER GI BLEEDING – ROOM M

OP361 MEDIUM- AND LONG-TERM RESULTS OF TREATMENT WITH LANREOTIDE IN CASES OF CHRONIC OR RECURRENT OBSCURE GASTROINTESTINAL BLEEDING OR DUE TO GASTROINTESTINAL ANGIODYSPLASIAS

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Introduction: Somatostatin analogues 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. For this purpose we conducted a retrospective, single-center study conducted under conventional clinical practice, following a defined management protocol, between 2003 and 2012. Patients with chronic or recurrent obscure GB or due to GIADs, refractory to or not candidates for iron therapy, endoscopic, surgical or angiographic treatments, were included. Curative patients and those ones with very limited life expectancy because of comorbidities (IVC-Society of American Society of Anesthesiologists Classification-ASA) were excluded. The diagnostic protocol included 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, 0.37–66 months).

Conclusion: NCAST 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. NCAST 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.
iron doses, and non-diagnostic endoscopies. Differences between data from 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 PATIENTS WITH ANGIODYSPASIAS AT MULTIPLE SITES OR LOCATED IN THE COLON: A POOLED ANALYSIS OF INDIVIDUAL PATIENT DATA


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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 gastrointestinal 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, 180 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 vs 5.0 ± 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...
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

OP356 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 UGH audit reported no difference2. We studied whether out of hours (OOH) admissions had more comorbidity, 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 30 day 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 the Kruskal-Wallis tests were used as appropriate. A two-tailed significance level of 5% was used.

Results: 2181 consecutive patients, 60% male, median age 66 years were seen. There were no significant differences in mortality, need for endoscopic therapy, secondary to PUD, in order to define high-risk patients that could benefit from alternative methods like angiography or surgery. Retrospective analysis of all cases of UGIB secondary to PUD that were submitted to two endoscopic therapies between 2010 and 2014 in a tertiary center. We recorded demographic, clinical, analytical and endoscopic data. Morbidities were evaluated according to the age adjusted charlson comorbidity index (ACCI). The main endpoint was rebleeding, defined as: objective evidence of UGIB, with hemodynamic instability and Hb decrease ≥2g/dL, or need for more than 3 units of blood in the 72-hour period after the endoscopic treatment.

Results: We identified 56 patients who underwent a second endoscopic therapy. The mean age was 76 years (males: 63%) and the mean ACCI was 7 (+3.1). The mean Rockall location of PUD was duodenal (80.4%) and 26.8% were classified as having a high-risk location (small gastric curvature / posterior wall of the bulb); the estimated mean size of PUD was 13.3 mm (+6.8). The mean number of blood units transfused was 3 (±2.4), Rebleeding occurred in 23% and in-hospital mortality was 4% (0.01). A multivariate analysis identified as having a higher risk (small gastric curvature / posterior wall of the bulb); the estimated mean size of PUD was 13.3 mm (+6.8). The mean number of blood units transfused was 3 (±2.4), Rebleeding occurred in 23% and in-hospital mortality was 4% (0.01). A multivariate analysis identified as having a higher risk (small gastric curvature / posterior wall of the bulb); the estimated mean size of PUD was 13.3 mm (+6.8). The mean number of blood units transfused was 3 (±2.4), Rebleeding occurred in 23% and in-hospital mortality was 4% (0.01). A multivariate analysis identified

Conclusion: In patients with UGIB secondary to PUD that require a second endoscopic therapy for rebleeding, the need for higher blood transfusion (>4) and large ulcers (>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 HOMOglobIN LEVELS: AS PREDICTIVE CLINICAL FACTORS FOR EARLY DEATH IN PATIENTS WITH PERCUTANEOUS ENDOSCOPIC 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 this 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 January 2008 to March 2011 was performed. We examined clinical and preparative laboratory data and extracted predictive factors of early death after PEG by using univariate and multivariate analyses.

Results: A total of 1077 patients (502 female (46.7%) and 575 male (53.3%); mean age 78 y.o.) were assessed. Predictors of poor survival after PEG included history of ischemic heart disease (odds ratio [OR] 2.32, 95% confidence interval [CI] 1.2–4.3, P < 0.01), blood urea nitrogen level ≥30 mg/dL (OR 3.14, 95% CI 1.8–5.5, P < 0.0001), C-reactive protein level ≥2.0 mg/dL (OR 4.04, 95% CI 2.2–7.3, P < 0.0001), albumin level ≤2.7 mg/dL (OR 4.2, 95% CI 1.2–13.2, P < 0.001), and hemoglobin level ≤11.2 g/dL (OR 4.0, 95% CI 2.0–8.0, P < 0.0001). Multivariate analysis on predictive factors of early death revealed a significant relationship with each and each of the following: history of ischemic
Aims & Methods: In this study, we aimed to unravel the molecular mechanism underlying tumor angiogenesis in colorectal cancer (CRC). We isolated endothelial and epithelial cells from surgically resected CRC tissues and corresponding normal colon tissues using antibodies against endothelial (CD146) and epithelial markers (EpCAM). RNA sequencing (RNA-seq) was carried out in 3 pairs of normal and tumor endothelial cells. Gene expression was validated by quantitative RT-PCR (qRT-PCR) and immunohistochemistry. Functions of a selected gene were analyzed by tumor conditioned medium (TCM) experiments, in vitro tube formation assay, cell cycle analysis, gene expression microarray and xenograft experiments.

Results: Through RNA-seq analysis, we identified a series of 18 genes which were upregulated in the endothelial cells isolated from CRC tissues. We further validated the results by qRT-PCR and immunochemistry in a larger number of clinical samples, and identified gene A as a novel candidate of the tumor endothelium-related gene. Expression of gene A was also upregulated in human umbilical vein endothelial cells (HUVECs) treated with TCM obtained from CRC cells. Knockdown of gene A expressed in vitro tube formation and induced G1 cell cycle arrest in HUVECs. Microarray analysis revealed that knockdown of gene A induced expression changes of approximately 300 genes in HUVECs, and gene ontology analysis showed that cell cycle-related genes were significantly enriched in the affected genes. To confirm our findings in vivo, we co-transplanted CRC cells with HUVECs into nude mice. We found that knockdown of gene A in HUVECs resulted in reduced micro vessel formations in the xenograft tissues. Finally, we evaluated the clinical implication of gene A in colorectal cancer. The Cancer Genome Atlas (TCGA) datasets of primary CRCs (n=411) revealed that higher expression of gene A is associated with worse overall survival, suggesting that upregulation of gene A in tumor endothelial cells may promote aggressiveness of CRC.

Conclusion: Our results suggested that gene A may play an important role in the angiogenesis in colorectal cancer, and that it could be a potential therapeutic target.

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?
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Introduction: Spontaneous bacterial peritonitis (SBP) develops in up to 25% of patients with cirrhosis and it is associated with significant short and long-term morbidity and mortality. With the ambularization of medical care, the use of antibiotics for primary and secondary prophylaxis of SBP has increased. 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: We compare clinical, analytical and microbiological features between nosocomial and community-acquired SBP, to assess the influence of the infection acquisition site when evaluated in hospital mortality and 1 year-mortality. Retrospective cohort study, conducted in 3 tertiary centers that evaluated all cases of 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 as same variable. Multiresistant bacteria (MDR) was defined according to the ECDC criteria (resistant to 3 antibiotic families, including beta-lactam antibiotics).

Results: We identified 222 episodes of SBP, from which 110 were considered as community-acquired; in-hospital mortality was 28.8% and 1 year-mortality was 56.9%. In 85 episodes we obtained microbiological isolation (MDR = 28%), with a predominance of gram negative (53.6%). Community-acquired SBPs were more frequently by gram negative bacteria and Nosocomial-acquired SBPs were more frequently by gram positive bacteria (p = 0.033); SBPs secondary to MDR-bacteria were more frequent in Nosocomial-acquired group (19/64 vs 6/36%; p = 0.003). No statistically significant differences were noticed between centers when evaluated by microbiological isolation rate, gram staining of MDR isolations. There were no statistically significant differences between Community-acquired SBP and Nosocomial-acquired SBPs for the variables age, gender, Child-Pugh, MELD, Hb, leukocytes, platelets, CRP, Na, INR, bilirubin, albumin, ascites fluid characteristics, gastrointestinal bleeding, acute kidney injury, renal and hemodynamic instability and diagnostic paracentesis. No complications were recorded.

Conclusion: Community-acquired SBPs were more frequently caused by gram negative bacteria and Nosocomial-acquired SBPs were more frequently by gram positive bacteria. Nosocomial-acquired SBPs secondary to MDR-bacteria were more frequent in Nosocomial-acquired group (19/64 vs 6/36%; p = 0.003). No statistically significant differences were noticed between centers when evaluated by microbiological isolation rate, gram staining of MDR isolations. There were no statistically significant differences between Community-acquired SBP and Nosocomial-acquired SBPs for the variables age, gender, Child-Pugh, MELD, Hb, leukocytes, platelets, CRP, Na, INR, bilirubin, albumin, ascites fluid characteristics, gastrointestinal bleeding, acute kidney injury, renal and hemodynamic instability and diagnostic paracentesis. No complications were recorded.

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

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United European Gastroenterology Journal 4/5(5)

OP372 ENDORINGSTM INCREASES ADR EVEN IN HIGH-RISK SCREENING COLONOSCOPY: RESULTS OF A SINGLE CENTRE PILOT STUDY
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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 colonoscopists 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 backward to allow intubation 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 non-gastroenterologists. Aims & Methods: A prospective data set was collected during screening colonoscopy (performed by two accredited colonoscopists) when the Endorings™ device was used and compared the results to outcomes from the previous 3 months, for the same two colonoscopists when the device was not in use (ie. historical controls).

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 28% increase in the number of polyps detected at any given procedure. There were no significant differences in completion rates, withdrawal time, use of sedation or comfort scores. The device was removed in 5/66 procedures due to interference with intubation (in the presence of either an angulated sigmoid or diverticula). There were no significant differences in complications rates of 0.9% with the device (n = 12), and 0.6% in the historical controls (n = 20) with ppr of 0.97. Likewise, proximal lesion detection and complications rates of 0.9% (95%CI −0.7, 1.5) per 10,000 endoscopies per two-year-period, p = 0.0013). Sedation induced the probability of procedure events (0.24% in sedated and 0.6% in unsedated patients, p = 0.025). Notably, all perforations occurred under sedation.

Conclusion: This study showed a strong improvement in quality of screening colonoscopies performed with 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.

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)
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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 attaches 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, randomised controlled trial. Ethics approval was obtained (ref. 5).
Conclusion: In the UK, bowel cancer screening is performed by highly experienced endoscopists with special accreditation. Our results suggest that in expert hands, ADR exceeds 60% even without Endocuff. In such settings, Endocuff Vision did not improve polyp detection rates (PDR) or ADR. However, Endocuff did not cause any adverse events, prolong procedure duration or cause additional injuries. These data demonstrate the safety and feasibility of Endocuff. However, no additional gain was demonstrated in expert hands.

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

Acknowledgements: The authors acknowledge the financial support from the NHS England, Leeds Teaching Hospitals (NHSFT), and University of Leeds (UK).

Disclosure of Interest: All authors have declared no conflicts of interest.
### Table 1 (OP375): Efficacy and safety endpoints

<table>
<thead>
<tr>
<th>Abstract legend</th>
<th>NER1006 2-day split-dosing N2D</th>
<th>Comparator: trisulfate solution TS</th>
<th>CI for the difference [P value]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></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>−0.15% [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 ascends [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 ascends</td>
<td>14.1%</td>
<td>17.1%</td>
<td>−11.36% [0.863]</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: Polyp detection rate, colon ascends</td>
<td>18.5%</td>
<td>23.9%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Polyp 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>BOCLRIR score [mean (SD)]</td>
<td>39.9 (17.70)</td>
<td>39.6 (17.51)</td>
<td>n.a.</td>
</tr>
<tr>
<td>SAFETY</td>
<td>Safety set, n = 262</td>
<td>Safety set, n = 265</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>

*P < 0.05; **P < 0.01; *P < 0.001; n.a. = not applicable

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**1L** NER1006 showed high efficacy and safety in overnight split-dosing administration.

**Disclosure of Interest:** M. DeMicco: Contractor for Norgine through Anahme Clinical Trials LLC; Principal Investigator for the NOCT study. L.B. Clayton: Employee of Norgine R. Ng Kwet Shing: Employee of Norgine M.S. Epstein: Contractor for Norgine through Investigative Clinical Research. Investigator for the NOCT study.

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**OP376** THE USE OF A SELF-EXPLANATORY BOOKLET FOR BOWEL PREPARATION WITHOUT ORAL INSTRUCTIONS OVERCOMES BARRIERS AGAINST SPLIT-DOSE ADOPTION FOR EARLY MORNING COLONOSCOPY: A RANDOMIZED CONTROLLED TRIAL

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**Introduction:** 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 whether additional oral explanation, aimed at reinforcing the benefits of split-dose, may further improve compliance, patients were randomized in two groups: group A-only booklet delivered; group B—oral explanation along with booklet. Patients’ data (demography, education, socioeconomic status), along with prep-related and procedural data, were collected by a structured questionnaire on colonoscopy day. Colon cleansing was evaluated using Boston Bowel Preparation Scale (BBPS). Proportions were compared by chi-squared test or chi-squared for trend, as appropriate. A logistic regression analysis was performed to disclose factors associated with compliance to split-dose prescription. A p-value <0.05 was considered significant for all comparisons.

**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 efficacy (HCS) result was good 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.

**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 unfeasible, 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**


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**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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**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 overt disease in the same geographic area. For the epidemiological analysis the MilleInRete dataset was used, where medical records of 139,104 subjects were stored by 99 general practitioners in the Veneto region. As indicators, transaminases elevation (>2 niv in at least two occasions) for liver disease and thrombocytopenia (<100,000/μL) for liver cirrhosis were used. Patients with thrombocytopenia due to hematologic disorders were excluded. Prevalence of patients with already diagnosed chronic hepatitis, cirrhosis and comorbidities was assessed using ICD-9-CM-1997 codes.

**Result:** Among 11,540 patients with elevated transaminases, 35% were already diagnosed as patients with liver disease of known etiology (viral hepatitis, alcohol abuse or hepatic steatosis), while in the remaining 65% no liver disease diagnosis
was recorded. Sex distribution of these patients was similar to that of the patients with liver enzymes alteration (M:F=0.91 vs 0.9, respectively), while age was higher in patients with elevated transaminases (mean age (yrs) = 55.5 vs 48.9, p < 0.0001). Patients with overt diagnosis of cirrhosis were 0.3% of the overall population, while thrombocytopenia, as indicator of occult cirrhosis, was detected in 13% of the remaining patients. The epidemiological profile of these two groups was similar [M:F=1:5.9]; mean age (yrs) = 65.6 vs M:F=1:6.7; mean age (yrs) = 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

OP378 THE NATIONAL BURDEN IN FRANCE OF HOSPITAL CARE FOR PATIENTS WITH HEPATIC ENCEPHALOPATHY: DATA FROM THE FRANCÉS NATIONAL HOSPITAL DATABASE (PMSI)

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Introduction: Hepatic encephalopathy (HE) is a complication of cirrhosis characterized by a broad spectrum of neuropsychiatric manifestations. According to the clinical symptoms there are two types of HE: covert and overt HE (OHE). In general, the prevalence of OHE is estimated at 10%–14% in cirrhotic patients, and 20% in patients with transjugular intrahepatic portosystemic shunt (TIPS). In France, the prevalence of OHE was estimated at 25,000 patients (21,000 to 30,000 patients). Yet little is published on the national burden of HE, especially in France. The purpose of this study was to use the retrospective national PMSI data (Programme Médicalisé des Systèmes d’Information) to assess the public health burden of patients with HE over a period of 7 years (2005–2011). Aims & Methods: An observational study was performed from the national PMSI database from 2005 to 2011. Given the absence of coding specificity of hepatic encephalopathy via ICD 10 code K72, K74, hepatic failure, not elsewhere classified, a medical expertise from the expression of the main symptoms of the disease was required. A negative binomial regression model was used to estimate the link between lengths of stay and HE patient's characteristics like age, sex, comorbidities (malnutrition, renal failure, bacterial infection and respiratory diseases), stays in reanimation, intensive care units and death. Result: The study collected respectively 13,484 patients on 2012 corresponding to 17,001 hospitalisations and 13,672 patients in 2013 corresponding to 17,491 hospitalisations. The mean age was 63.1 ± 13.8 years in 2013 and 62.7 ± 13.9 years in 2012. Thirty percent of patients were admitted to the intensive care units. In nearly all hospital stays, the illness was medically managed (87% of stays in 2013 and 89% in 2012). Nevertheless, there are 12% of surgical stays (1,664 stays in 2013 and 1,514 stays in 2012). The mean length of HE stay was 15 days (SD 19 days) and the median was 10 days. The length of stay was 48% longer for patients with malnutrition, and 52% longer in case of a bacterial infection. The length of stay was 12% and 14% longer for patients with renal failure and respiratory diseases, respectively. More 40 million euros per year are spent by Social Security in France for HE hospitalisations with a mean cost per hospitalisation estimated at € 62,411. Conclusion: The mean length of stay in patients with HE was high (15 ± 19 days). The binomial model confirmed the significant longer length of stay induced by patients with comorbidity such as malnutrition, renal insufficiency, bacterial infection and respiratory disease. The annual economic burden of HE hospitalisations in France amounted to € 40 million.

Disclosure of Interest: H. Hagege: Herve Hagege has acted as a medical expert for Norgine and Alfa Wassermann
C. Béreau: Christophe Béreau has acted as a medical expert for Norgine and Alfa Wassermann
C. Blein: Cécile Blein is an employee of HEVA, who were contracted by Norgine and Alfa Wassermann to participate in this study.
A. Ribot-Mariotte: Emmanuelle Robert-Mariotte was an employee of Alfa Wassermann at the time the study was undertaken.
I. Leurs: Irina Leurs was an employee of Norgine at the time the study was undertaken.

All other authors have declared no conflicts of interest.

References

OP379 THE IMPACT OF RIFAXIMIN-ALPHA ON NHS HOSPITAL RESOURCE USE IN UK PATIENTS WITH HEPATIC ENCEPHALOPATHY: A RETROSPECTIVE OBSERVATIONAL STUDY (IMPRESS)

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Introduction: In clinical trials rifaximin-α (RFX) has shown to reduce the risk of an overt episode of hepatic encephalopathy (HE) and the number of HE-related hospitalisations, but there are limited data describing its impact on healthcare resource use in real-world UK practice. This study compared hospital resource use pre- and post-RFX initiation in UK patients.

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/WA/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 (40%) patients (10% Class A, 54% B, 36% C). Resource use in the 6-12 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 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. Aspinal: Consultant and UK advisory board member for Norgine
A. Radwan: Employee of Norgine
G. Shaia: Employee of Norgine
H. Sodatoum: Employee of Norgine
R. 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.

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>
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<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Hospitals with overnight stay per patient</td>
<td>101</td>
</tr>
<tr>
<td>Total bed days</td>
<td>101</td>
</tr>
<tr>
<td>Total bed days per inpatient</td>
<td>101</td>
</tr>
<tr>
<td>Critical care bed days per inpatient</td>
<td>19</td>
</tr>
<tr>
<td>Emergency room visits per patient</td>
<td>63</td>
</tr>
</tbody>
</table>
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 births to women with HBV and 2,150 births to women with HCV using data from Swedish healthcare registries. Births to women without HBV (n = 1,428,361) and births with undetermined status for HCV (n = 1,429,165) were used 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 preeclampsia (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 was associated with an increased risk for preeclampsia and HBV with a decreased risk of preeclampsia. Further studies should corroborate these findings.

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

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Conclusions: The recently recognised alternative RAS axis comprising angiotensin converting enzyme 2 (ACE2), the effector peptide angiotensin (Ang) (1–7) and the Mas receptor is gaining interest. This study aimed to investigate the expression of Ang (1–7) and the AT2 receptor in IBD and non-IBD control colonic segments.

Methodology: Immunohistochemistry and qRT-PCR were performed in healthy and diseased tissue samples from 14 IBD patients and 14 non-IBD controls. qRT-PCR was used to quantify mRNA expression of ACE, ACE2, Ang II, Ang (1–7), AT1R, AT2R and Mas receptor.

Results: Significant differences in the expression of Ang (1–7) and AT2 receptor were noted across the groups. Circulating renin (5.24% vs. 17.40% p = 0.028) and Ang (1–7) (mean 22.8, 20.1–25.4 pg/ml) were both increased in the IBD compared with controls. No significant correlations between circulating RAS components and markers of disease activity (faecal calprotectin, C-reactive protein, platelet or white cell counts, or albumin) were noted.

Conclusion: Increased expression of Ang (1–7) in IBD compared with controls was observed. This study suggests that the alternative RAS may be involved in the pathogenesis of IBD.

Disclosure of Interest: No conflicts of interest.
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 disease.

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-TNF therapy. Myeloid DC expressed a gut-homing profile (CLA- and gut-homing (CLA+) 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-TNF therapy.

Results: Production of TNFα by myeloid DC was significantly reduced (p = 0.016) in those patients who received vitamin D alongside anti-TNF therapy, beyond that of those who received anti-TNF therapy alone (mean ± standard deviation TNFα production 4.29 ± 1.21 for TNFα treated patients and 5.49 ± 1.62 for TNFα treated patients (p = 0.025). There was a significant correlation between increase in vitamin D level and decrease in TNFα production by myeloid DC (p < 0.001).

Conclusion: High dose parenteral vitamin D, given as an adjunct to anti-TNF 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 infection; thus the ability of vitamin D to further block TNFα production may contribute to the pathogenesis of Crohn's disease. Vitamin D modulates DC homing marker expression. This study highlights the central role that this dendritic cell subset plays in the pathogenesis of Crohn's disease.

Disclosure of Interest: P. Hendy: Advisory board for: Falk, AbbVie

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

Reference


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-kB after their activation. Previous studies of our group revealed a strong expression of TLR2 and 4 on inflammatory iMACs leading to a higher susceptibility of CD patients to LPS, in parallel with a specific loss of gp96.

Aims and Methods: We aim to study the impact of the gp96-knockdown on TLR-function in the human monocytic cell line MM6 and in a conditional gp96-LysMcre knock-out mice. MM6 cells were stably transduced with lentiviral gp96-knockdown vector. The lentiviral vector particles were produced by co-transfection of HEK293T cells with transfer, packaging and envelope plasmids using Fugene HD Transfection Kit. After transduction, cells were treated with LPS (100 ng/ml) for 2 hours. Furthermore, in order to analyze the relevance in vivo, conditional LysMcre-gp96 knock-out (KO) mice were also generated after crossing gp96lox/lox mice with LysMCre. Peritoneal macrophages were isolated from both, wild-type (WT) and KO mice, and treated with LPS (100 ng/ml) for 2 hours. In transduced MM6 cells and peritoneal macrophages, TLR2 and TLR4 expression was analyzed by flow cytometry and the expression of NF-kB, IκBα, IL-8, IL-6 and TNF-α was confirmed 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% by Western blot, flow cytometry experiments revealed 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 pIκBα/IκBα in gp96-knockdown (1.6 fold induction) and in KO peritoneal macrophages (5 ± 1.5); and in protein expression of pNF-kB 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 mRNA expression of IL-10 (8 fold induction and 800 pg/ml respectively) in gp96 shRNA compared with mock-transduced cells. These results were strongly reinforced since LPS also induced a significant increase in the mRNA expression of IL-8 (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.

WEDNESDAY, OCTOBER 19, 2016
10:30-12:00

GASTRIC AND JUNCTIONAL CANCERS – ROOM 1.86

OP389 A NEW, BIOLOGICALLY RELEVANT CLASSIFICATION FOR ADENOCARCINOMA AT THE GASTRO-OESOPHAEGAL JUNCTION

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Introduction: Adenocarcinomas at the gastro-oesophageal junction (GOJ) are currently stratified according to the Siewert classification by location of the main tumour mass (Siewert I: 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). This classification has not been validated against a new genomic classification for gastric adenocarcinomas that has been proposed by the Cancer Genome Atlas project. In this study, we aimed to validate the genomic classification for GOJ and to compare the performance of the new and the current classification.

Methods: Data were extracted from the TCGA dataset and the Siewert dataset. The genomic classification was performed using the cBioPortal (cBioPortal.org) and the performance was assessed using the PAM50 signature. The Siewert classification was validated against the cBioPortal dataset.

Results: The cBioPortal dataset consists of 455 tumours, of which 278 were confirmed by qRT-PCR. Clustering analysis revealed two main clusters of patients: one with a higher copy number alteration, and one with a higher mutation rate of the tumour. The genomic classification for GOJ was confirmed by a 2 fold enrichment of the cBioPortal dataset.

Conclusion: The genomic classification for GOJ is validated against the cBioPortal dataset and is confirmed by the Siewert classification.

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 WITH 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 of Slit-Robo signaling. However, the involvement of SRGAP1 activation and functional role in gastric carcinogenesis has not been investigated.

Aims & Methods: We aim to investigate the biological functions of SRGAP1 and comprehensively reveal its regulation by deregulated miRNAs in gastric carcinoma. First, we performed the mRNA expression and protein expression of SRGAP1 in MKN28, MGC-803 and SGC-7901 cells and confirmed expression of these genes within the respective subgroups. Comparison of the recurrence and survival of gastric cancer 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-kB after their activation. Previous studies of our group revealed a strong expression of TLR2 and 4 on inflammatory iMACs leading to a higher susceptibility of CD patients to LPS, in parallel with a specific loss of gp96.

Results: After checking that the efficiency of lentiviral knockdown was more than 90% by Western blot, flow cytometry experiments revealed 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 pIκBα/IκBα in gp96-knockdown (1.6 fold induction) and in KO peritoneal macrophages (5 ± 1.5); and in protein expression of pNF-kB 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 mRNA expression of IL-10 (8 fold induction and 800 pg/ml respectively) in gp96 shRNA compared with mock-transduced cells. These results were strongly reinforced since LPS also induced a significant increase in the mRNA expression of IL-8 (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.
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 up-regulated and epithelial marker (E-cadherin) was down-regulated in MKN45-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 with high level of HOXB7 were also significantly increased in MKN45-B7 tumor-implanted nude 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 CANCER
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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 cancer patients with gastric cancer in a category the category of high risk 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 category 4 lesion (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 neoplasms was defined as ≥ 1 cm, adenoma with villous component, adenoma with HGD, three or more polyps or 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 < 0.05). The risk factors of high-risk colorectal neoplasms were associated with age, DM, colon cancer family history, and presence of gastric cancer category 4 lesion. The risk factors of colon cancer were associated age, and colon cancer family history, and presence of gastric cancer category 4 lesion.

Conclusion: Increase of high-risk colorectal neoplasm 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 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-esophageal 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 forthcoming Issue of Systematic Reviews. We searched the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE, and searched reference lists of studies. The search was not restricted to English language publications only. Randomized controlled therapy and/or targeted therapy versus BSC or versus a control arm, in patients with esophageal or gastro-esophageal junction cancer were included. Two authors independently extracted data.

Results: For the comparison of palliative chemotherapy or targeted therapy versus BSC, five trials with a total of 751 patients were included in the meta-analysis for overall survival (OS). This analysis demonstrated a significant benefit in OS in favor of the group receiving palliative chemotherapy and/or targeted therapy compared to BSC (hazard ratio (HR) 0.81 (0.71 to 0.92)). A similar trend was observed for progression free survival (PFS), including two trials and 542 participants, with a HR of 0.58 (95%CI 0.28 to 1.18). For the comparison of adding a cytostatic and/or targeted agent to a control arm, ten trials, with 1288 patients in total were included for the meta-analysis of OS. This analysis demonstrated a significant benefit in favor of the arm with 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, for the studies included, was not systematically assessed.

Discussion: Palliative chemotherapy and targeted therapy 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.

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

OP395 ECONOMIC EVALUATION OF ANTIBIOTIC THERAPY VS APPENDICECTOMY FOR TREATMENT OF UNCOMPPLICATED ACUTE APPENDICITIS: RESULTS OF THE APPAC RANDOMIZED CLINICAL TRIAL
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Abstract: The aim of this study was to determine how the addition of an antibiotic to a control arm in patients with uncomplicated acute appendicitis affected the economic costs of the appendectomy and the clinical outcome. The study design was a randomized double-blind clinical trial. The trial was carried out in university hospitals in Finland. Patients with uncomplicated acute appendicitis were eligible for the study. Randomization was performed using a computer-generated random sequence in a 1:2 ratio to antibiotic therapy versus appendectomy. Patients were monitored for the first 30 days after surgery. Primary outcome measure was the cost of surgery. Secondary outcomes were the effect of the antibiotic on the clinical outcome and postoperative costs. The study was approved by the institutional review boards of the participating hospitals. The final version is expected to be published in the Cochrane Database of Systematic Reviews. The cost-effectiveness ratio was calculated as the incremental cost per additional year of survival, 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 therapy treatment to the control arm. Subanalysis with second line therapies showed a similar benefit as first line therapies. Rumurciunab 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, for the studies included, was not systematically assessed.

Conclusion: Palliative chemotherapy and targeted therapy significantly increased OS compared to BSC in patients with esophageal or gastrooesophageal junction carcinoma. Additional patients with early stage esophageal and gastroesophageal cancer who reported this outcome, often improved in the arm with an additional agent.

Disclosure: All authors have declared no conflicts of interest.
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 treatment of uncomplicated acute appendicitis in our Appendicitis Acuta (APPAC) randomized clinical trial conducted in Finland from November 2009 until June 2012. A total of 530 adult patients aged 18 to 60 years with CT-scanner confirmed uncomplicated acute appendicitis were enrolled at six Finnish hospitals. Patients were randomly assigned using computer-generated randomization (n = 273). The cost estimates were based on the cost levels of the final quarter of year 2012. All costs were recorded, whether generated by the initial visit and subsequent treatment or possible recurrent appendicitis during the one-year follow-up period.

Results: In the operated 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 treatment costs together, with diagnostic medicine having a minor role. Patients in the operated group were prescribed significantly more sick leave days (16.96, SD 8.30) compared with the antibiotic group (9.17, SD 6.89) (p < 0.001). When the age and sex of the patient as well as the hospital of care were controlled simultaneously, the appendectomy treatment option generated significantly more costs in all models.

Conclusion: To our knowledge, this is the first randomized study comparing antibiotic therapy and appendectomy for uncomplicated acute appendicitis to reach conclusion analysis. Avoiding resection among uncomplicated appendicitis 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 acute appendicitis. Further studies evaluating the optimal treatment of uncomplicated acute 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

OP396 SURGERY VERSUS CONSERVATIVE TREATMENT FOR REDUCED AND ONGOING DIVERTICULITIS: RESULTS OF A MULTICENTER RANDOMIZED CONTROLLED TRIAL (DIRECT-TRIAL)

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Introduction: Patients with recurrent or persisting complaints following an episode of diverticulitis are managed with either conservative measures or elective appendectomy. To date no studies have been done comparing these two treatment modalities. We aimed to determine which treatment is superior in terms of improving quality of life. (DIRECT trial,NTR1478 (www.trialregister.nl)).

Aims & Methods: An open-label, multicenter, randomized clinical trial was performed in 24 teaching and 2 academic hospitals in the Netherlands (DIRECT trial). Randomization was performed with either recurrent or persistent abdominal complaints after an objectively described episode of diverticulitis were included. Patients were randomly assigned to either conservative treatment, according to current day practice, or elective (laparoscopic) sigmoidectomy using a stratified digital envelope randomization system. Primary endpoint was quality of life measured by the Gastro-intestinal Quality of life Index (GIQLI) after six months.

Results: Between July 1, 2010 and April 1, 2014, 109 patients were randomized when the data safety and monitoring board prematurely terminated the trial because of increasing difficulties in recruitment. Fifty-three patients were randomized to resection and 56 to conservative treatment. The GIQLI score was significantly higher among patients randomized to resection (114.4 (SD 22.3) vs 100.4 (SD 22.7) p = 0.0001). Seven (13.2%) patients underwent elective resection due to ongoing abdominal complaints. There was no mortality.

Conclusion: Elective sigmoidectomy is superior to conservative management in terms of quality of life in patients with recurrent and persistent abdominal complaints after an episode of diverticulitis.

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

References

OP397 PREVALENCE OF SESSILE SERRATED ADENOMAS/POLYPS IN DISTAL COLON DURING SCREENING COLONOSCOPY: FLEXIBLE SIGMOIDOSCOPY: A SINGLE BOWEL CANCER SCREENING CENTRE EXPERIENCE FROM UK

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Introduction: Sessile Serrated Adenomas/Polyps (SSA/P) are responsible for nearly 20% of colorectal cancer (CRC). Despite the utility of novel image enhancing techniques including narrow band imaging it is difficult to differentiate hyperplastic (HP) polyps from SSA/P. 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 30 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/P in proximal colon was 4.5%.

Site Number of polyps Total number of polyps Number of SSA/Ps Prevalence of SSA/Ps
Rectum 222 08 3.6%
Sigmoid colon 320 13 4%
Descending colon 133 02 1.5%
Splenic flexure 37 00 0%
Transverse colon 217 07 3.2%
Heaptic flexure 30 01 2.7%
Ascending colon 168 09 5.4%
Heaptic flexure 114 09 7.9%
Site not specified 07 00 0%

Conclusion: Our cohort showed a slightly higher prevalence of SSA/P in rectum and sigmoid colon. Therefore, it becomes clinically relevant to differentiate SSA/Ps from HP polyps in recto sigmoid before adapting a diagnose and disregard approach for small (6-9 mm) hyperplastic looking polyps in this location.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP598 SERRATED POLYPOSIS SYNDROME: A SURGICAL PERSPECTIVE
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Introduction: Serrated Polyposis 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 unresectable 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 developed metachronous tumours; of these only three have recorded formal post-operative endoscopic surveillance. None of these patients met SPS criteria at the time of index surgery.

Conclusion: Three had total IRA as management of their second tumour. The median interval to development of second CRC was 24 months. In the limited resection group seven (8%) patients required further surgical intervention for endoscopically unmanageable polyp load. All had IRA as their second procedure. Total polyp burden (median 40 v 25, p < 0.01), proximal polyp burden (median 25 v 15, p = 0.002) and number of proximal polyps >10mm (median 10 v 2, p = 0.005) were higher in this group compared with those having surgery for CRC alone.

Surgery for High Polyp Burden All 31 patients had a diagnosis of SPS and under- went IRA. The median polyp count was 43 (IQR 34-56.5) and median proximal polyp burden was 31 (IQR 26.8-47.5). Surgery for Unresectable Polyp Fourteen patients had unresectable polyps and had segmental resections. None have developed CRC to date. Polyp burden in this group was equivalent to those having CRC surgery.

Conclusion: Over a third of SPS patients required colorectal resection. The vast majority for CRC, of whom only half were known to fulfil criteria for SPS at the time of their cancer resection. 2. Developing metachronous cancer is uncommon. Segmental resection and close endoscopic surveillance may be appropriate for at least some of this patient cohort and more extensive surgery reserved for those whose SPS cancers present concurrently with higher polyp counts. Surgical decision making should be guided by the endoscopic assessment of the SPS.

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

OP599 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.

Aims & Methods: We included 82 colorectal cancer patients who underwent colonoscopy with adequate bowel cleansing and caecum intubation in the Polish National Colorectal Cancer Screening Program between January 2000 and December 2008. They were followed for colorectal cancer incidence and death through national registries until December 2013. We estimated adjusted hazard ratios (HR) for individuals with different adenoma characteristics compared to individuals without adenomas and derived a novel risk classification system.

Results: Among 159,928 individuals (median age 56 years; 37.6% 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 ≥20mm 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 ≥3 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 2.2–9.95% CI –11.9–16.3).

Conclusion: Limiting surveillance recommendations to patients with adenomas ≥20mm in diameter or high-grade dysplasia or ≥3 adenomas significantly reduces the need of surveillance colonoscopies without increasing the risk for colorectal 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. 1, 2 Japanese guidelines, however, recommend that post-polypectomy surveillance 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 1–4mm and 5–9mm, high-risk adenomatous polyps, CRC, and finally to death from CRC. 4 High-risk polyps included intramuscular cancers and adenomas with a diameter ≥10mm, 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 results were 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; 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 the resection of high-risk polyps, low-risk polyps, and no polyps were 1, 3, and 5 years, respectively. In all strategies, a fecal immunochemical 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 are as follows: strategy 1, 23,004 QALYs and $US1,024.88; 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


OP401 NEW NBI MAGNIFYING ENDOCOPIC CLASSIFICATION FOR COLORECTAL TUMORS PROPOSED BY THE JAPAN NBI EXPERT TEAM (JNET)

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Introduction: There have been many narrow-band imaging (NBI) magnifying endoscopic classifications advocated (Sano, Hiroshima, Showa, and Jikei classifications) so far in Japan. NBI magnifying endoscopy for qualitative and quantitative 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 polypoid 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 polyp/ sessile serrated polyp (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 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 i) 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 1) 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 submucosal invasive cancer.

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

Table (OP401)

<table>
<thead>
<tr>
<th>JNET</th>
<th>Type 1</th>
<th>Type 2A</th>
<th>Type 3</th>
</tr>
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<tbody>
<tr>
<td>Vessel pattern</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>(mesh/spiral pattern)</td>
<td></td>
</tr>
<tr>
<td>Surface pattern</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>Most likely histology</td>
<td>Hyperplastic poly/ Sessile serrated polyp</td>
<td>Low grade intramucosal neoplasia</td>
<td>High grade intramucosal neoplasia/ Shallow submucosal invasive cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Deep submucosal invasive cancer</td>
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OP402 SUBCLASSES OF TYPE-II PIT PATTERN REVEAL ALTERNATIVE TUMORIGENIC PATHWAYS OF COLORECTAL SERRATED LESIONS


Introduction: Colorectal serrated lesions (SLs) include hyperplastic polyp (HP), traditional serrated adenoma (TSA) and sessile serrated adenoma/polyp (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 (MINT-1, −2, −12, −31, 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 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 compared to Type II-O plus tumor pit and 214 tumor pit. Type II-O plus tumor pit and 214 tumor pit were identified Type II-L plus tumor pit, which was specific to TSA with KRAS mutation and CIMP-low (sensitivity, 60%; specificity, 96%).

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.

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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-PIV 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 (as 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. 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) classes. 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 unlabeled 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 23 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>
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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>
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<tr>
<td>Stoma present, n (%)</td>
<td>7 (88)</td>
<td>11 (100)</td>
<td>10 (29)</td>
<td>10 (32)*</td>
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<td>Colon-in-continuity, n (%)</td>
<td>1 (13)</td>
<td>1 (9)</td>
<td>22 (63)</td>
<td>24 (77)*</td>
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<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>
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<td>Baseline PS, mean (SD), L/wk</td>
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<td>15.9 (10.4)</td>
<td>11.5 (5.9)</td>
<td>11.2 (6.4)*</td>
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<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>
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