The optimal therapeutic approach to ileocecal Crohn’s disease (CD) remains unclear.

Aims & Methods: The objective of this study was to compare infliximab with laparoscopic 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 (MD 0.475, 95% CI 0.325–0.726, p = 0.005). Infliximab was stopped at Kings College London - ISS on November 25, 2016ueg.sagepub.comDownloaded from
**OP003 MULTIVARIATE MODELLING OF GUT MICROBIAL PROFILES PREDICTS RESPONSE TO A DIET LOW IN FODMAPS**

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**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 intervention study (Böhm 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 c20/5 bacteria on diethylpyrocarbonate (DEPC) treated faecal material for each patient. Data were analyzed by multivariate discrimination analysis and graded from 1-5, relative to a healthy reference group. A dysbiosis index (DI) ≤2 signify normal microbiota composition. responders (n=14), 19 non-responders (n=19), responders (n=14), 19 non-responders (n=19). 20 responders (n=20), 20 non-responders (n=20). 20 responders (n=20), 20 non-responders (n=20). 20 responders (n=20), 20 non-responders (n=20).

**Results:** Faecal bacterial profiles differ significantly. Responders consumed significantly less protein, fat, and alcohol. Composition after the intervention. Patients on a low-FODMAP diet ate significantly less carbohydrates, fibre, mono- and oligo-saccharides, fructose and total FODMAPs, and had significant reduction in potentially beneficial Bifidobacterium after the intervention. Compared to baseline, patients on a low-FODMAP diet experienced improved response (n=0.005) which was even more prominent in non-responders. An OPLS-DA model of the low-FODMAP intervention demonstrated satisfactory model efficacy in distinguishing responders from non-responders in clinical response (AUROC 0.652; Q2 cca 0.541). Fecal microbial profiles differed between responders and non-responders. An OPLS-DA model of the traditional diet group was inadequate, showing good model fit but lacking predictive power. The model was not able to predict responders from non-responders.

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

**Disclosure of Interest:** L. Öhman: Unrestricted research grants from AstraZeneca; L. Collin: unrestricted research grants, speaker honoraria. All other authors have declared no conflicts of interest.

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

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**Introduction:** Infected necrotizing pancreatitis is a potentially lethal disease that almost always requires an invasive intervention. In recent years, the surgical step-up approach has become standard of care replacing primary open necrosectomy. A new, minimally invasive alternative is the endoscopic step-up approach. We conducted a multicenter randomized trial comparing a surgical and endoscopic step-up approach in patients with infected necrotizing pancreatitis. Among these patients, clinical remission and clinical response were observed in 39% and 71% of patients achieving PBO-q8w (a situation similar to a drug holiday), 41% and 55% in the q12w-q8w group and 32% and 46% in the q8w-q8w group when assessed 16 weeks later (Table 1). Median change in CDAI after adjustment was −121, −141 and −78.5 in the PBO-q8w, q12w−q8w and q8w−q8w groups, respectively. Of 467 patients not in response to UST following IV induction in UNITI-1, 20.5% and 28.9% were in clinical response and remission 8 weeks after one additional UST dose (80 mg SC). Among the 251 of these patients continuing dosing at week 8 of maintenance, 68.1% were in response and 50.2% were in remission at week 44. No increase in adverse events was seen among patients who dose adjusted.

**Conclusion:** In patients who met LOR criteria, dose adjustment from UST 90 mg q12w to 90 mg q8w provided some additional clinical benefit compared to patients who remained on UST 90 mg q12w. Additionally, patients who were initial induction non-responders can benefit from continued treatment with at least 1 SC UST dose 8 weeks after IV induction.

**Table 1:** Proportion of subjects achieving clinical response and remission 16 weeks after dose adjustment

<table>
<thead>
<tr>
<th>Dose</th>
<th>Clinical Response</th>
<th>Clinical Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBO−UST q8w</td>
<td>71%</td>
<td>39%</td>
</tr>
<tr>
<td>q12w−UST q8w</td>
<td>55%</td>
<td>41%</td>
</tr>
<tr>
<td>q8w−UST q8w</td>
<td>46%</td>
<td>32%</td>
</tr>
</tbody>
</table>
C. Gasink: Employee of Janssen Research & Development, LLC.
D. Jacobson: Employee of Janssen Research & Development, LLC.
L.L. Gao: Employee of Janssen Research & Development, LLC.
J. Johanns: Employee of Janssen Research & Development, LLC.
P. Szapary: Employee of Janssen Research & Development, LLC.
J. Colombel: Investigator for Janssen Research & Development, LLC.
S. Targan: Investigator for Janssen Research & Development, LLC.
S. Ghosh: Investigator for Janssen Research & Development, LLC.
W. Sandborn: Investigator for Janssen Research & Development, LLC.

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

Aims & Methods: The first 75 patients (49 CD, 26 UC) who initiated VDZ therapy (300 mg IV administered) in our tertiary referral center were sampled at trough during induction (w2 and w6) and early maintenance (w10, w14 and w22) treatment. Clinical response (clinical symptoms and physical global assessment) was correlated to VDZ TC. All patients with UC received sigmoidoscopy. The relation between serum VDZ trough concentrations (TC) and clinical, biological and endoscopic outcomes in real-life practice. We included 72 patients (47 CD, 25 UC), of whom 14 (30%) were excluded: 7 CD, 6 UC. UC patients with endoscopic healing at w22 had significantly higher VDZ TC throughout w2 to w22, compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001). Biological response and remission were achieved in 52% (14/27) and 30% (8/27) of patients with CD. Significantly higher VDZ TC were observed at w6 in case of biological response (23.8 mg/mL [16.1–33.8]), n = 42) compared to patients who did not receive a w10 infusion (13.1 mg/mL [6.9–19.3], n = 28) (< .0001).

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.

Disclosure of Interest: A. Gilis: Lecture fee(s) MSD, Janssen Biologics, Abbvie, Pfizer, Takeda. Consultancy: UCB. Conflict: with license of infliximab, anti-infliximab and adalimumab ELISA from Institution to apDna and with lateral flow infliximab to Biopharm AG. M. Ferrante: Financial support: research from Janssen Takeda, Lecture fees: Takeda, Abbvie, Boehringer, Pfizer. S. Vermeire: Grant/research support Takeda, Abbvie Consultancy/speakers fees from Abbvie, MSD, Takeda, Pfizer. S. Ben-Horin: Prof. Ben-Horin has received consulting and/or advisory board fees from Janssen, Takeda, Celltrion, Abbvie, and Schering-Plough and research support from Celltrion and Abbvie. All other authors have declared no conflicts of interest.

Table 1: Vedolizumab trough concentrations, in mg/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>CD</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>w6</td>
<td>33.5 [21.8–38.5] (23)</td>
<td>16.6 [9.0–31.4] (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 [9.7–16.8] (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 < .05; ** p < .01; *** p < .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 mg/mL [18.6–38.0]), compared to patients who did not achieve endoscopic healing (16.6 mg/mL [11.0–29.3]) (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 mg/mL [22.3–37.1], n = 16) and w6 (32.0 mg/mL [17.8–37.7], n = 16) compared to absence of clinical response (21.6 mg/mL [16.0–25.2] and 16.6 mg/mL [11.0–20.6], resp. n = 7) (p = .03 and p = .02).

Disclosure of Interest: U. Kopylov: Dr. Kopylov received consultancy fees from Janssen, research support from Janssen and Takeda and lecture fees from Janssen, Takeda, Abbvie and CTS.
Y. Chowers: Prof. Chowers received consulting and lecture fees as well as grant support from Takeda, Abbvie, Janssen, Pfizer, Ferring and Protalix.
R. Elaiikin: Prof. Elaiikin has received consulting and lecture fees from Takeda.
S. Ben-Horin: Prof. Ben-Horin has received consulting and/or advisory board fees from Janssen, Takeda, Celltrion, Abbvie, and Schering-Plough and research support from Celltrion and Abbvie.

All other authors have declared no conflicts of interest.
1. Introduction: Tumour necrosis factor antagonists (anti-TNFs) are effective at inducing and maintaining disease remission in patients with moderate to severe IBD, including patients with a physician global assessment of moderate (45%) at study entry. Mean disease duration was 8 years (SD ± 7.18) and mean disease duration was 8 years (SD ± 13.7); 51% were male. Most patients had a Charlson comorbidity index (CCI) score of 0–1 (83%), 15% were current smokers, mean BMI was 24.8 (SD ± 3.9) and mean age was 43.6 (SD ± 12.4) years.

2. Results: The study included 1195 patients (45% U.S., 55% CD; 96.8% 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 Charlson comorbidity index (CCI) score of 0–1 (83%), 15% were current smokers, mean BMI was 24.8 (SD ± 3.9) and mean age was 43.6 (SD ± 12.4) years.

3. Discussion: The study used real-world data to identify predictors of non-response or non-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 and natalizumab) 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-response 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 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-response or loss of response.

4. Conclusion: The step-up approach remains the dominant strategy in IBD, growing need of studying de-escalation strategy in IBD. The cumulative risks of first intestinal resection in CD, and colectomy in UC were 78.2%, 17.7% and 4.1% of UC patients, respectively. Subsequently, 36.8% and 56.6% CD and 80.3% UC patients, respectively. The study included 1195 patients (45% U.S., 55% CD; 96.8% 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 Charlson comorbidity index (CCI) score of 0–1 (83%), 15% were current smokers, mean BMI was 24.8 (SD ± 3.9) and mean age was 43.6 (SD ± 12.4) years.

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

6. 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 CPR values during the baseline period were used.

7. 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 CD included higher CRP and higher number of liquid or soft stools per day. These predictors should be considered when evaluating treatment options for patients.


9. B. Bokemeyer: Grant/support research from: Abbvie, Ferring, UCB, Consultant for: Abbvie, MSD, Shire, Ferring, UCB, Hospira, Takeda, Movetis, Speaker bureau with: Abbvie, Ferring, MSD, Merckle, Falk, HLR, UCB. J. Lindsay: Grant/support research from and is on speaker bureau with: MSD, Abbvie, Hospira, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Vifor Pharma, Atlantic Health care, Actavis (Warner Chilcott), and Tillotis. M. Smyth: Employee of Takeda Development Centre Europe Ltd, London, United Kingdom. S. Ramagopalun: Employee of Evidera and was commissioned by Takeda Development Centre Europe Ltd. to conduct the study. J.M. Khalid: Employee of Takeda Development Centre Europe Ltd, London, United Kingdom.

10. A. Armuzzi: Grant/research support from: MSD, Consultant for: Abbvie, Celltrion, Hospira, Takeda, Biogaran, Boehringer-Ingelheim, Lilly, Pfizer, Amgen, Sandimmune, Celgene, Biogen Idec, BMS. A. Armuzi: Grant/support research from: MSD, Consultant for: Abbvie, Celltrion, Hospira, Janssen, Lilly, MSD, Mundipharma, Pfizer, Sofar, Samsung, Takeda, Speaker bureau with: Abbvie, Astra-Zeneca, Chiesi, Ferring, Hospira, MSD, Mundipharma, Otsuka, Takeda, Zambon. J.P. Gispert: Grant/support research from and is on speaker bureau with MSD, Abbvie, Hospira, Kern Pharma, Takeda, Janssen, Pfizer, Ferring, Faes Pharma, Shire Pharmaceuticals, Dr. Falk Pharma, Chiesi, Casen Flet, Gebro Pharma, Otsuka Pharmaceutical, Vifor Pharma, Otsuka. G.C. Nguyen: Consultant for: Janssen, Abbvie, and Takeda.
**Introduction:**

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**Aims & Methods:** Data from BELCRO (Belgian observational prospective cohort of 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 PCDAI/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 severity 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 age, gender, WBC or CRP at diagnosis and treatment between both groups. Percentages of infliximab and adalimumab use were similar in both groups, including drug switching and dose or interval adjustments. When stratified by follow-up clinic, infliximab in paediatric follow-up was less frequently associated with failure to reach sustained remission compared to comparison groups.

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 = 15)</th>
<th>Sustained remission (n = 55)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediatric follow-up and infliximab</td>
<td>3 (27)</td>
<td>37 (67)</td>
<td>.01</td>
</tr>
<tr>
<td>Paediatric follow-up and adalimumab</td>
<td>1 (9)</td>
<td>8 (15)</td>
<td>.63</td>
</tr>
<tr>
<td>Adult clinic follow-up and infliximab</td>
<td>6 (55)</td>
<td>14 (25)</td>
<td>.05</td>
</tr>
<tr>
<td>Adult clinic follow-up and adalimumab</td>
<td>2 (18)</td>
<td>4 (7)</td>
<td>.25</td>
</tr>
<tr>
<td>Paediatric follow-up and adjustments</td>
<td>1 (9)</td>
<td>8 (15)</td>
<td>.63</td>
</tr>
<tr>
<td>Adult follow-up and adjustments</td>
<td>1 (9)</td>
<td>3 (11)</td>
<td>.65</td>
</tr>
</tbody>
</table>

Higher average disease severity (2.1 (2.0-2.3) vs. 1.6 (1.3-1.8); p < .001), adult clinic follow-up (73% vs. 27%; p < .01), surgery for CD (1 (0-3) vs. 0 (0-3); p = .01), active disease at diagnosis (95% vs. 24%; p < .05) were associated with failure to reach sustained remission. Both colonic disease and adult follow-up (AUC = 0.66; both p = .04) correlated with average disease severity (no correction for multiple testing). No other correlations were found.

**Conclusion:** Patient phenotype at diagnosis does not predict failure to reach sustained remission despite anti-TNF exposure. Mild disease may not trigger sustained remission despite anti-TNF exposure. Both colonic disease and adult follow-up could be underlying mechanism of the prevention of gastric cancer by H. pylori eradication.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
OP012 THE EFFECT OF CURRENT HELICOBACTER PYLORI INFECTION ON GASTRIC CANCER IN A LARGE POPULATION
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Introduction: Although the association between risk of gastric cancer and Helicobacter pylori (H. pylori) in case-control study have evaluated, the effect of current H. pylori infection on the risk of gastric cancer has not been studied in a large general population.
Aims & Methods: Their first Health check-up persons, who underwent comprehensive screening including endoscopy and H. pylori test from 2003 to 2013, were enrolled. Current infection of H. pylori was defined as positive rapid urease test. Negative current infection was defined as negative rapid urease test and absence of previous H. pylori eradication. Adjusted regression analysis was performed and estimated odds ratio (OR) and 95% confidence interval (CI).
Results: Among 35519 persons with 19396 men, 113 gastric cancers and 158 gastric adenomas were detected. In adjusted analysis, age (OR 1.06, 95% CI 1.04–1.08), current infection of H. pylori (OR 2.39, 95% CI 1.53–3.74), first degree relatives with gastric cancer (OR 2.08, 95% CI 1.30–3.32), and high glucose (OR 1.66, 95% CI 1.04-2.65) increased the risk of gastric cancer, whereas high HDL (≥60 mg/dL) reduced the risk of gastric cancer (OR 0.49, 95% CI 0.22–0.94). In current infection of H. pylori, age was a common risk factor of gastric cancer. First degree relatives (OR 3.23, 95% CI 1.39–7.50) increased gastric cancer risk in the absence of H. pylori, whereas high glucose (OR 1.98, 95% CI 1.16–3.39) increased the risk in the presence of H. pylori.
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
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
Medicine and Therapeutics, The Chinese University Of Hong Kong, Institute of Digestive Disease, Hong Kong/Hong Kong Prc
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Introduction: We have recently identified that Apelin (APLN) was highly expressed in 18 paired liver cell carcinoma and liver tumor tissues compared to adjacent normal liver specimen 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 investigated by silencing of APLN in two NASH-HCC cell lines (HKCI-2 and HKCI-10), whilst no or very low expression was observed in a normal liver cell line (MIHA) and human normal liver tissues. Ectopic expression of APLN (in Huh7, Miha, HKCI-2 and HKCI-10), whilst no or very low expression was observed in a normal liver cell line (MIHA) and human normal liver tissues. Ectopic expression of APLN in (Huh7, Miha, HKCI-2 and HKCI-10) was found to promote cell proliferation, accelerate G1/S phase progression by increasing cyclin D1 (9) expression, and increased 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 was investigated by analyzing APLN expression in a large tumor cohort.
Results: Liver cancer was induced in genetically obese mice (db/db, deficient in insulin) and wild-type mice with diethylnitrosamine. mRNA analysis of mice HCC tissues and adjacent non-HCC tissues revealed that APLN was a top candidate gene consistently up-regulated in HCC tumor tissues compared to adjacent non-tumor tissues. APLN was also overexpressed in human HCC tissues as compared with adjacent normal tissues at mRNA level (28 pairs of non-alcoholic fatty liver disease/ASH-HCC and 26 pairs of HCC) and protein level (9 pairs of NAS-HCC patients). APLN was ubiquitously expressed in liver cells (7404, HepG2, HuH6, HuH7, PLC5, SKHEP1 and two NASH-HCC cell lines HKCI-2 and HKCI-10), whilst no or very low expression was observed in a normal liver cell line (MIHA) and human normal liver tissues. Ectopic expression of APLN (in Huh7, Miha, HKCI-2 and HKCI-10) was found to promote cell proliferation, accelerate G1/S phase progression by increasing cyclin D1 (9) expression, and increased 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 was investigated by analyzing APLN expression in a large tumor cohort.
Conclusion: APLN is a novel liver cancer-promoting gene in HCC. 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 GENOCIDIC TUMOR-INDUCED SENESCENCE TOWARDS TUMOR GROWTH PROMOTION
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Introduction: Oncogenic-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 in mice bearing full-bloned tumour 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, C2CR2 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. Furthermore, peritumoral tissue of 226 HCC patients was hierarchical clustered based on the expression of 35 senescence-associated genes (2). Senescence-associated gene signature expression was then compared with chemokine expression and survival. In addition, human peritumoral tissue was analyzed by immunohistochemistry for the presence of senescence and myeloid cell markers.
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 C2CR2 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 cell inhibition through senescence-induced CCR2 (3). iMC lead to accelerated tumor growth. Accordingly, in C2CR2 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: Senescence surveillance is mediated by CCR2-CCL2 signaling and the ensuing myeloid cell accumulation harbor 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-induced immunosuppression induced by liver tumors.
Disclosure of Interest: All authors have declared no conflicts of interest.
References
OP015 COLD FORCEPS AVULSION (CFA) WITH ADJUVANT SNARE TIP SOFT COAGULATION (STSC) IS AN EFFECTIVE AND SAFE STRATEGY FOR THE MANAGEMENT OF NON-LIFTING LARGE LATERALLY SPREADING COLORECTAL LESIONS (NL-LSLS)

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

Aims & Methods: The study aimed to evaluate the characteristics of NL-LSL and the safety and efficacy of endoscopic treatment by Cold Forceps Avulsion (CFA) followed by thermal ablation of the avulsion site by Snare Tip Soft Coagulation (STSC). Amongst a prospective observational study of patients referred for wide field EMR of LSL > 20 mm, LSLs which could not be completely resected by snare due to NL were labelled NL-LSL. These were divided into previously attempted non-lifting LSLs (PANL-LSL) and naïve, non-lifting LSLs (NNL-LSL). [MB1] Such lesions had completion of resection using a standardized approach with CFA and STSC. The NL area was isolated by circumferential snare excision of all adjacent tissue including adenoma and/or normal mucosa to free the lateral margins. This then allowed effective CFA of NL adenoma. Systematic CFA was then performed to remove all visible NL adenoma. The exposed submucosa of the avulsion site and its margins were treated with controlled thermal ablation using STSC (ERBE eff 4, 80W). Scheduled surveillance colonoscopy was performed at 5 months (SC1) and 18 months (SC2) post the index procedure. The primary outcome was endoscopic and histological evidence of adenoma clearance. The secondary outcome was safety. Standard statistical analyses were performed to compare standard LSL with NL-LSL.

Results: From January 2012 to April 2016, 677 patients (mean age 69 years, 50.6% male) with 780 lesions (median size 35 mm (IQR 25–45 mm), 65.4% proximal colon) were referred for WF-EMR. 33 lesions were excluded due to interval growth (32 vs 13.8%, p=0.003) than standard LSL. NNL (n=50) were also more likely to be non-granular (46 versus 33.9%, p=0.12) and were associated with previous biopsy (32 versus 13.8%, p=0.001) and carbon particle suspension injection within 10 mm of the lesion (26 vs 3.8%, p<0.001). Neither intra-procedural bleeding nor deep injury were more common in NL-LSL treated with CFA and STSC. The technique was technically successful in all cases. One perforation was recognised secondary to CFA in a previously attempted lesion and was successfully closed with endoscopic clips with no sequelae. Endoscopic recurrence at SC1 was not significantly different for PANL-LSL treated with CFA and STSC than LSLs treated with complete snare excision, whereas NNL-LSL recur more frequently (16.0 vs 12.2%, p=0.578 and 28.2 vs 12.2%, p=0.005 respectively).

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

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

OP016 SCISSORS TYPE KNIFE SIGNIFICANTLY IMPROVED SELF-COMPLETION RATE OF COLORECTAL ENDOSCOPIC SUBMUOSAL DISSECTION PERFORMED BY SUPERVISED RESIDENTS: A PROSPECTIVE RANDOMIZED TRIAL

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Introduction: Endoscopic colorectal submucosal dissection (ESD) is currently not a common treatment for unskilled endoscopists because of technical difficulties. Recently, the scissors-type knife, SB knife Jr type (SB Jr) was launched to reduce the difficulty of colorectal ESD, although it can be a time-consuming procedure. Aims & Methods: The aim of the present study was to evaluate the efficacy and safety of the combined SB Jr and Flushknife for colorectal ESD compared with using the Flushknife alone performed by supervised residents. This was a prospective randomized controlled trial in a cancer referral center. Eighty-five patients undergoing submucosal dissection of colorectal lesions, were enrolled and randomly assigned to undergo ESD using the Flushknife alone (Flush group) or the SB Jr supported Flushknife (SB Jr group). The procedures were conducted by two residents. Primary endpoint was self-completion rate by the residents.

Abstract No: OP015

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

<table>
<thead>
<tr>
<th>Patient</th>
<th>PANL n = 33</th>
<th>p</th>
<th>NNL n = 50</th>
<th>p</th>
<th>LSL n = 650</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>70.2 (8.6)</td>
<td>.121</td>
<td>73.0 (9.5)</td>
<td>.&lt; .001</td>
<td>66.9 (12.1)</td>
</tr>
<tr>
<td>Male, (%)</td>
<td>18 (54.5)</td>
<td>.598</td>
<td>29 (88.0)</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>.001</td>
<td>23 (46.0)</td>
<td>.004</td>
<td>299 (33.9)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>4 (12.5)</td>
<td>.001</td>
<td>5 (10.0)</td>
<td>.001</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>.012</td>
<td>11 (23.9)</td>
<td>.981</td>
<td>95 (15.2)</td>
</tr>
<tr>
<td>Transverse</td>
<td>5 (15.6)</td>
<td>.224</td>
<td>14 (30.0)</td>
<td>.282</td>
<td>132 (20.5)</td>
</tr>
<tr>
<td>Ascending and caecum (+ICV)</td>
<td>10 (31.3)</td>
<td>.036</td>
<td>15 (32.6)</td>
<td>.944</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>50 (100)</td>
<td>.&lt; .001</td>
<td>179 (27.6)</td>
</tr>
<tr>
<td>Previous biopsy (%)</td>
<td>na</td>
<td>.001</td>
<td>16 (32.0)</td>
<td>.001</td>
<td>90 (13.8)</td>
</tr>
<tr>
<td>SPOT mark within 10 mm of lesion (%)</td>
<td>na</td>
<td>.&lt; .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 (92.6)</td>
<td>.324</td>
<td>44 (90.0)</td>
<td>.147</td>
<td>482 (77.5)</td>
</tr>
<tr>
<td>Serrated adenoma</td>
<td>2 (7.4)</td>
<td>.012</td>
<td>4 (10.0)</td>
<td>.001</td>
<td>135 (21.7)</td>
</tr>
<tr>
<td>Cancer</td>
<td>0 (0)</td>
<td>.001</td>
<td>0 (0)</td>
<td>.001</td>
<td>0 (0.6)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0)</td>
<td>.001</td>
<td>0 (0)</td>
<td>.001</td>
<td>0 (0.2)</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
<td></td>
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<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>
Use of surgical techniques like TEMS and TAR for resection of RPDLs.

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 for resection of RPDLs. This is a prospective observational study of patients who underwent KAR for RPDLs over the study period. The polyp characteristics and histology were done on a day case basis and were carried out under sedation by two endoscopists using high-definition gastroscopes with a distal transparent cap. The polyp margins were randomized 1:1 to either thermal ablation of the margin of the post EMR mucosal defect with KAR with a mean follow-up of 32 months (range 1–83 months). All procedures were done in a day case basis and were carried out under sedation by two endoscopists using high-definition gastroscopes with a distal transparent cap. The polyp margins were randomized 1:1 to either thermal ablation of the margin of the post EMR mucosal defect with KAR or active arm of the SCAR study. Relative risk (RR); Confidence interval (CI) 0.01. Overall, there was one complication where the patient had delayed bleeding which was managed conservatively. None of the patients experienced perforation, or post-procedural sepsis.

Table 1: Lesion characteristics and histology

<table>
<thead>
<tr>
<th>Lesion size, median (range), mm</th>
<th>50 (12–150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphology, n (%)</td>
<td>LST – G, 29 (72.5) 2 (5) 2 (5) 7 (17.5) nodular mixed LST – G, 4 (10.5) homogenous LST – NG Is</td>
</tr>
<tr>
<td>Scarring, n (%)</td>
<td>13 (32.5)</td>
</tr>
<tr>
<td>Histology, n (%)</td>
<td>Adenoma with LGD Adenoma with HGD 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 TAR, 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: Endoscopic and histological recurrence in patients randomised to null versus active arm of the SCAR study. Relative risk (RR); Confidence interval (CI)

<table>
<thead>
<tr>
<th>Endoscopic recurrence (95% CI)</th>
<th>0.01</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/136 (0.7%)</td>
<td>20/97 20.6% 9/136 (6.6%)</td>
</tr>
</tbody>
</table>

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

Disclosure of Interest: All authors have declared no conflicts of interest.
OP019 EVALUATION OF THE LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION PERFORMED WITH A SINGLE HEMOCLOC technique FOR EARLY COLORECTAL NEOPLASMS


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Introduction: Endoscopic submucosal dissection (ESD) is one of the most useful methods for the precise removal of early colorectal neoplasms. It is minimally invasive and is an attractive alternative to surgery. Together with hemoclip/giant needle and a hook knife, hock needle, or needle knife are conventionally used to perform ESD. However, because these devices are used without fixation of target tissue, there is the potential risk of complications due to an unexpected incision. To reduce the risk of complications associated with using a conventional knife to perform ESD, we used a scissors-type knife (stag beetle [SB] knife Jr, Akita Sumitomo Bakhelt Co.) that maintains an adequate dissection layer and prevents an unexpected muscular layer injury. We previously reported that performing colorectal ESD with an SB knife Jr is an easy, safe, and technically efficient method. However, the long-term outcomes of this method are unknown.

Aims & Methods: We aimed to evaluate the feasibility and long-term outcomes of ESD performed with an SB knife Jr for treating early colorectal neoplasms. ESD was performed for 227 lesions in 211 patients (male:female ratio = 116:95; mean age = 69.1 ± 14.1 years) between October 2010 and March 2016. We evaluated the patients’ clinicopathological characteristics, in bloc resection rate, histological complete resection rate, R0 resection rate, tumor size, procedure time, complications, and long-term outcomes, including local recurrence, and the survival rate.

Results: The tele-ESD neoplasms were as follows: right colon, 94 lesions (41.4%); left colon, 58 (25.6%), and rectum, 75 (33.0%). Regarding the macroscopic type of lesions, there were 95 (41.9%) laterally spreading tumors (LSTs) of the muscosal layer (34.8%), LSTs of the submucosal layer, 76 (33.9%), LSTs of the submucosal and epithelial type, and 48 (21.1%) polypoid lesions. Histological examination findings showed that 102 lesions were closed in the hemoclip group (hemoclips) and twin-grasper group (hemo-clips). The mean number of hemoclips used per case and total closure time were significantly lower in the twin-grasper group than the hemoclip group. Histological examination findings showed that 102 lesions were closed in the hemoclip group (hemoclips) and twin-grasper group (hemo-clips). The mean number of hemoclips used per case and total closure time were significantly lower in the twin-grasper group than the hemoclip group.

Conclusion: The twin-grasper-clip 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.
It is important highlights that only one session of Spyglass + EHL was performed in each patient of our protocol. Better success rates can be achieved with two or three 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 Spyglass 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.

References

MAGNIFIED

MONDAY, OCTOBER 17, 2016
10:30-12:00
PREVENTION OF GI CANCERS: NUTRITION AND CHEMOPREVENTION – ROOM 1.61/1.62

OP023 CD24 INDUCES THE ACTIVATION OF b-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/b-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 b-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 crossed to generate double KO transgenic mice. Genotypes were routinely crossed to generate double KO transgenic mice. Genotypes were routinely crossed to generate double KO transgenic mice. Genotypes were routinely crossed to generate double KO transgenic mice.
OP024 LOSS OF PTPN2 IN MACROPHAGES AGGRAVATES COLITIS

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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. Inflammases 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 important activator of sterile inflammatory innate immune functions, while IL-18 is involved in epithelial cell protection.

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

Results: PTPN2-deficient macrophages show enhanced levels of cleaved caspase-1 and IL-1β upon in vitro activation of the NOD-like receptor protein 3 (Nlrp3) and absent in melanoma 2 (AIM2) inflammasomes, finally resulting in enhanced secretion of active IL-1β and IL-18. This effect was mediated by increased phosphorylation of the inflammasome adaptor apoptosis associated speck-like protein containing CARD (ASC), a mechanism we previously showed promote inflammasome activation. In vivo, PTPN2-LysMCre mice suffered from pronounced acute colitis, accompanied with enhanced secretion of mature IL-1β and IL-18, but concurrent decreased IL-10 production. On the other hand, no differences were observed in T cell subsets or other T helper cell associated cytokine expression. In chronic colitis, PTPN2-LysMCre mice again showed enhanced inflammasome activation in the intestine, and further developed metastasis to squamous epithelium in the distal part of the colon epithelium, 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 tumours upon AOM-DSS treatment. Interestingly, when IL-1β-/- mice were also knock down for acute colitis severity in PTPN2-LysMCre mice did not differ from that observed in WT animals. Further, inhibition of IL-1β restored susceptibility to AOM-DSS induced colitis in PTPN2-LysMCre mice.

Conclusion: PTPN2 is an important regulator of inflammasome activation, and loss of PTPN2 in macrophages enhances acute colitis. Further, during chronic intestinal inflammation, macrophage-specific loss of PTPN2 promotes metastasis to squamous epithelium, but at the same time protects from tumour formation. This indicates an important, previously under-estimated macrophage-specific role for PTPN2 during intestinal inflammation and tumour induction.

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

OP025 LOW PROCUREMENT YIELD AND DIAGNOSTIC ACCURACY OF EUS-GUIDED FINE NEEDLE BIOPSY OF TRANSUDENAL LESIONS USING THE 19-GAUGE FLEXIBLE NEEDLE: A LARGE MULTICENTER PROSPECTIVE STUDY

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Introduction: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is the procedure of choice to obtain samples for reaching the definitive diagnosis of lesions of the gastrointestines (GI) tract (1). The percutaneous biopsy procedure is safe and very accurate, especially when rapid on-site evaluation (ROSE) of the adequacy of the collected specimens is performed. However, in centers where ROSE is not available, it has been suggested that the performance of EUS-fine needle biopsy (EUS-FNB) can result in a greater chance to reach a diagnosis than a typical EUS-FNA sample. Based on a previous study (2), which reported a 19-gauge flexible needle to be able to sample transudendal lesions and be diagnostic in all 32 included patients, an algorithm for EUS-tissue acquisition (EUS-TA) of solid lesions from the duodenum depending on the availability of ROSE has been proposed. Thus, in institutions with no availability of ROSE, for lesions derived from the duodenum, which represent the most difficult sampling position because of the stiffness induced by the needle assembly on the echoendoscope shaft, the authors recommended the use of a 19-gauge needle made of a wire with increased flexibility (1). The aim of the present study was to test the validity of this recommendation we performed a prospective multicenter study aimed at evaluating the technical feasibility, procurement yield, and diagnostic accuracy of this newly developed 19-gauge nitinol flexible needle in patients with solid lesions or enlarged lymph nodes that could be punctured only from the duodenum. Consecutive patients with solid lesions who needed to undergo EUS sampling from the duodenum were prospectively enrolled in 6 tertiary care referral centers. Puncture of the lesion was performed with the 19-gauge flexible needle (Expect™ 19 Flex and Slimline Expect™ 19 Flex) and at least 3 needle passes were performed in each case. The feasibility, procurement yield, and diagnostic accuracy were evaluated.

Results: 246 patients (144 males, mean age 65.1 ± 12.7 years) with solid lesions (203 cases, 82.5%) or enlarged lymph nodes (43 cases, 17.5%) were enrolled. The mean size of the target lesion was 32.6 ± 12.2 mm. The procedure was technically successful in all patients, without an overall complication rate of 7.8%. Two centers had suboptimal procurement yields of 66.7% and 64.2% (table). Major complications occurred in six patients (2.4%): two cases of bleeding, two cases of perforation, and two cases of acute pancreatitis. For patients with suspected pancreatic or periampullary lesions, the overall diagnostic yield was 70.7% (95% CI, 64.3–76.6), 100% (95% CI, 79.6–100), 53.3% (95% CI, 2.3–94.9), 0.3% (95% CI, 0.2–0.4), and 73.6% (95% CI, 67.6–79), respectively. On multivariate analysis, the only determinant of successful EUS-FNB was the center in which the procedure was performed.

Conclusion: The findings of our study, with a procurement yield and diagnostic accuracy of only 76.8% and 73.6%, respectively, redefine the role of the 19-gauge flexible needle for transduodenal EUS-FNB. Thus, the correct diagnosis was missed in about 1 every 4 patients. Since the prevalence of malignant disease in our population was 86%, this finding cannot be considered negligible. The results of our study are of particular interest since we showed that the diagnostic performance of the 19-gauge flexible needle has a wide intercenter variability, not only between centers, but also within the same center. Therefore, the use of this particular needle assembly should be carefully considered in the context of the specific expertise of the endoscopist. In conclusion, our results suggest
that the use of the 19-gauge flexible needle for transduodenal FNB cannot be wise was 5 cm with vascular invasion 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**


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

All other authors have declared no conflicts of interest.

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


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**Introduction:** For 10 years, EUS-guided biliary drainage has been an option as EUS guided cholecledo-duodenostomy or hepatico-gastrostomy. Two small randomized studies showed no difference between EUS guided BD vs Percutaneous drainage. The aim of this work was to evaluate in a multicenter randomized study the percutaneous biliary drainage (PBD) vs EUS-guided biliary drainage (EBD) in patients with an obstructive jaundice when ERCP failed or impossible due do 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, severe cardiac or pulmonary failure, and 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 yield between the type of needles and use of suction at 80% power and type specificity between cohorts. To detect a 15% difference in diagnostic accuracy and cell block yield between the 22 and 25G needles, the use of suction must be avoided in centers using ROSE as it increases specimen bloodiness and number of passes needed to achieve diagnostic adequacy, particularly with 22G needles.

**Disclosure of Interest:** R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc.
Introduction: United States of America significantly different 86.7% EUS-GE vs. 94.2% ES (p = 0.002). Rates and severity of AEs (as per the ASGE classification) were high in the PTB arm than in the EUS-guided biliary drainage. By Kaplan-Meyer analysis to assess survival after first biliary stenting and cox regression analysis, the following factors were significantly associated with improved survival. Chemotherapy was restarted after a median of 27 days. When drainage was efficient survival improved from 13.5 days to 40.2% female) were included: 30 in EUS-GE and 52 in ES. Technical and clinical success were not determined via endoscopy and fluoroscopy), 3) clinical success (ability to tolerate oral intake without vomiting), and 4) procedure-related adverse events (AEs). A total of 82 patients (mean age 66-years old, 13.3% and 40.2% female) were included: 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 = 0.002). Rates and severity of AEs (as per the ASGE classification) were higher in the PTB arm than in the EUS-guided biliary drainage. By Kaplan-Meyer analysis to assess survival after first biliary stenting and cox regression analysis, the following factors were significantly associated with improved survival. Chemotherapy was restarted after a median of 27 days. When drainage was efficient survival improved from 13.5 days to 40.2% female) were included: 30 in EUS-GE and 52 in ES. Technical and clinical success were not determined via endoscopy and fluoroscopy), 3) clinical success (ability to tolerate oral intake without vomiting), and 4) procedure-related adverse events (AEs). A total of 82 patients (mean age 66-years old, 13.3% and 40.2% female) were included: 30 in EUS-GE and 52 in ES. Technical and clinical success were not determined via endoscopy and fluoroscopy), 3) clinical success (ability to tolerate oral intake without vomiting), and 4) procedure-related adverse events (AEs). A total of 82 patients (mean age 66-years old, 13.3% and 40.2% female) were included: 30 in EUS-GE and 52 in ES. Technical and clinical success were not determined via endoscopy and fluoroscopy), 3) clinical success (ability to tolerate oral intake without vomiting), and 4) procedure-related adverse events (AEs). A total of 82 patients (mean age 66-years old, 13.3% and 40.2% female) were included: 30 in EUS-GE and 52 in ES. Technical and clinical success were not determined via endoscopy and fluoroscopy), 3) clinical success (ability to tolerate oral intake without vomiting), and 4) procedure-related adverse events (AEs).

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

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

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

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

Results: A total of 205 patients (mean age 38.4±12.5 years, 181 males) underwent EUS-Guided drainage with BFMS. Technical success was achieved in 203 patients (99%). Peri-procedure adverse events occurred in 8 (3.9%) patients (bleeding in 6 and perforation in 2). WON resolved with BFMS in 158 (77%). 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 nasso-cystic placement through BFMS followed by irrigation with saline and hydrogen peroxide improved 16 out of 20. At final step, DEN improved outcome in 19 out of 23. BFMS migrated in 5 (2.9%) patients (2 internal, 3 external). Four patients failed to achieve clinical success, requiring surgery (n = 2) or additional percuta- neous drainage (n = 2). Overall, clinical success was achieved in 198 (96.5%) patients.

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

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

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 a drainage expectation when chemothera- py cannot 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. Demographical, 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 restarted 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). Multivariable 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 1.68, 95% CI [1.36-2.06], p < 0.0001), and fever before drainage (HR 2.97, 95% CI [1.39-6.36], p = 0.003).

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.
Bile calprotectin in relation to variables of PSC activity

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>B-calpro, mg/l, median [25%-75%]</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>ERC-score ≤ 4</td>
<td>94</td>
<td>0.4 [0.1–3.9]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ERC score &gt; 4</td>
<td>116</td>
<td>13.8 [1.6–96.3]</td>
<td></td>
</tr>
<tr>
<td>Bi-Neutrophils</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 0</td>
<td>74</td>
<td>0.2 [0.1–1.1]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>- 1</td>
<td>100</td>
<td>5.3 [0.9–22.9]</td>
<td></td>
</tr>
<tr>
<td>- 2</td>
<td>36</td>
<td>172.8 [39.1–286.8]</td>
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</tr>
<tr>
<td>Dysplasia</td>
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<td></td>
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<tr>
<td>- No</td>
<td>203</td>
<td>4.0 [0.2–41.0]</td>
<td>0.023</td>
</tr>
<tr>
<td>- Yes</td>
<td>14</td>
<td>34.7 [4.8–99.5]</td>
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<tr>
<td>S-CA19-9 kU/l</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 26 (UNL)</td>
<td>198</td>
<td>2.7 [0.2–28.5]</td>
<td>0.003</td>
</tr>
<tr>
<td>≥ 26 (UNL)</td>
<td>12</td>
<td>57.4 [19.4–179.3]</td>
<td></td>
</tr>
<tr>
<td>S-ALP, U/l</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤ 105 (UNL)</td>
<td>101</td>
<td>1.2 [0.9–26.9]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt; 105 (UNL)</td>
<td>109</td>
<td>6.1 [0.5–81.9]</td>
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<tr>
<td>S-AST, U/l</td>
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<td></td>
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<tr>
<td>≤ 40 (UNL)</td>
<td>141</td>
<td>1.4 [0.1–21.0]</td>
<td>&lt;0.0001</td>
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<tr>
<td>&gt; 40 (UNL)</td>
<td>69</td>
<td>8.3 [1.0–89.6]</td>
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<td>S-IgG, g/l</td>
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<td></td>
</tr>
<tr>
<td>≤ 15 (UNL)</td>
<td>177</td>
<td>2.8 [0.2–27.0]</td>
<td>0.008</td>
</tr>
<tr>
<td>&gt; 15 (UNL)</td>
<td>33</td>
<td>19.5 [1.3–112.1]</td>
<td></td>
</tr>
</tbody>
</table>

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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.

References
Bile duct when the enhanced, biliary wall thickness was recognized at more than 10 mm upstream of the stenosis.

Results: Autoimmune pancreatitis (AIP) was accompanied in 88% (42/48) of IgG4-SC patients at the initial diagnosis. On MDCT imaging, the long thickened bile duct rate was higher in IgG4-SC cases (76%/6% vs. AIP, 4% and 32% of REC, respectively). By IDUS, a continuous circular-symmetric wall thickness more than 10 mm upstream from stenosis was recognized in 84% of IgG4-SC cases and in 36% of ECC cases. In IgG4-SC cases, bile biopsy revealed one or more positive pathological diagnostic criteria in only 13% of cases. In ECC cases, the sensitivity of biopsy was 92%, and brush cytology increased this by 6%. Among three out of six IgG4-SC patients without AIP, pancreaticoduodenectomy was performed without clinical diagnosis. The remaining three underwent steroid trial after negative work up for malignancy.

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

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

References

OP035 SELECTIVE TARGETING OF FXRα ISOMORPHS BY NOVEL BILE ACID DERIVATIVES IS ASSOCIATED WITH INHIBITION OF LIPOXICITY IN LIVER CELLS

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2Faculty of Pharmacy, University of Coimbra, Coimbra/Portugal

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 generic ablation leads to hepatic steatosis and hyperlipidaemia. The FXR gene expresses four biologically active variants (FXRα–1), which regulate hepatic and lipid metabolism in an isoform-dependent manner.

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 cholic (CA), deoxycholic (DCA), chenodeoxycholic (CDCA) and ursodeoxycholic (UDCA) acid scaffolds were incubated in HepG2 cells. BA FXR activation was determined by transcriptional activity using reporter and luciferase reporter constructs. As a result of the diverse structural modifications, BA derivatives specifically and significantly activated FXRα isoform only. Interestingly, 2 novel CA-, 1 DCA- and 4 UDCA-derivatives were stronger activators of both FXRα and a2, compared with their corresponding precursors. Further, 3 novel CA-, 2 DCA-, 3 CDCA- and 4 UDCA-derivatives specifically and significantly activated FXRα and a4. Incubation of HepG2 cells with the FAs mixture led to a significant 25% reduction in cell viability and a ~10–15% increase in cell death, concurrently with a dose-dependent accumulation of lipid droplets. Pre-incubation with cells with CA-derivatives preferentially activating FXRα or a2, significantly reduced intracellular lipid accumulation, but also intracellular lipid accumulation, by 25% and 35% as detected by Oil red O (ORO) staining. Additionally, mRNA levels of both direct and indirect key FXR-targets, namely SHP, SREBP1-c, PPAR-a, CYP7a1 and VLDLR, were assessed after incubation of primary mouse hepatocytes with the select BA-derivatives.

Results: As a result of the diverse structural modifications, BA derivatives showed differential activation of the FXRα-4 isoforms, when compared to their precursor BAs. From the precursor BAs, only CDCA, a natural FXR ligand, significantly activated FXRα and a2 isoforms, with CA and UDCA displaying a modest activation of FXRα isoform only. Interestingly, 2 novel CA-, 1 DCA- and 4 UDCA-derivatives were stronger activators of both FXRα and a2, comparing with their corresponding precursors. Further, 3 novel CA-, 2 DCA-, 3 CDCA- and 4 UDCA-derivatives specifically and significantly activated FXRα and a4. Incubation of HepG2 cells with the FAs mixture led to a significant 25% reduction in cell viability and a ~10–15% increase in cell death, concurrently with a dose-dependent accumulation of lipid droplets. Pre-incubation with cells with CA-derivatives preferentially activating FXRα or a2, significantly reduced intracellular lipid accumulation, but also intracellular lipid accumulation, by 25% and 35% as detected by Oil red O (ORO) staining. Additionally, mRNA levels of both direct and indirect key FXR-targets, namely SHP, SREBP1-c, PPAR-a, CYP7a1 and VLDLR, were assessed after incubation of primary mouse hepatocytes with the select BA-derivatives.

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

OP034 COMPARISONS OF IMAGING AND BILIARY BIOPSY BETWEEN IGGA-RELATED SCLEROSING CHolangitis AND EXTRAHEPATIC CHOLANGIOCARCINOMA

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Introduction: The comparison of imaging and biliary biopsy between IgG4-related sclerosing cholangitis (IgG4-SC) and extrahepatic cholangiocarcinoma (ECC) is not well established. The aim of this study is to compare the diagnostic accuracy of imaging and biliary biopsy between IgG4-SC and ECC.

Aims & Methods: We compared the diagnostic accuracy of imaging and biliary biopsy between IgG4-SC and ECC. We also compared the sensitivity and specificity of imaging and biopsy for the diagnosis of IgG4-SC and ECC.

Results: The sensitivity of imaging for the diagnosis of IgG4-SC was higher than that of ECC (76% vs.53%, p = 0.001). The specificity of imaging for the diagnosis of IgG4-SC was lower than that of ECC (100% vs. 95%, p = 0.0001). The sensitivity of biopsy for the diagnosis of IgG4-SC was higher than that of ECC (92% vs. 72%, p = 0.02). The specificity of biopsy for the diagnosis of IgG4-SC was lower than that of ECC (100% vs. 94%, p = 0.0001). The positive predictive value of imaging for the diagnosis of IgG4-SC was higher than that of ECC (91% vs. 66%, p = 0.0001). The negative predictive value of imaging for the diagnosis of IgG4-SC was lower than that of ECC (76% vs. 95%, p = 0.0001). The positive predictive value of biopsy for the diagnosis of IgG4-SC was lower than that of ECC (86% vs. 97%, p = 0.0001). The negative predictive value of biopsy for the diagnosis of IgG4-SC was higher than that of ECC (100% vs. 90%, p = 0.0001).

Conclusion: Imaging has a high sensitivity for the diagnosis of IgG4-SC, but a low specificity. Biopsy has a low sensitivity for the diagnosis of ECC, but a high specificity. Therefore, a combination of imaging and biopsy is necessary for the diagnosis of IgG4-SC and ECC.

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

References
OP036 THE IMPACT OF PNPLA3 (rs738409 C>G) POLYMORPHISM ON DISEASE COURSE IN PRIMARY SCLerosING CHOLANGITIS (PSC)

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Introduction: PNPLA3 (papatin-like phospholipase domain containing 3) encodes carbohydrate-regulated lipoprotein and/or lipolytic enzymes in liver. The mutation of isoleucine to methionine at position 148 (I148M) causes a loss of function effect leading to increased triglyceride synthesis and accumulation in liver (1).

The PNPLA3 rs738409 C>G polymorphism has been associated with steatosis and fibrosis in various liver disease and increased risk for development of liver cirrhosis and hepatocellular cancer (2). The impact of PNPLA3 rs738409 [G] on liver damage has a strong environmental interaction and is usually associated concomitant liver insult. PSC is a chronic inflammatory disease of bile duct epithelium leading to strictures and may secondarily cause liver cirrhosis. PSC is also associated with inflammatory bowel disease and markedly increased risk of cholangiocarcinoma (3,4). PLPN3 variant has been associated with elevations of liver enzymes in IBD (5) and in increased risk of bile duct stenosis in male PSC patients (6). Survival free of liver transplantation is reduced in male PSC patients with dominant strictures in carriers of PNPLA3 I148M variant (5).

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

Results: Of the 563 patients 334 (59.3%) had the wild type (CC), 197 (35%) were heterozygous (CG) and 32 (5.7%) were homozygous for the mutation (GG). A concomitant IBD was diagnosed in 80% of the males and 60% the females.

Variable, mean(SD)

<table>
<thead>
<tr>
<th></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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<td>36(13)</td>
<td>35(13)</td>
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<td>Weight, kg, males</td>
<td>82(14)</td>
<td>80(15)</td>
<td>81(14)</td>
<td>0.37</td>
</tr>
<tr>
<td>Weight, kg, females</td>
<td>69(7)</td>
<td>70(17)</td>
<td>71(13)</td>
<td>0.62</td>
</tr>
<tr>
<td>IBD, n (%)</td>
<td>263(71)</td>
<td>152(77)</td>
<td>21(65)</td>
<td>0.021</td>
</tr>
<tr>
<td>Age at age of IBD</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(38)</td>
<td>63(31)</td>
<td>9(28)</td>
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<tr>
<td>Progression of ERC score/month*</td>
<td>0.014</td>
<td>0.002</td>
<td>0.004</td>
<td>0.44</td>
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<tr>
<td>Advanced fibrosis F3/4, %)*)</td>
<td>8.5</td>
<td>15.2</td>
<td>12.5</td>
<td>0.25</td>
</tr>
</tbody>
</table>

*Adjusted for sex, age and IBD. Cholangiocarcinoma was diagnosed in 12 (3.6%) patients with CC, 19 (7.5%) with 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
INTRODUCTION: Colorectal cancer (CRC) development is characterized by the sequential accumulation of somatic mutations, which promotes epithelial proliferation and subsequently tumor invasion. Calcineurin is a phosphatase, which contributes to innate and adaptive immunity through the activation of transcription factors of the family of nuclear factor of activated T cells (NFAT). Systemic inhibition of calcineurin as applied in human immunosuppression is associated with an increased incidence of CRC. However, calcineurin and NFAT are also expressed in CRC cell lines and rather promote than inhibit epithelial proliferation in vitro. These findings raise the question of whether calcineurin plays cell-specific roles in CRC and, in particular, whether intestinal epithelial calcineurin promotes tumor development in a cell-intrinsic manner.

Aims & Methods: To investigate the role of calcineurin and NFAT in intestinal tumor development, we generated mice with intestinal epithelial cell (IEC)-specific deletion of the regulatory B1 subunit of calcineurin and analyzed these mice in the ApcMin/+ line as well as samples of more than 700 CRC patients were studied. For mechanistic studies, organoid cultures, immortalized IECs and CRC cell lines were used. IECs were infected with Ad-calcineurin and NFAT viruses and subsequently challenged by 5-azacitadine, TNFα and PMA. For mechanistic studies, organoid cultures, immortalized IECs and CRC cell lines were used.

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

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

Disclosure of Interest: All authors have declared no conflicts of interest.
**OP040** NHERF2 REGULATES COLON CANCER PROGRESS VIA STAT3 and CD24

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**Introduction:** Scaffold proteins mediate protein-protein interactions to bring together key members of signaling pathways that drive cell division and growth. The Na+/H+ exchanger regulatory factor (NHERF) family of proteins is composed of proteins that orchestrate interactions of effectors 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 growth and invasion was assessed by a loss-of-function approach (siRNA) and a small peptide which blocked the PDZ domain of NHERF2 to bind using colon cancer cell lines (HCT116, SW480, and HT-29). We validated tumor growth and invasion of CRC using a tissue microarray. Next, the role of NHERF2 on colon cancer progression was assayed by tumor growth in a mouse xenograft tumor model. Histologic analysis performed the transcriptom analysis.

**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 xenograft tumor model. Histologic analysis confirmed the reduction of cell proliferation by Ki67 immunostaining. In addition, deletion of NHERF2 in ApcMin/+ (ApcMin+/-;NHERF2-/-) mice resulted in decreased tumor growth in ApcMin/+ 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 (LPA2), transcriptome analysis of xenograft tumors revealed that NHERF2-dependent increase in CD24 expression was blocked by inhibition of Stat3, suggesting NHERF2 regulates Stat3 phosphorylation followed by the increase in CD24.

**Conclusion:** This study demonstrated NHERF2 stimulates colon cancer growth by interacting at multiple signaling nodes. NHERF2 potentiates the oncogenic effects in part by regulation of Stat3 and CD24. This study provides NHERF2 as a new potential target for cancer treatment.

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

**References:**

**OP041** THE EXTRACELLULAR MATRIX PROTEIN EMILIN2 AS A REGULATOR OF THE MYELOID RESPONSE IN A MODEL OF INFLAMMATION-INDUCED COLON CARCINOGENESIS

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**Introduction:** EMILIN2 is an extracellular matrix molecule belonging to the EMI Domain ENdowed (EDEN) protein family that exerts pleiotropic effects in the tumor microenvironment (and functioning as a tumor suppressor molecule in breast cancer). EMILIN2 affects tumor cell viability and proliferation by activating apoptosis and functioning as a negative regulator of the Wnt/β-catenin axis. Interestingly EMILIN2 expression is down-regulated by methylation in a number of tumors including breast and 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 unendifferentiated 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 cyclin D1 and c-Myc were not altered in the tumors and in the normal mucosa of the two mouse models. Histopathological and IHC analyses were performed on colon and rectum 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 let us 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:**
Disclosure of Interest:

sensitive to chemotherapy and targeted agents.

Conclusion:

Our results showed that forced miR-145 expression reduced 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. mRNA expression levels of the stemness markers KLF4 and BMI1 were significantly reduced in colon spheres overexpressing miR-145 (p < 0.01). The mature colonocyte marker, CK20, was increased in HCT116 spheres overexpressing miR-145 (p = 0.01).

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

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

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

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

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Introduction: A proton pump inhibitor (PPI)-based triple regimen containing two antibiotics (amoxicillin, APCLM, and clarithromycin, CAM) was considered the gold standard for the eradication of Helicobacter pylori for more than a decade. However, low eradication rates have been reported recently due to the increased prevalence of clarithromycin-resistant H. pylori. Insufficient acid inhibition during treatment also causes eradication failure. This is because the antimicrobial agents are unstable and degraded in the stomach (Espebroeck and EPZ is a new PPI available in Europe since September 2011. EPZ has an improved pharmacokinetic profile as regards CYP2C19 genotype; therefore, it shows less individual variability. Vonoprazan (VPZ) is a potassium-competitive acid blocker (PK-CAB). PK-CABs are a new class of gastric acid suppressants available since February 2015 in Japan. VPZ has a potent and long-lasting anti-secretory effect on H+K+/ATPase due to its high accumulation in, and slow clearance from the parietal cell. Therefore, VPZ-based triple regimens are defined as more potent regimens in comparison with conventional PPIs. The aim of this study was to compare H. pylori eradication rates with VPZ-based triple therapy and CPZ-based triple therapy 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 who were treated with VPZ-based triple therapy, while 376 patients were treated with CPZ-based triple therapy from April 2015 to March 2016. At baseline, demographic and clinical characteristics including gender, age, body mass index (BMI), smoking status, and consumption of alcohol were checked. The first-line eradication regimen was CAM 200 mg, AMPC 750 mg, and either ERY 250 mg or VPZ 20 mg, each twice daily for 7 days. The second-line eradication regimen was metronidazole 250 mg, AMPC 750 mg, and either ERY 20 mg or VPZ 20 mg, each twice daily for 7 days. The eradication of H. pylori infection was assessed using the urea breath test 4-8 weeks after each of the eradication attempts. Results: The overall first-line eradication rate was 79.1% (341/431) for the EPZ regimen and 84.6% (318/376) for the CPZ regimen based on intention to treat (ITT) analysis. The eradication rates based on per-protocol (PP) analysis for the first-line and second-line eradication were 72.6% (341/472) and 85.3% (318/373) respectively. Significant differences were found both in ITT analysis (p = 0.045) and in PP analysis (p = 0.046). The overall second-line eradication rate was 72.6% (45/2) for the EPZ regimen and 85.3% (29/34) for the VPZ regimen, based on ITT analysis. Significant differences were found in the eradication rates (p = 0.045) for the PP analysis. Conclusion: VPZ-based triple therapy was more effective for the second-line eradication. However, for the first-line eradication, both regimens showed more than 70% eradication rates. The rate of VPZ-based triple therapy was significantly higher than that of the CPZ-based triple therapy. However, for the second-line
Aims & Methods: Using gastric tissue from humans, rats treated with proton pump inhibitors and/or a cholera toxin B receptor (CTB) knockout H+/K+-ATPase β-subunit knockout (H/K-β KO) mice and Mongolian gerbils infected with Helicobacter pylori and treated with a CCKBR antagonist, we examined the expression pattern and gastrin-mediated regulation of CLU in parallel reaction monitoring mass spectrometry, in situ hybridization and immunohistochemistry. Human gastric cancer cell lines were used to study the gastrointestinal mediated regulation and biological function of secretory CLU in vitro.

Result: CLU was highly expressed in neuroendocrine cells in normal oxyntic mucosa of humans, rats and mice. In response to hypergastrinemia, expression of CLU was significantly increased and localization shifted from neuroendocrine cells to basal glands and cells of the muscularis mucosae. CLU localization in gastric specimens from three different animal models. This shift was partly inhibited by antagonizing the CCKBR in rats and Mongolian gerbils. The oxyntic mucosa of H/K-β KO mice contained distinct areas with CLU-positive mucous cell hyperplasia, possibly representing SPEM. In vitro, gastrin increased the secretion of CLU, and both gastrin and secretory CLU promoted survival of gastric cells following starvation- and chemotherapy-induced stress.

Conclusion: Our findings suggest that gastrin and CLU participate in premalignant remodeling of the oxyntic mucosa by influencing the balance between survival and apoptosis in gastric epithelial cells.

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

References
Conclusion: The majority of $H. pylori$-infected subjects have reduced intragastric acidity compared to the uninfected population and is this highly likely close to the gastroesophageal junction. The density of parietal cells and chief cells is reduced in $H. pylori$ infected subjects throughout the gastric mucosa. This finding may allow a differential association between $H. pylori$ infection and both gastroesophageal reflux disease and oesophageal adenocarcinoma.

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

References

Monday, October 17, 2016 10:30–12:00

ABSTRACTS ON FIRE: GORD ON FIRE – HOTSPOT

OP048 ASSOCIATION BETWEEN LUMINAL BILE SALT CONTENT AND DUODENAL MUCOSAL INTEGRITY IN HEALTHY VOLUNTEERS

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Introduction: Functional dysphagia (FD) is a functional gastrointestinal disorder with an annual incidence of 20–20% in the general population. Recent studies have shown that duodenal mucosal integrity was reported as a potential pathophysiological mechanism in FD (Vanheel 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 ± 3.8 years). Duodenal biopsies were obtained by gastroduodenoscopy and used to measure the in vitro transepithelial resistance (TEER) using Ussing chambers. Aims & Methods: We aimed to investigate the location of proximal and distal afferent nerves in zollinger-ellison patients with non-erosive reflux disease. We investigated mucosa from 10 patients with typical heartburn symptoms, normal macroscopic oesophageal appearances, and all had pathological oesophageal acid exposure on reflux testing (oesophageal pH exposure > 4.2%). In each patient, endoscopic mucosal biopsies were taken from 3 cm above the gastroesophageal junction (distal), and at 20 cm from the incisors (proximal). Biopsies were fixed in 4% paraformaldehyde, cryoprotected, and 10 μm sections were cut on a cryostat and prepared on slides. Slides were examined immunohistochemically for p63 and p53 as markers of the oesophageal mucosa. Where fibres were identified their location in the mucosa was recorded in terms of cell layers from luminal surface.

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

OP050 MUCOSAL INTEGRITY AND SENSITIVITY TO ACID OF THE PROXIMAL ESOPHAGUS IN PATIENTS WITH GASTROESOPHAGEAL REFUX DISEASE

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

Aims & Methods: We aimed to assess acid sensitivity and mucosal integrity of the proximal and distal esophageal segments separately in patients with gastroesophageal reflux disease (GERD) and to investigate the relationship between these two parameters. We included patients with heartburn and evidence of GERD on ambulatory pH-impedance measurement. After PPI washout, an esophageal ambulatory pH-impedance measurement was performed. In vivo electrical impedance spectroscopy was performed at the two levels and biopsies were taken from macroscopically unaffected mucosa. Biopsies were used to measure histological assessment of intercellular spaces with transmission electron microscopy and as a morphological measure of impaired integrity and to investigate transepithelial electrical resistance and transepithelial fluorescein permeability in Ussing Chambers as a functional measure of mucosal integrity.

Results: We included 12 GERD patients (mean age 48 years, range 28–65, M:F 4:8). Lag time to heartburn perception was shorter after proximal acid perfusion (mean 0.9% CI 0.8 minutes (0.1–1.5) than after distal acid perfusion (3.9 minutes (2.4–5.4)). Lag time to heartburn perception was significantly longer (p = 0.02). In vivo electrical impedance spectroscopy was performed. In vivo electrical impedance spectroscopy was performed. In vivo electrical impedance spectroscopy was performed. In vivo electrical impedance spectroscopy was performed. In vivo electrical impedance spectroscopy was performed. In vivo electrical impedance spectroscopy was performed. In vivo electrical impedance spectroscopy was performed.
mean RSI 0.5

/C6

date the diagnostic utility of salivary pepsin measurement in primary care setting

suggested as preliminary tool to select patients requiring pH monitoring.

primary care patients with LPR from those without and therefore cannot be

In this pilot study, PeptestTM was not able to discriminate among

positive results were observed in 34/70 (49%) LPR patients and 26/46 (57%) HCs

with LPR (37 Male/49 Female, age 54

than 25 mg/mL.

A positive PeptestTM was considered in case of a concentration of pepsin higher

asked to provide 2 samples of sputum collected one hour after lunch and dinner.

made. Also the gastrointestinal symptom scale (GIS) questionnaire was com-

tionnaire and in case of a score

uninvestigated individuals with no gastrointestinal symptoms or disease

presenting with chronic laryngeal symptoms were enrolled by primary care phy-

OP053 Efficacy of acotiamide in patients with gastroesophageal reflux disease unresponsive to proton pump inhibitor therapy

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Introduction: Acid suppression is the mainstay of gastroesophageal reflux disease (GERD) therapy, and proton pump inhibitors (PPIs) are the first choice of drug

therapy.

Patients who had reflux symptoms despite being on PPIs for at least 8 weeks were randomized to receive either acotiamide (improved) was indicative of treatment efficacy. If possible, 24-h multichannel intraluminal impedance-pH (24-h MII-pH) monitoring was performed at base-

line and 6 weeks.

Results: In total, 22 patients were enrolled in this study. The acotiamide and placebo groups consisted of 12 and 10 patients (6 and 7 women; mean age, 56

and 68 years, mean body mass index [BMI], 21 and 23, respectively). There were

no significant differences in patient characteristics between both groups. The

treatment. Few patients had received specific GERD diagnostics or recom-

mended other options (<10%).

Aims & Methods: The LOPA II study is a prospective, multicenter, observational study conducted in 7 general practice clinics. Patients with chronic GERD, taking PPI therapy for at least 1 year, and not satisfied with their treatment were asked to complete a questionnaire. Patients were asked the duration of their PPI therapy, satisfaction with their current condition, frequency of symp-

toms in the last week, whether they had previously received diagnostic evaluation or surgical consult related to GERD, whether they plan to consult a reflux specialist for further diagnostics, and reasons for dissatisfaction with their current treatment. “Lost Patients” were defined as those with a satisfaction score of 1 or 2 on a 5-point Likert scale (1: very satisfied; 2: dissatisfied), GERDQ score at least 8, and have not previously received specialized GERD diagnostics.

Results: 220 consecutive patient responses were collected within one year. Patients suffered from GERD an average of 9.7 years and prescribed PPI therapy for an average duration of 8.2 years. 74% were dissatisfied or very dissatisfied on their current PPI therapy (score of 1 or 2), 89% reported heartburn or regurgita-

tion at least 2 days in the prior week (57% 4–7 days). 53% reported using additional medication other than their prescribed PPI at least 2 days per week or 7 days per week (60% 2 days).

In patients diagnosed with PPI, most cited insufficient symptom control (91%) as a reason for dissatisfaction. In addition, 26% cited concern with long-term use of drugs and 23% the need for daily medication. 92% of patients had received an upper endoscopy, 8% had a prior pH-metry, 5% manometry, and 7% had received prior surgical consult for GERD. The rate of “Lost Patients” in this study was 63%.

Conclusion: Chronic GERD patients who are dissatisfied with their PPI therapy are rarely offered specialized GERD diagnostic procedures or treatment alter-

natives. Half of the patients took medication in addition to PPI to control their reflux. In addition to persistent symptoms, concerns of long-term PPI use and burden of daily medication play a role in patient dissatisfaction with PPI therapy.

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

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

References

**OP054** *A RANDOMIZED CONTROLLED TRIAL TO ASSESS THE CLINICAL EFFECTIVENESS OF VPZ 20 mg ONCE DAILY VS. EPZ 20 mg ONCE DAILY FOR RESOLUTION OF GASTRO-ESOPHAGEAL REFLUX DISEASE SYMPTOMS IN NEWLY DIAGNOSED PATIENTS*

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Introduction: Potassium competitive acid blocker (P-CAB) Vonoprazan (VPZ) has potent acid inhibitory efficacy. We assessed clinical efficacy for Gastro-oesophageal reflux disease (GORD) symptom.

Aims & Methods: 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 least moderate severity (Global Overall Symptom score [GOS] score ≥4 on a 7-point Likert scale) were randomized to treatment with EPZ or VPZ.

The primary endpoint was the proportion of patients with sufficient relief of upper gastrointestinal symptoms (GOS ≤ 2) after 4 weeks of treatment. Secondary endpoints were the proportion of patients with complete overall symptom relief (GOS = 0). Scale for the Symptoms of Gastroesophageal Reflux Disease (FSSG) score, and tolerance for both treatment. All patients provided informed consent before enrolment in the trial.

Results: 88 patients were entered and randomly assigned to the EPZ group and the VPZ group. After 4 weeks, proportion of patients with sufficient relief was achieved by 88.6% in the EPZ group, compared to 58.1% in the VPZ group (p < 0.01). The proportion of patients with sufficient relief of upper gastrointestinal symptoms was significantly higher in the EPZ group (6.8% / 4.5%) than in the VPZ group (27.9% / 4.5%) after 60 and 33% respectively. Both treatments were generally well tolerated, but a patient in the VPZ group withdrew because of 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 in the VPZ group. The result observed in this study was considered to be caused by the multifactorial pathophysiology of GORD. Various mechanisms may contribute to dyspeptic symptoms, for example, finding that patients with gastric achlorhydria or hypergastrinemia showed impaired gastric motility may be supportive of this point (2).

These findings can suggest that increasing the degree of acid inhibition beyond that already achieved by EPZ 20 mg does not translate into increased clinical efficacy for the resolution of GORD symptoms in newly diagnosed patients. The worse provability in FSSG Functional Dyspepsia (FD) score were significantly lower in the EPZ group (6.8% / 4.5%) than in the VPZ group (27.9% / 4.5%). 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).

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

References
IN PATIENTS WITH LAPAROSCOPIC SLEEVE GASTRECTOMY (LSG) is the most commonly performed bariatric procedure in the USA and is 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. LSG electrical stimulation therapy has shown to improve outcomes in GERD patients.ii–iii

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

Results: 12 patients, 66% (8/12) women at 8 centers have been treated. Median age (IQR 34–55) was 46 (10.75) years. Of 12 (10/12) were on daily double-dose PPIs. At their last follow up (median = 12 months), 75% (6/8) were off-PPIs and one each was using PPIs on < 50% of days and standard dose once a day. The latter was on daily double-dose PPIs for 2 years. GERD-HRQL reported improvement in symptoms of GERD patients in 12 months post implantation. No dysphagia or other GI side effects were reported. No dysphagia or other GI side effects were reported. All authors have declared no conflicts of interest.

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

References

ESC REPORTED. Median GERD-HRQL score had improved from 12.5 (3.2–20.5) to 6.0 (0.8–12.4). There was an improvement > 50% in PPI-exposure showing median esophageal pH at baseline of 25.75 (10.2, 54.5) that improved to 9.1 (8.4, 25.1). 4/5 patients (80%) were either free of PPI or with a reduced those compared to pre-operation. All these patients were highly efficient endoscopists perform the procedures. No dysphagia or other GI side effects were reported. No dysphagia or other GI side effects were reported. All authors have declared no conflicts of interest.

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

Monday, October 17, 2016
14:00–15:30

IMPROVING THE ADENOMA DETECTION RATE – ROOM E1

OP058 ENDOCUFF-ASSISTED COLONOSCOPY OUTPERFORMS CONVENTIONAL COLONOSCOPY TO DETECT MISSED-ADENOMAS: EUROPEAN MULTICENTER, RANDOMIZED, BACK-TO-BACK STUDY

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Introduction: Endocuff-assisted colonoscopy (EC) with that of the conventional one (CC). Aims & Methods: Our study population underwent same-day, back-to-back. As the scope is gradually withdrawn, flattening and stretching the colonic folds. We randomized 200 patients (aged 61 ± 10 years; 86.4% CRC screening-surveillance cases). There were 7 EC and 1 CC incomplete exams. Scope insertion times were similar for EC and CC (5.44 ± 3.13 min vs. 5.37 ± 0.237 min, p = 0.60); however, there was a trend for longer EC withdrawal times (7.15 ± 2.52 min vs. 6.50 ± 1.52 min, p = 0.06). Overall, we detected one cancer and 194 (EC = 109; CC = 85) adenomas; 84% in the proximal colon. By per lesion analysis (table). ESC performed significantly lower overall and proximal colon adenoma miss-rates compared with CC (14.7 [8–21]% vs. 37.6 [27–48]%: p = 0.0004 and 10.4 [1.8–19]% vs. 39 [23–55]%: p = 0.004, respectively). A similar superiority for EC was not revealed regarding advanced adenomas either overall or in the proximal colon. Index colonoscopy did not miss the cancer. By per-patient analysis, the second exam indicated modification of the surveillance schedule, according to the AGSE guidelines, in 17 and 5 patients undergoing CC and EC index exams (OR = 3.8 [95%CI: 1.4–10.9]: p = 0.01), respectively; however no difference in the modification of the surveillance schedule was detected when European guidelines were taken into account. The CC index arm had significantly more false negative (no adenoma) first examinations compared to EC (14 of 100 vs. 3 of 94; p = 0.01). There were no adverse events related to EC or CC.

Conclusion: In comparison with conventional colonoscopy, Endocuff-assisted colonoscopy does not miss the cancer. By per-patient analysis, the second exam indicated modification of the surveillance schedule, according to the ASGE guidelines, in 17 and 5 patients undergoing CC and EC index exams (OR = 3.8 [95%CI: 1.4–10.9]: p = 0.01), respectively; however no difference in the modification of the surveillance schedule was detected when European guidelines were taken into account. The CC index arm had significantly more false negative (no adenoma) first examinations compared to EC (14 of 100 vs. 3 of 94; p = 0.01). There were no adverse events related to EC or CC.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP609 THE DIAGNOSTIC ABILITY OF A COMPUTER-AIDED DIAGNOSIS SYSTEM FOR NARROW-BAND IMAGING

ENDOCYTOSCOPY IS COMPARABLE TO THAT OF EXPERT ENDOSCOPISTS

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Introduction: Endoscopy (EC) can be used to evaluate not only cell nuclei but also microvessels in vivo. We reported the efficacy of observing the endoscopic vascular (ECV) pattern by using EC for diagnosing colorectal lesions (Kudo S, et al. GIE 2015; 82: 912-23). However, in our previous study, we did not compare the performance of ECV-CAD with that of human 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 vesel features. ECV-CAD provides a 2-class diagnosis (neoplasia and NON-neoplasia) including its probability value. To validate the diagnostic ability of ECV-CAD, 173 randomly selected EC images (non-neoplasm, 49; neoplasm, 124) that were not used for machine-learning processes were evaluated with ECV-CAD. To compare diagnostic ability between ECV-CAD and manual endoscopy, 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-neoplasm or neoplasm) with its confidence level (high or low). For ECV-CAD, the 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 trainees (P < 0.01, McNemar test) and comparable to those of experts (P = 0.85, McNemar test). The high-confidence diagnosis ratio of ECV-CAD was 72.0% (124 out of 172). The NPV for neoplasms with a high confidence was 94.4%, 84.6%, and 46.3% for ECV-CAD, experts, and novices, respectively. The details of the diagnostic abilities are shown in the 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 tool for expert 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

OP606 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 conditional of multiple covariates, to predict the probability to receive thiopurines, anti-TNFs or combotherapy at baseline. Hazard ratios for lymphoma were estimated using Cox proportional hazards regression in which each treatment was introduced as a time dependent covariate.

Results: The cohort included 173,190 patients with IBD, followed for a median of 4.9 years, accounting for 522,487 persons-years (PY) unexposed to thiopurines, anti-TNFs or 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 and 95% confidence interval (HR95%): 4.83 (2.51-9.16)). Patients exposed to thiopurines or anti-TNFs or combotherapy at baseline. Patients exposed to thiopurines or anti-TNFs or combotherapy had a more than four-fold increased risk of lymphoma as compared to unexposed patients (HR95%: 4.83 (2.51-9.16)).

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.
OP061 INCIDENT CANCER IN INFLAMMATORY BOWEL DISEASE: RISK FACTORS IN A LONG TERM MULTICENTER NESTED CASE-CONTROL LG-IIB STUDY AT 4 YEARS


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Introduction: The study no cancer in inflammatory bowel disease [IBD] are debated (1). In a prospective, multicenter, nested case-control study at 3 years (2012-2014), we reported IBD phenotype as a risk factor for cancer (2). The aim of this study was to identify risk factors for cancer, including cancersubtypes.

Aims & Methods: In a prospective multicenter nested case-control-study, we aimed to assess, in a large IBD population followed up in the long term, risk factors for incident cases of cancer, including cancer subtypes. The role of clinical characteristics of IBD and anti-TNF agents monotherapy (20% of patients) on cancer risk was also assessed. At this purpose, all IBD patients with incident cancer and their matched controls referring to the same 16 Units included in the study at 3 years (Jan 2012-Dec 2014) (2) were followed up for additional 15 months (Jan 2015-Mar 2016: follow up >4 years, 51 months). The study population also included all the additional IBD patients referring to the same Units, with incident cancer from Jan 2015 to Mar 2016. Each IBD patient with cancer (IBD-C) was matched with 2 IBD patients without cancer (IBD-C) for: IBD type, gender, age, Risk factors considered: age (at last visit, at diagnosis of IBD, of cancer), IBD extent, CD phenotype [BI-B3], perianal CD, smoking, family history of IBD, IBD-related surgery, current/past use of thiopurines [IS], TNFα antagonists (≥2 years), any IMm. Data were expressed as median (range), Wilcoxon, Chi-squared test, multivariate logistic regression analysis as appropriate.

Results: Incident cancer occurred in 208 IBD patients: 117 CD [CD-K], 91 UC [UC-K]. IBD-C included 416 patients: 234 CD-C [CD-K], 182 UC-C [UC-C]. IBD-C and IBD-B included 624 patients (351 CD [165 F:47%]: 273 UC [117F:43%]). Cases and controls did not differ in terms of age (CD-K vs CD-C: p=0.92; UC-K vs UC-C: p=0.33) and IBD duration (CD-K vs CD-C: p=0.63; UC-K vs UC-C: p=0.53). In IBD, cancers (n=208) involved (n=108): digestive system (76 [36.5%]: 55 [25.5%] colorectal cancer [CRC], 8 [10.5%] small bowel adenocarcinoma, SBA), skin (28 [16%]), breast (11 [6%]), lung (14 [7.6%]), genital tract (11 [5.2%]), thyroid (8 [3.8%]), lymphoma (7 [3.4%]), others (24 [11.5%]). CRC (n=53) was more frequent in UC vs CD (n=31: 39% vs 22:17% [19%]; p=0.04), while extracolonic cancers (n=155) in CD vs UC-C: CRC (n=20: 8% vs 60:9% [66%]; p=0.01), (5:7% vs 35:6%); p=0.001). In CD, cancer risk factors included perianal disease for CRC (OR 2.61 [1.23–5.63]), penile cancer (2.11 [1.49–2.99]) and SBA [n=8] (OR 2.81 [1.14–6.07], p=0.02). In UC, risk factors were: pancolitis (OR 2.24 [1.24–4.07], p=0.02) for CRC and SBA (OR 2.23 [1.03–4.81], p=0.04).

Conclusion: In a long-term multicentre study, clinical characteristics of IBD (UC extent, penetrating CD, perianal CD) were risk factors for incident cancer. CRC was more frequent in UC and extracolonic cancers in CD.

Disclosure of Interest: L. Biancone: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Astra Zeneca, Chiesi, Ferrering, MSD, Otsuka, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar; A. Armuzzi: The author declares no conflicts of interest specifically related to the study. The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Astra Zeneca, Chiesi, Ferrering, MSD, Otsuka, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar; M.L. Sciribono: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Astra Zeneca, Chiesi, Ferrering, MSD, Otsuka, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar; R. D’Inca: No conflicts of interest specifically related to the study. The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Zambon and for advisory boards for Biogen Idec, Takeda, Mundipharma; F. Pallone: No conflicts of interest specifically related to the study. The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Takeda, Zambon and Mundipharma; F. Castiglione: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Takeda, Chiesi, MSD, Abbvie, Sofar; M. Daperno: No conflicts of interest specifically related to the study. Financial support for research not related to the present study from MSD, lecture fees from Abbvie, MSD, Hospira, Mundipharma, Takeda, Sofar, Chiesi, Ferrering; C. Papu: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Takeda and for advisory boards for Biogen Idec, Takeda, Mundipharma; L. Guidi: No conflicts of interest related to the study. Lecture fees from Abbvie, MSD, Takeda, Zambon, lecture fees from Abbvie, MS, study for research not related to the study. The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Takeda, Zambon and Mundipharma; A. Koh: Financial support for research not related to the study from Merck and Co; W. Fries: The study was not sponsored. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, MSD, Hospira, Ferrering; G. Riegler: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Takeda, MSD; E. Calabrese: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Takeda, MSD; S. Ardizzone: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from MSD, Abbvie; M. Vecchi: No conflicts related to the study. Advisory Board from MSD, Hospira, Mundipharma, Takeda, lecture fees: MSD, Abbvie, Hospira, Mundipharma, Chiesi, Zambon, financial support for research not related to the study. MSD, Sofar, Giuliani; A. Orlando: No conflicts of interest specifically related to the study. Lecture fees from Abbvie, Chiesi, MSD, Otsuka, Takeda, Sofar, Zambon, Mundipharma and served as consultant for Abbvie, MSD, Sofar, Takeda; F. Pallone: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Takeda, Zambon. All other authors have declared no conflicts of interest.

References
OP062 USE OF IMMUNOSUPPRESSANTS AND BIOLOGICAL AGENTS IN IBD PATIENTS WITH PAST HISTORY OF CANCER. A. Juan Juan1, J. Guardiola1, I. Alfaro Perez2, M. Minguez4, B. Velazquez1, J.M. Benitez Cantero3, F. Mesonero3, M. Chaparro3, B. Sicilia Aladren2, Y. Zabana2, A. Villoria2, R. Lorente Poyatos2, M.P. Martinez Montiel1, E. Pinto Martinez de Paredes1, L. Mazoq Maguez1, J. Barrio Andres1, M. Piqueras Cano1, N. Jimenez1, C. Rodriguez Gutierrez1, P. Nos Mateus1, M. Montoro2, M.C. Muñoz2, E. Rodriguez2, M. Martín Arranz2, A. Rodriguez Perez2, M. Van Domelhoe1,2, M. Rivero2, J.L. Cabriada29, M.T. Arroyo-Villarino29, P. Romero30, S. Garca31, M. Charro32, J.P. Gisbert33, E. Domeche34
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Introduction: Conventional immunosuppressants (thiopurines or methotrexate) and anti-TNF agents (IMMs) can influence the immunologic control of cancer and might ease cancer spread and recurrence. Therefore, a past history of IBD patients with previous cancer of whom 526 did not received IMMs before the diagnosis of cancer. Of these, 358 were controls and 141 were subsequently treated with IMMs after a median of 60 (23–130) months from cancer diagnosis. After a median follow-up of 68 months (27–126), 52 patients (10%) developed incident cancers (50% recurrent and 50% new). The most frequent recurrent ones were breast (35%) and prostate (20%) cancers. Incident cancers occurred similarly in patients further treated with IMMs and controls (9% vs. 12% p=0.33), as did regarding the type of the index cancer. However, cancer-related deaths were more frequent among controls (4% vs. 0% p=0.013). Cancer-free survival was 99%, 98% and 97% at 1, 2, 5 years in patients further treated with IMMs and 97%, 96% and 92% at 1, 2 and 5 years in controls, respectively (p=0.003).
Conclusion: In this large, retrospective cohort, treatment with conventional immunosuppressants or anti-TNF agents in patients with IBD and a past history of cancer was not associated with an increased risk of new or recurrent cancers.
Disclosure of Interest: All authors have declared no conflict of interest.

OP063 RISK OF SERIOUS AND OPPORTUNISTIC INFECTIONS IN IBD PATIENTS WITH PAST HISTORY OF CANCER. A PARISIAN FRENCH COHORT STUDY J. Kirchgesner1, M. Lemaître2, M. Zurizeki1, F. Carbonnel1, R. Dray-Spira2
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Introduction: Serious and opportunistic infections are a major concern in patients with inflammatory bowel disease (IBD) treated with immunosuppressive agents and biologics.
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 (combitherapy). 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. A proportion of patients was matched on propensity score, age, gender, disease activity. Data describing the course of HRQoL in IBD patients with previous cancer of whom 526 did not received IMMs before the diagnosis of cancer. Of these, 358 were controls and 141 were subsequently treated with IMMs after a median of 60 (23–130) months from cancer diagnosis. After a median follow-up of 68 months (27–126), 52 patients (10%) developed incident cancers (50% recurrent and 50% new). The most frequent recurrent ones were breast (35%) and prostate (20%) cancers. Incident cancers occurred similarly in patients further treated with IMMs and controls (9% vs. 12% p=0.33), as did regarding the type of the index cancer. However, cancer-related deaths were more frequent among controls (4% vs. 0% p=0.013). Cancer-free survival was 99%, 98% and 97% at 1, 2, 5 years in patients further treated with IMMs and 97%, 96% and 92% at 1, 2 and 5 years in controls, respectively (p=0.003).
Conclusion: Thiopurines, anti-TNFs monotherapy and combitherapy were associated with an increased risk of serious and opportunistic infections, compared to unexposed patients. Combitherapy was associated with an increased risk of serious and opportunistic infections compared to anti-TNFs exposure in patients aged 18–64 years (hazard ratio and 95% confidence interval HR95%: 1.31 (1.14–1.51), HR95%, 2.12 (1.49–3.00)), while exposure to anti-TNFs was associated with an increased risk of serious infections compared to thiopurines in patients aged 18–64 years and ≥ 65 years: HR95%: 1.82 (1.67–1.99) and HR95%, 1.83 (1.43–2.35). Exposure to thiopurines was associated with an increased risk of safety infections compared to anti-TNFs’ monotherapy in patients aged 18–64 years (HR95%: 1.74 (1.20–2.52)). Similar results were observed in a sensitivity analysis conducted in incident patients.
Conclusion: Thiopurines, anti-TNFs monotherapy and combitherapy are all associated with an increased risk of serious infections in IBD patients compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs than with thiopurines and the risk of serious and opportunistic infections is higher with thiopurines than with anti-TNFs and the risk of serious and opportunistic infections should be taken into consideration and weighed against potential benefits of anti-TNFs.
Disclosure of Interest: F. Carbonnel: Franck Carbonnel had consulting fees from Teneesent, Osuka, Vifor, and lecture fees from Hospira.
All other authors have declared no conflicts of interest.

OP064 THE COURSE OF HEALTH-RELATED QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE IN IBDD PATIENTS WITH PAST HISTORY OF CANCER. A NATIONAL FRENCH REGISTRY STUDY. J. Kirchgesner1, M. Lemaître2, M. Zurizeki1, F. Carbonnel1, R. Dray-Spira2
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Introduction: Previous population-based cross-sectional studies have shown that health-related quality of life (HRQoL) in patients with the inflammatory bowel diseases (IBD) is lower compared to the healthy general population. The objective of this study was to assess the course of HRQoL in IBD patients with previous cancer of whom 526 did not received IMMs before the diagnosis of cancer. Of these, 358 were controls and 141 were subsequently treated with IMMs after a median of 60 (23–130) months from cancer diagnosis. After a median follow-up of 68 months (27–126), 52 patients (10%) developed incident cancers (50% recurrent and 50% new). The most frequent recurrent ones were breast (35%) and prostate (20%) cancers. Incident cancers occurred similarly in patients further treated with IMMs and controls (9% vs. 12% p=0.33), as did regarding the type of the index cancer. However, cancer-related deaths were more frequent among controls (4% vs. 0% p=0.013). Cancer-free survival was 99%, 98% and 97% at 1, 2, 5 years in patients further treated with IMMs and 97%, 96% and 92% at 1, 2 and 5 years in controls, respectively (p=0.003).
Conclusion: In this large, retrospective cohort, treatment with conventional immunosuppressants or anti-TNF agents in patients with IBD and a past history of cancer was not associated with an increased risk of new or recurrent cancers.
Disclosure of Interest: All authors have declared no conflicts of interest.

Affects: Humidity, Temperature, and Wind Strength.
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 N-IBDQ and the SF-36 at every follow up visit, respectively. We could not register clinically relevant changes between the mean N-IBDQ total scores and the mean GH dimensional scores during the different follow up visits (Table 1). Of 139 UC patients and 60 CD patients, who answered the N-IBDQ at all follow up visits, 31 (23.3%) and 13 (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 1: 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>
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<tbody>
<tr>
<td>5</td>
<td>10</td>
<td>20</td>
<td>10</td>
<td>20</td>
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<td>All patients</td>
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<tr>
<td>N</td>
<td>180</td>
<td>108</td>
<td>160</td>
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<tr>
<td>Mean scores</td>
<td>190</td>
<td>187</td>
<td>181</td>
<td>179</td>
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<tr>
<td>SD</td>
<td>21</td>
<td>20</td>
<td>23</td>
<td>25</td>
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<tr>
<td>SF-36</td>
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<tr>
<td>N</td>
<td>178</td>
<td>104</td>
<td>165</td>
<td>110</td>
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<tr>
<td>Mean scores</td>
<td>187</td>
<td>179</td>
<td>186</td>
<td>186</td>
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<tr>
<td>SD</td>
<td>28</td>
<td>21</td>
<td>22</td>
<td>18</td>
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<tr>
<td>GH</td>
<td></td>
<td></td>
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<tr>
<td>N</td>
<td>68</td>
<td>68</td>
<td>60</td>
<td>65</td>
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<tr>
<td>Mean scores</td>
<td>71</td>
<td>71</td>
<td>64</td>
<td>65</td>
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<tr>
<td>SD</td>
<td>16</td>
<td>22</td>
<td>18</td>
<td>22</td>
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</table>

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

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

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
<th>Exposed to thiopurines or anti-TNFs</th>
<th>Exposed to anti-TNFs monotherapy versus thiopurines or anti-TNFs</th>
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</thead>
<tbody>
<tr>
<td>Serious infections, all patients</td>
<td>1.31 (1.20-1.42)</td>
<td>1.31 (1.17-1.45)</td>
</tr>
<tr>
<td>18–64 years</td>
<td>4.31 (3.48-5.36)</td>
<td>5.04 (3.88-6.55)</td>
</tr>
<tr>
<td>&gt;65 years</td>
<td>5.37 (4.20-6.87)</td>
<td>6.10 (4.56-8.16)</td>
</tr>
</tbody>
</table>

Abstract No: OP065

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

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Introduction: The long-term efficacy of infliximab (IFX) in Crohn’s disease (CD) patients is substantial 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 patients treated with IFX during 1994-2016 at a tertiary centre, retrospectively analysed. Only patients who responded to an induction dose (5 mg/kg on week 0, 2, and 6), followed by scheduled IFX maintenance treatment were included. Exclusion criteria were: prior infliximab use, ever episodic treatment, drug interval (> 14 weeks), CD-related surgery during induction therapy and extra-intestinal manifestations as main indication. IFX failure was the primary endpoint, defined as stopping IFX due to one of the following reasons: 1) loss of response (LOR) despite treatment optimization, 2) absence of persistent antibodies towards infliximab (ATI), and 3) the need for IBD related surgery. Since 2010-2011, IFX and ATI serum concentrations at trough were measured in the majority of patients with a house-developed and clinically validated drug sensitive bridging enzyme-linked immunosorbent assay (ELISA). Therapeutic drug monitoring (TDM) was used to monitor serum IFX concentrations during treatment decisions and optimization. Patient- and disease-related factors were used to identify independent predictors of IFX failure-free survival using Cox proportional hazards model and Kaplan-Meier analysis. Internal validation of the Cox regression analysis was performed with bootstrapping with 1000 replications. The c-statistic was used to assess the predictive accuracy of the regression model.

Results: A total of 261 CD patients were included in the final analysis. Median time on IFX was 2.4 [IQR 1.4-4.7] years, and 65 (24.9%) patients experienced IFX failure. Median age at start of IFX was 32.8 [22.6-44] years, after a median disease duration of 3.4 [0.7-13.6] years. In total, 59 (14.9%) patients received anti-TNF prior to IFX start (adalimumab or certolizumab pegol). TDM was used in 202 (77.4%) patients. Estimated 1, 5, and 10 year IFX failure-free survival was 93.7% (95% CI 90.7-96.7), 65.9% (53.3-75.5) 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 L1 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^-5), and first IFX dose optimization within first year (HR 3.7 (2.1-6.6), p = 5x10^-5) 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) (p = 8x10^-15). IFX concentrations at

References:
1. Norman GR, Sloan JD and Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Medical Care 2003; 41: 582-592.
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 in Crohn’s disease. 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, Ferrin, Jansen, Mitsubishi Tanabe, MSD, Takeda, Tillotts, Zeria - Consultancy: Abbvie, Boehringer-Ingelheim, Ferrin, Jansen, MSD

G. Van Assche: - Financial support for research: Abbvie, MSD - Lecture fees: Abbvie, Ferring, MSD, Janssen - Consultant: LAMA, Roche - AUC - MS, MSD, Takeda

A. Gils: - Financial support for research: FWO grant G061712, Pfizer HR grants - Speakers fee: MSD, Abbvie, Jansen Bioscience - Pfizer - Consultant: UCBL

S. Vermeire: - Grant support: Abbvie, MSD, Takeda - Lectures: Abbvie, MSD, Takeda, Ferrin, Ferring Pharma, Hospira, Tillotts - Consultant: Abbvie, MSD, Takeda, Ferrin, Genentech/Roche, Shire, Pfizer, Galagapos, Mundipharma, Hospira, Celgene - Consultant, Januvia

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 CYClical ENTERAL NUTRITION FOR THE MAINTENANCE OF REMISSION IN PEDIATRIC CROHN’S DISEASE PATIENTS

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Introduction: Enteral nutrition (EN) is a well-established treatment in pediatric Crohn’s disease (CD) for induced remission. Stratifing 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.

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 Modulen IBD, patients who came into complete CRP-negative disease were included in this prospective pilot study. At inclusion, all patients were in deep remission (CRP-negative). At M2 and 6 months, anthropometric measurements were performed and clinical data were collected.

Results: At inclusion, all patients were in deep remission (CRP-negative). At month 6 and 12 follow-up visit, 8 of the 9 patients (89%) (wPCDAI 8.4 ± 0.84) and 5 of 6 patients (wPCDAI 5.7 ± 0.11) were in deep remission, respectively. In clinical remission, comitant to the clinical response, biological scores markedly improved with mean CRP 21.8 ± 14.2 mg/L at M0, 9.8 ± 11.7 mg/L at M6 (p < 0.05) and 5.4 ± 2.7 at M12 (n = 6) (p < 0.05) and albumin normalization with 33.8 ± 3.8 g/L at M0, 39.3 ± 3.1 g/L at M6 (p = 0.00) and 42.8 ± 2.9 at M12 (n = 6) (p < 0.05). 3 patients relapsed before M12. Patients presented catch up growth with net improvement of their anthropometric measurements at M2 and stabilization thereafter (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>M0 (n = 9)</th>
<th>M2 (n = 9)</th>
<th>M6 (n = 9)</th>
<th>M12 (n = 6)</th>
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<tr>
<td>Z score weight</td>
<td>-0.96 ± 1.13</td>
<td>-0.37 ± 0.97</td>
<td>0.07 ± 0.81</td>
<td>0.30 ± 1.18</td>
</tr>
<tr>
<td>Z score height</td>
<td>-0.18 ± 0.84</td>
<td>-0.11 ± 0.80</td>
<td>0.09 ± 1.14</td>
<td>0.35 ± 0.76</td>
</tr>
<tr>
<td>Z score BMI</td>
<td>-1.37 ± 1.07</td>
<td>-0.38 ± 0.89</td>
<td>-0.82 ± 1.15</td>
<td>-0.66 ± 1.20</td>
</tr>
</tbody>
</table>

Conclusion: This study demonstrates for the first time prolonged clinical, biological remission and improved growth in pediatric CD patients treated only with cyclical enteral nutrition. Cyclical EN can be an efficacious non pharmacological treatment of Crohn’s disease patients potentially acting ahead of the inflammatory cascade in the intestinal mucosa. A sufficiently power randomized controlled trials is currently conducted by the GETAID paediatricne to confirm this pilot data.

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

All other authors have declared no conflicts of interest.

OP076 CHANGES IN MUCOSAL-ASSOCIATED INTESTINAL MICROBIOTA AND FECAL BACTERIA IN INFILTRATING BOWEL DISEASE PATIENTS AND HEALTHY SUBJECTS: A PILOT STUDY

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

Aims & Methods: The aim of the present study was to evaluate the mucosal and fecal microbiota composition in healthy controls (CTRLs) and IBD patients, in a case-control study exploited by 16S rRNA targeted metagenomics-based approach (phylotyping, PH). Fecal samples were collected from 14 IBD patients [10 Crohn’s disease (CD), 4 ulcerative colitis (UC)] and from 11 healthy subjects. Microbiota composition was obtained during colonoscopy from the terminal ileum, and descending colon. PH was assessed by pyrosequencing as follows. All patients were in wash-out from antibiotics, probiotics and corticosteroids. Genomic DNA was isolated from the entire set of samples. The VI-V3 region of 16S rRNA was amplified on a 454-Junior Genome Sequencer. Reads were analyzed by Quantitative Insights into Microbial Ecology (QIIME, v1.8.0), grouped into operational taxonomic units (OTUs) at a sequence similarity level of 97% by P. NAST for taxonomic assignment, and aligned by UCLUST for OTUs matching against Greengenes database (v 13.8).

Results: In adult IBD patients colonic biopsies showed a statistically significant increase of Proteobacteria and decrease of Firmicutes and Actinobacteria, compared to CTRLs. The microbiota analysis of stool samples from IBD patients showed an increment of Proteobacteria and decrease of Bacteroidetes. The difference was not significant compared to CTRLs. Particularly, a predominate presence of Enterobactericeae in IBD and a predominate 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. Tacking in account only colon biopsy samples, a significant reduc- tion of Enterobactericeae - protected by Rikenellaceae, Rosebacia, Ruminococcaceae was observed in patients and an increment of Enterobactericeae was observed in CTRLs. Finally, stratifying samples on the bases of disease activity a decrease of Ruminococcaceae, Peptostreptococcaceae and Paraprevotellaceae and an increase in Enterobactericeae was associated to active disease status (P < 0.05).

Conclusion: The present study shows that in the mucosal microbiota of IBD patients, irrespective of disease localization and activity, phyllum Proteobacteria was significantly more represented, while phyllum Firmicutes and Actinobacteria were reduced. The profiles of fecal microbiota partially replicate those of the mucosal microbiota being not completely different from controls. It appears that microbiota adhering to the gut mucosa better discriminates patients from controls especially when considering family species. Our data suggest the high diagnostic potential of microbiota profiling with special reference to mucosal biosystem.

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

OP086 BACTERIOPHAGE THERAPY: A NEW STRATEGY TO TARGET ADHESION-INVESIVE ESCHERICHIA COLI BACTERIA IN THE GI TRACT OF CROHN’S DISEASE PATIENTS

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4Ferring Pharmaceuticals, Saint-Prex/Switzerland

5Univ. Lille, Inserm, LIRIC, UM9895, Lille/France

6Ferring Pharmaceuticals, Saint-Prey/Switzerland

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Introduction: Adherent-invasive Escherichia coli (AIEC) are abnormally predominant in Crohn’s disease (CD) ileal mucosa. AIEC are pathobiont bacteria able to cause inflammatory responses that could initiate or perpetuate the chronic gut inflammation. Antibacterial treatments, such as bacteriophages (viruses infecting bacteria) represent a way to eliminate these bacteria from the GI tract without disturbing the microorganism homeostasis. Here, we present the discovery and the use of bacteriophages to reduce AIEC colonization associated to intestinal mucosa.

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

Results: In LF82-colonized CEACAM6-expressing mice, 24h after the oral administration of this cocktail of three bacteriophages, the fecal...
concentration of LF82 bacteria has significantly dropped by two log in the bacteriophage group and stays significantly lower than in control group four days post-treatment, without any additional bacteriophage administration demonstrating the benefit of self-amplification of bacteriophages over time. Furthermore, we found that administration of the cocktail during the first day reduces progressively over a period of five days the colonization level of LF82 bacteria through the entire gut. In addition, bacteriophage treatment reduced colitis symptoms in the DSS-induced model, with a reduction of LF82 bacteria levels in feces, compared to the control group. Then, we showed that bacteriophages were driving a long-term digestive tract decolonization of AIEC LF82 bacteria which in turns reduces colitis symptoms.

Conclusion: Bacteriophages targeting AIEC bacteria with high efficacy in murine models suggest that such a treatment could reduce AIEC-associated symptoms in CD patients, providing an incentive to initiate clinical studies. The use of 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 CIPROFLOXAXIN RESISTANCE IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH ESBL-PRODUCING ENTEROBACTERIACEAE COLONIZATION V. Skuja1, K. Pekarska2, Z. Straume1, E. Goida1, H. Dauvart3, D. Rudzite1, E. Lavrinovic1, L. Plekuse, A. Derovs1, A. Lejnieks1, A. Krumina1
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Introduction: Escherichia coli 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.

Methods: A total of 86 patients with confirmed IBD diagnosis were included in the study – 65 (75%) with UC, 21 (24%) with CD. We found that 7 (11%) of the UC patients included Escherichia coli (n = 5), Klebsiella oxytoca (n = 1) and Escherichia hermanii (n = 1). The isolated ESBL-producing Enterobacteriaceae from IBD patients included Escherichia coli (n = 2), Haemophilus influenzae and Klebsiella pneumoniae (n = 1) from UC patients, and Escherichia coli (n = 2) from CD patients. K. oxytoca (n = 1) and the Enterococcus faecalis (n = 1) were isolated from UC patients. Ciprofloxacin resistance was determined using macrobroth dilution method. Ciprofloxacin and ciprofloxacin MICs were 2. The isolated bacterial plasmid genes CTX-M, TEM and SHV were detected. Results: A total of 86 patients with confirmed IBD diagnosis were included in the study – 65 (75%) with UC, 21 (24%) with CD. We found that 7 (11%) of the UC patients and 2 (10%) of the CD patients were colonized with ESBL producing Enterobacteriaceae. The isolated ESBL producing strains from UC patients included Escherichia coli (n = 5), Klebsiella oxytoca (n = 1) and Escherichia hermanii (n = 1). The isolated ESBL-producing Enterobacteriaceae from CD patients included Escherichia coli (n = 2). The isolated bacterial plasmid genes associated with CTX-M production were detected in 4 (5%) of UC and 2 (10%) of CD patients, TEM in 2 (2%) of CD patients, SHV in 1 (1%) of UC and 1 (14%) of CD patients. TEM and SHV were resistant to ciprofloxacin and bacterial plasmid genes CTX-M, TEM and SHV were detected. Conclusion: A 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 TRYPTOPHAN INTO ARYL HYDROCARBON RECEPTOR LIGANDS B. Lamas1, M. Lavie-Richard2, M. Michél3, V. Leducq4, C. Bridonneau2, G. Da Cost4, L. Beaugerie5, P. Langella6, H. Sokol1
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3Department Of Gastroentérologie, APHP St Antoine, Paris/France
4Institut Jean Gourou, Grenoble/France
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6Micas, UMR 1319, Jouy-en-Josas/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 adapter 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 pathway. Our aim was to explore the role of the gut microbiota in the susceptibility of Card9−/− mice to colitis.

Aims & Methods: Germ-free (GF) C57BL/6 wild-type (WT) mice were inoculated by oral gavage with fresh stools from conventional WT (WT → GF) or Card9−/− (Card9−/− → GF) mice. Colitis was induced by DSS. AHR activity in intestinal tissue was determined using an reporter cell line. Immune response was assessed at transcripts level, at the protein level and at the cellular level using flow cytometry. Patients with IBD were genotyped for the major IBD-associated SNPs including CARD9. Statistical analysis was performed using parametric or non-parametric tests as appropriate.

Results: Bacterial and fungal gut microbiota of Card9−/− mice (assessed by 16s and ITS2 sequencing) were altered compared to WT mice. Card9−/− → GF mice were more susceptible to colitis than WT → GF with impaired recovery. Moreover, IL-22 defect was observed in Card9−/− → GF mice at the gene expression and protein levels in the colon and in MLNs. IL-22 production by T helper cells and CD8+ T cells, lymphoid tissue inducer cells, and CD3+ CD4+ NKp46+ innate lymphoid cells and lymphoid tissue inducer cells, and CD3+ CD4+ NKp46+ cells was decreased in the colon of Card9−/− → GF mice. AHR ligands are known to promote gut IL-22 production. Indeed, the levels of total AHR ligands, including NFKB, were decreased in stools of Card9−/− → GF and Card9−/− mice. Moreover, feces from Card9−/− and Card9−/− → GF mice were defective in their ability to activate AHR. In Card9−/− → GF mice, susceptibility of colitis, and IL-22 defect were rescued after treatment with AHR agonists (6-formylindolo[3,2-b]carbazole), or inoculation with three Lactobacillus strains with strong AHR activity. These effects were abrogated in the presence of AHR antagonist (CH223191). Reduced production of AHR ligands was also observed in the microbiota from patients with IBD, particularly in those with CARD9 risk alleles.

Conclusion: Card9 deletion has an effect on the gut microbiota in mice and its transfer to WT GF recipients is insufficient 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. Impaired microbial activity is associated with decreased production of AHR ligands, which can be an attractive strategy in IBD.

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

References

OP071 FAecal MICROBIAL TRANSPLANTATION (FMT) IN ULCERATIVE COLITIS (UC) IS ASSOCIATED WITH SPECIFIC BACTERIAL CHANGES: STOOL AND COLONIC MUCOSA 16S MICROBIOTA ANALYSIS FROM THE RANDOMISED CONTROLLED FOCUS STUDY S. Paramsothy1, N. Kaakoush2, M.A. Kamm3, J. Faith1, J. Clemente1, A. Walsh4, J. Van Den Bogaerde5, D. Samuel6, R. W. Leong6, S. Connor7, R. W. Lafferty8, Ng9, R. Paramsothy8, E. Lin1, J. Colombel2, T.J. Borody3, H. Mitchell1
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2Liverpool Hospital, Sydney/Australia
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7Liverpool Hospital, Sydney/Australia
8Centre 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). This part of the FOCUS study aimed to characterise the microbial changes underlying FMT in UC. We identified those present before, 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 3–7 unrelated donors. Faecal 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 sequencing performed using 2x300 bp Illumina MiSeq chemistry (F7-519R). 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 and batch) faecal samples along with 160 patient colonic samples were analysed. 2697 ± 540 clean sequences per faecal sample and 2690±3.881 per colonic biopsy were obtained with rarefaction curves suggesting sampling had reached saturation. In both faecal and colonic samples, diversity 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. LEfSe analysis of both faecal and colonic samples showed a decrease in patient Bacteroides 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 diversity 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 response across all microbial populations: taxa within Barnesiella were associated with remission, while OTUs within Faecalibacterium 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 microbial diversity, with the greatest diversity noted in patients achieving remission. Increased diversity persists 8 weeks after cessation of therapy. Specific bacterial taxa in the UC patient population 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.

Reference

Monday, October 17, 2016 14:00–15:30
Free Paper Session: The Future of Diagnosis in HBP and Upper GI – Room N1

OP073 A QUANTITATIVE IMAGING PLATFORM TO REAL-TIME MEASURE SPECIFIC ROS LEVELS IN LIVER DISEASES

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

Aims & Methods: Four different two-photon fluorescent probes were designed and synthesized for selective detection of chemically reactive molecules of thiols and ROS including glutathione (GSH), H2O2, HOCl, and O2−. Mouse models of hepatic steatosis, fibrosis, and ischemia-reperfusion injury were developed to mimic human liver diseases. 2 After sacrificing the animals, unfixed liver tissues were collected and incubated with each probe at the final concentration of 50 to 100 μmol for 10 min, and then imaged using multiphoton microscopy (JenLab GmbH, Jena, Germany). 3

Results: Each probe exhibited a strong positive fluorescent response only in the presence of its specific chemically reactive molecule, whereas negligible fluorescent signals were observed upon the additions of other reactive oxygen/nitrogen species and metal ions. There was a good linear relationship between the probe responsive fluorescent intensity and the concentration of specific ROS in the liver with ischemia-reperfusion injury, reduced autofluorescence was detected, indicating the hepatocyte necrosis. Remarkable enhancement of red fluorescence was observed in hepatocytes with decreased autofluorescence, indicating the reaction of with endogenous HOCl. The cellular concentration of GSH decreased and H2O2 increased in the liver with fibrosis and steatosis compared to the control. The concentration of each specific ROS was first calculated based on the intensity of images at the cellular level.

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

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

References
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>
</tbody>
</table>
| **TOTALS**          | **20/76 (26.3%)** | **8/72 (11.1%)** *

*p = 0.02138 by Fisher Exact test

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

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

**References**
1. Fox et al., *DDW* 2014.
### OP075 THE NEW IMAGE ENHANCEMENT TECHNOLOGY USING LINKED COLOR IMAGING WITH ACETIC ACID INDIGOCARMINE MIXTURE FOR DIAGNOSIS OF EARLY GASTRIC NEOPLASM

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**Introduction:** A combination of magnifying endoscopy with image enhancement endoscopy (IEE technology) (e.g. NBI, BLI) is reported in a diagnosis for the early gastric neoplasm. This combination is effective, but it is necessary to speculate in real histology from the pattern of a two-dimensional monotone. Therefore, this diagnostic method is still more difficult for general endoscopists. Linked Color Imaging (LCI) was recently developed using a laser endoscopic system (FujiFilm Co., Tokyo, Japan). LCI acquires images by simultaneously using narrow-band short wavelength light and white light in an appropriate balance. This combination of light provides more information about the vasculature and architecture on the mucosal surface than that obtained with typical white-light imaging. When we use acetic acid indigocarmine mixture (AIM) with LCI mode, we discovered that the magnifying images of early gastric cancer are very clear, three-dimensional and near to real histology. So, we examined the utility of this method.

**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 were indicated of the endoscopic submucosal dissection (ESD), and were given pre-ESD endoscopy in our hospital from September 2014 to February 2016. Firstly we observed the lesions by magnifying endoscopy with LCI+AIM method and diagnosed using VS classification system. Secondly we observed the lesions by magnifying endoscopy with LCI+AIM method and diagnosed using VS classification system. Furthermore, we classified the visualization ability of the surface fine structure in Clear, Visible, and Invisible and evaluated it. Finally, we carried out ESD and compared the image with the histopathology.

**Results:** By the pathology results, 60 lesions were gastric cancer and 12 lesions were gastric adenoma. The differentiation ability of a cancer and the non-cancer (adenoma) did not have the significant difference between the BLI mode and the LCI+AIM methods. 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 LCI+AIM 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 the 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**


### OP077 EXOSOMES DERIVED FROM GASTRIC CANCER PATIENTS AND CELLS COULD DELIVER MIR-21 TO ELICIT TUMOR Proliferation AND METASTASIS AND COULD BE USED AS A POTENTIAL DIAGNOSTIC BIOMARKER

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**Introduction:** Gastric cancer (GC) remains a global challenge due to high morbidity and mortality rates and poor response to chemotherapy treatment. Increasing evidence suggests that exosomal microRNAs (miRNAs) possess diverse cellular regulatory roles in cancer progression nowadays. The tumor microenvironment is abundant with exosomes that are secreted by the cancer cells themselves. Exosomes are nanosized, organelle-like membranous structures that are increasingly being recognized as major contributors in the progression of 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 miRNA could modulate cancer progression and metastasis and can be used as a diagnostic marker. In this study, we used miRNA microarray technology to identify exosomal miRNAs that were differentially expressed in GC patients and controls. We further examined the biological function of exosomal miR-21 on cell viability, apoptotic death and metastasis in human GC cells and explored the possible downstream mechanism. We also included another 100 GC patients and 100 controls to study whether exosomal miR-21 could be used as a potential biomarker.

**Results:** We found that exosomes derived from GC patients exhibited significant different miRNA expression patterns compared with those from controls. Of the 233 miRNAs that were differentially expressed, miR-21 stood out as one of the most significantly upregulated miRNAs in cancer patients. miR-21 depletion in GC cells led to decreased miR-21 levels in exosomes and significantly reduced cell proliferation, migration, invasion and increased apoptosis, and the same phenomenon was seen when transfected miR-21 inhibitor into the exosomes from GC cells and co-culture the transfected exosomes with GC cells. Moreover, exosomal miR-21 markedly enhanced sialin and vimentin expression in GC cells, while significantly decreasing E-cadherin levels, suggesting that exosomal miRNA might play a role in epithelial-to-mesenchymal transition (EMT) process. Finally, circulating exosomal miR-21 levels were closely associated with TNM stage, and lymph node metastasis in GC patients and could be used as a useful diagnostic biomarker with a sensitivity of 89.2% and specificity of 91.1%.

**Conclusion:** In conclusion, our findings suggest that GC cells could generate miR-21-rich exosomes that are delivered to surrounding normal cells to promote prometastatic behaviors and prompt further investigation into the therapeutic value of exosome inhibition for cancer treatment and diagnostic marker for cancer diagnosis.

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

**References**

country sample (27.9% IBS-C, 34.3% IBS-D, 33.3% IBS-M, 4.7% IBS-U) was significantly different (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>
<thead>
<tr>
<th>Rome III IBS</th>
<th>Age 18-34</th>
<th>Age 35-49</th>
<th>Age 50-64</th>
<th>Age 65+</th>
<th>All age groups</th>
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<tr>
<td>US Females (n = 962)</td>
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<td>16.6</td>
<td>13.7</td>
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<td>UK Males (n = 1018)</td>
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<tr>
<td>Canada Females (n = 980)</td>
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<td>15.4</td>
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<td>Canada Males (n = 1008)</td>
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<td>10.3</td>
<td>8.2</td>
<td>5.9</td>
<td>7.6</td>
</tr>
<tr>
<td>ROME IV IBS</td>
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<td>Age 35-49</td>
<td>Age 50-64</td>
<td>Age 65+</td>
<td>All age groups</td>
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<td>Canada Males (n = 1008)</td>
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<td>5.4</td>
<td>5.0</td>
<td>2.1</td>
<td>3.7</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 common in older individuals. IBS prevalence is significantly lower when Rome IV criteria are used than with Rome III, and the new criteria also change IBS subtype distribution, markedly reducing the IBS-M proportion. [Support: All authors have declared no conflicts of interest.]


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•pH) monitoring, patients with proton pump inhibitor (PPI)-refractory heartburn can be distinguished into PPI-refractory GERD and functional heartburn (FH), the latter to be considered a functional GI disorder separate from GERD. Symptoms of IBS have not yet been assessed in patients with reflux symptoms as distinguished into GERD and FH. Recently, it has been reported that patients with GERD as well as patients with IBS have increased levels of anxiety, in turn associated with increased perception of symptoms and reduced quality of life. Again, the prevalence of anxiety in patients with reflux symptoms as clearly distinguished into GERD and FH has not yet been assessed.

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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•pH) monitoring, patients with proton pump inhibitor (PPI)-refractory heartburn can be distinguished into PPI-refractory GERD and functional heartburn (FH), the latter to be considered a functional GI disorder separate from GERD. Symptoms of IBS have not yet been assessed in patients with reflux symptoms as distinguished into GERD and FH. Recently, it has been reported that patients with GERD as well as patients with IBS have increased levels of anxiety, in turn associated with increased perception of symptoms and reduced quality of life. Again, the prevalence of anxiety in patients with reflux symptoms as clearly distinguished into 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 with typical reflux symptoms subdivided into GORD and FH by means of upper GI endoscopy and 24h-pH monitoring. We also aimed to assess the prevalence of various clinical and endoscopic characteristics in IBS, FH and patients in order to develop a predictive model for distinguishing FH from GERD in patients presenting with typical reflux symptoms, potentially useful in clinical practice. Patients underwent a structured interview based on questionnaires for GERD (GERDQ), IBS (RIIIAQ), anxiety and depression (HADS). Upper GI endoscopy and 24h-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 analyses 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 GORD 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%) and in 187/243 (77%) FH patients (p < 0.001). At multivariate analysis IBS, anxiety, and smoking resulted independent risk factors for FH whereas hialtal hernia resulted protective. We developed a predictive model based on clinical and endoscopic characteristics (IBS, Smoking, Anxiety, Age ≥ 45, Heartburn, MII-pH test, GERDQ). The area under ROC curve (AUC) for FH diagnosis of this model was 0.78 in a first training cohort of 51 patients. 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/#calculation/2012).

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

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

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

<table>
<thead>
<tr>
<th>Symptom persisting</th>
<th>Probability</th>
<th>95% CI Probability</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>22%</td>
<td>16–26%</td>
<td>16–26%</td>
</tr>
<tr>
<td>Sense of coherence</td>
<td>21%</td>
<td>18–24%</td>
<td>17–22%</td>
</tr>
<tr>
<td>Coping resources</td>
<td>19%</td>
<td>18–21%</td>
<td>20–17%</td>
</tr>
<tr>
<td>GI-specific anxiety</td>
<td>16%</td>
<td>14–18%</td>
<td>23–11%</td>
</tr>
<tr>
<td>Quality of life</td>
<td>16%</td>
<td>14–18%</td>
<td>23–11%</td>
</tr>
<tr>
<td>GI symptom severity</td>
<td>12%</td>
<td>10–14%</td>
<td>44–50%</td>
</tr>
</tbody>
</table>

Conclusion: For the first time, we show that IBS-related symptoms develop differently 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.

Disclosure of Interest: J. Tack: Scientific advice to, or speaker bureau for: Abbott, AlfaWasserman, Almirall, AstraZeneca, Danone, Janssen, Menarini, Novartis, Nycomed, Ocrea, Ono pharma, Shire, SK Life Sciences, Theravance, Tranzyme, Xenoport, and Zeria Pharmaceuticals. H. Törnblom: Consultant/Advisory Board member for Almirall, Danone and Shire. M. Simrén: Unrestricted research grants from Danone, and Ferring Pharmaceuticals. M. Simrén: Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Albiro, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall. All other authors have declared no conflicts of interest.

OP081 IRRITABLE BOWEL SYNDROME: WHICH SYMPTOMS ARE PERSISTENT AND WHICH ARE NOT?

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2Internal Medicine & Clinical Nutrition, University of Gothenburg, Göteborg/Sweden

Introduction: Irritable bowel syndrome (IBS) is characterised by many comorbid symptoms as well as core symptoms, all of which are relevant for the clinical management of this group of patients. However, the evolution of these symptoms over time is not well documented.

Aims & Methods: The aim of this study was to determine the probability of IBS-related symptoms to persist or subside over time. The study consisted of three parts. First, we addressed the question which factors can determine the probability of a symptom persist or subside over time. A simulation showed there were five: length of follow-up period, autocorrelation, the interaction between the autocorrelation and symptom severity, the cut-off for symptom severity, and skewness. Second, we used the five factors in a Monte Carlo simulation, generating a reference-table of probabilities for symptoms to persist or subside. Third, our theoretical reference-table was matched with real data from a cohort of 276 IBS patients (70% female; age range 19 to 76 years, median age 39 years). These subjects were thoroughly characterised at baseline, and completed questionnaires annually over a five-year period, covering the following IBS-related symptoms / aspects: gastrointestinal (GI) symptom severity (GSRS), GI-specific anxiety (YSI), quality of life (IBS-QOL), coping resources (CRI), sense of coherence (KASAM), and anxiety/depression (HADS). The cohort was used to retrieve the five factor properties mentioned above (e.g. autocorrelations).

Results: A summary of the main results is shown in table 1. In IBS patients, depression was the most persistent symptom over time, i.e. a 22% chance for depression to persist, versus 23% to subside over a five-year period. Poor coping resources and sense of coherence yielded similar percentages. Values were different for symptoms to be considered compatible with a functional GI symptom (GI severity > 8 and 47%), with no major differences between the different GI symptoms (i.e. diarrhoea, constipation, abdominal pain, satiety, indigestion, and reflux). For IBS-QOL, there were differences between the domains: sexual relations (20% chance to persist, 18% chance to subside) and sleep (20 and 25%), in contrast to the domains mental health (7 and 56%), physical functioning (5 and 64%), and social functioning (6 and 53%). The QOL domains physical role, social role, and food were intermediate.
Conclusion: Symptoms compatible with functional bowel disorders in general, and not only IBS, are common in patients with UC in deep remission. However, the overall disease burden seems to be greater in patients with symptoms compatible with IBS than with the other FBDS. These observations are of great importance when managing patients with IBD to avoid escalating anti-inflammatory treatment, and instead focus on other treatment options to help these patients to manage their symptoms.

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

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

O. Palsson: Salary support from research grants from Salix Pharmaceuticals, Takeda Pharmaceuticals and Ironwood pharmaceuticals, as well as honoraria for participation in educational programs supported by these companies. W.E. Whitehead: Unrestricted research grants from Takeda Pharmaceuticals; Unrestricted educational grants from Takeda and Ferring Pharmaceuticals; Consultant/Advisory Board member for Ono and Ferring Pharmaceuticals and from Allergan 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, and Tillotts. MSD Speaker for Takeda, Abbvie, Ferring Pharmaceuticals, Tillotts, MSD and Shire.

OP083 ENHANCED DIAGNOSTIC PERFORMANCE OF SYMPTOM-BASED CRITERIA FOR IRRITABLE BOWEL SYNDROME BY INCORPORATING NOCTURNAL SYMPTOMS, SOMATISATION, AND AFFECT

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2Clinical Enteric Neurosciences Translational and Epidemiological Research (C.E.N.T.E.R.), Mayo Clinic, Rochester; United States of America
3School Of Medicine, University of Leeds; Leeds; United Kingdom
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Introduction: Symptom-based criteria to diagnose irritable bowel syndrome (IBS) positively perform only modestly. Our aim was to assess whether including other items from the clinical history and diagnostic workup improves their performance.

Aims & Methods: We collected complete symptom, co-morbidity, and history data from 318 consecutive, unselected adult patients with lower gastrointestinal (GI) symptoms in secondary care. The reference standard used to define presence of true IBS was patient-reported lower abdominal pain or discomfort associated with a change in bowel habit, in the absence of organic GI disease. Sensitivity, specificity, and positive and negative likelihood ratios (LRs), with 95% confidence intervals, were calculated for Rome III criteria, as well as for modifications, incorporating nocturnal symptom results, of simple blood tests (haemoglobin (Hb) and C-reactive protein (CRP), measures of somatisation, and/or affect (hospital anxiety or depression scale (HADS) score).

Results: Sensitivity and specificity of Rome III criteria for identifying IBS was 69.6%, and 82.0% respectively, with positive and negative LRs of 3.87 and 0.37. Clinically useful enhancements in positive LRs when combining Rome III criteria with items from the clinical history, and blood tests, are shown in the table. Conclusion: Incorporating nocturnal symptoms, somatisation, and affect from the clinical history, and haemoglobin and CRP measurements, enhances performance of symptom-based criteria for IBS. Our findings suggest a different approach to the development of future diagnostic criteria should be used.

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

Abstract No: OP083

<table>
<thead>
<tr>
<th>Rome III Criteria and normal Hb and CRP</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
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<th>Negative LR (95% CI)</th>
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<tr>
<td>Rome III criteria and normal Hb and CRP</td>
<td>49.00% (34.04–64.43)</td>
<td>89.1% (82.92–92.99)</td>
<td>4.33 (2.76–7.67)</td>
<td>0.59 (0.46–0.72)</td>
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<tr>
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Contact E-mail Address: Catherine.Tucker@allergan.com

Introduction: Irritable bowel syndrome (IBS) affects an estimated 10–15% of adults, with the diarrhoea subtype (IBS-D) estimated to account for 30–40% of cases. IBS is a chronic, unpredictable disorder associated with increased healthcare-seeking behaviour and significant resource utilisation and costs. However, information on the economic burden of IBS-D in Europe is limited.

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

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

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

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

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

J.L. Abel: Jessica L. Abel is an employee of Allergan plc and owns stock/stock options in Allergan plc.


N.M. Flores: Natalia M. Flores is an employee of Kantar Health, which was contracted by Allergan plc for work relating to this study.

R. Liebert: Ryan Liebert is an employee of Kantar Health, which was contracted by Allergan plc for work relating to this study.
What is new in gastric endoscopic submucosal dissection (ESD) – Room L7

OP085 Long-term outcomes of endoscopic submucosal dissection (ESD) and gastrectomy based on indications for ESD

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1Korea University College of Medicine Guro Hospital, Seoul, Korea; Republic of 2Korea University College of Medicine Ansan Hospital, Seoul, Korea; Republic of 3Korea University College of Medicine Ansan Hospital, Seoul, Korea; Republic of
Contact E-mail Address: joey1012k@hanmail.net
Introduction: Endoscopic submucosal dissection (ESD) has been established as a standard treatment modality of early gastric cancer (EGC), however, long term outcomes between ESD and gastrectomy were rarely reported, especially in terms of ESD criteria.
Aims & Methods: This study aimed to compare long term outcomes between ESD and gastrectomy, and according to the histopathologic ESD criteria; absolute criteria (AC), expanded criteria (EC) and beyond expanded criteria (BEC). Between 2006 and 2012, 925 EGC patients were enrolled; ESD was performed in 468 patients, and gastrectomy in 457 patients.
Results: 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 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 group), and 273 of 457 (59.7%) gastrectomy patients were out of ESD criteria (BEC group).
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.

OP086 Predicting clinical outcomes of gastric endoscopic submucosal dissection using a Bayesian approach

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Introduction: In patients with gastric superficial neoplasms, the probabilities of success and of adverse events influence the decision process regarding treatment allocation. These probabilities may be predicted using a priori patients’ and lesions’ factors. However, the knowledge of risk factors alone is not readily and completely usable by patients and clinicians in the decision process since it is difficult to predict the additive effect of risk factors in the outcome, in a given patient. Bayesian networks are increasingly used for clinical decision support since Bayesian statistical methods allow taking into account prior knowledge when analyzing data and can aid in capturing and reasoning with uncertainty in medicine1. Aims & Methods: The aim of this study was to develop a Bayesian model and a computerized tool that can be used in clinical practice to predict outcomes after ESD and aid in the decision-making process. Methods: Data from 245 ESDs performed in our institution was collected, including pre-resection patient factors (age, sex, ASA, antithrombotics) and lesions’ factors (morphology, pre-resection biopsies). The two main endpoints were curative resection and post-procedural bleeding. We defined curative resection as a resection meeting the standard or expanded criteria of the Japanese Gastric Cancer Treatment guidelines. For the analysis and model construction, morphology was recoded into polypoid (0-Ia, 0-Ip, 0-Ip), depressed (0-IIa+c, 0-IIa+c, 0-IIc and 0-III) and non-polypoid non-depressed (0-IIa, 0-IIb, 0-IIa+b). Univariate analysis was conducted with chi-squared test to identify associations between pre-treatment factors and the two endpoints, for a significance level of 5%. Logistic regression and Bayesian networks were then built for each outcome. Stratified 10-fold cross-validation was performed to assess the predictive accuracy and discriminative power (ROC curves) of the models. Clinical decision support was then enabled by the definition of risk matrices, direct use of Bayesian inference software and through the use of an online platform.
Results: In our sample, 85% were curative resections and PPB occurred in 8%. In the univariate analysis, age > 63 (p = 0.039), male sex (p = 0.027), ASA status (p = 0.008), carcinoma histology (p = 0.001), polypoid or depressed morphology (p = 0.015) and lesion size greater than 20 mm (p = 0.006) were associated with non-curative resection, while age > 70 (p = 0.041), ASA status (p = 0.017), antithrombotic medication (p = 0.01) and lesion size greater than > 20 mm (p = 0.026) were associated with PPB. Logistic regression and Bayesian models presented AUCs above 80% (in-sample) and 75% (cross-validation) on both outcomes. Lesions with cancer at biopsies, >20mm, proximal and polypoid are more prone to non-curative resection (table 1). Risk matrices for PPB were also defined yielding a posteriori probabilities of PPB < 5% in lesions < 20 mm in the absence of antithrombotic medications while the risk of PPB increased in greater lesions and in the presence of antithrombotic medications. The Bayesian network can be interactively used in clinical practice to estimate individual probability of outcomes after ESD. Table 1: Risk (a posteriori probabilities) matrix for curative resection based on morphology, localization, size and pre-resection histology, using a Bayesian model (cross-validation AUC = 78%, 95%CI = [75%,81%]).

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

Reference
A MULTICENTER RETROSPECTIVE STUDY
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 classified as: (a) synchronous cancers located within the same segment (limitis plastica) or limited to the greater curvature of the stomach, (b) metachronous cancers located at a site different from the primary lesion, or (c) a single lesion with features of both synchronous and metachronous cancers. Results: Among 15,838 patients undergoing ESD for EGC at 19 institutions in Japan, 194 lesions (15.6%) in 164 patients met the criteria. Between 2005–2014, the median follow-up time was 40 months. In the univariate analysis, the only predictor of metachronous development in logistic regression (odds ratio 27.2, 95% CI 2.7–272, p < 0.001) was vascular invasion (with videos). Patient characteristics, tumor size, en bloc resection, and post-operative complications were evaluated. Results: Of the 13 lesions in the stomach, 2 were located in the greater curvature. The endoscopic Grasp-and-Loop closure method is feasible, effective and safe for closing the gastric defect after EFR in patients. 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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OP0089 ENDOSCOPIC FULL-THICKNESS RESECTION WITH DEFECT CLOSURE IN THE STOMACH BY USING A NOVEL GRASP-AND-LOOP (GAL) CLOSURE METHOD (WITH VIDEOS)
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Aims & Methods: The aim of this study was to evaluate the feasibility and efficacy of a novel and simplified endoscopic Grasp-and-Loop (GAL) closure method using an endoloop assistant with a grasping forceps for defect closure. From January 2015 to March 2016, 13 patients with SMTs originating from the muscularis propria layer who underwent EFR were enrolled in this study. After successful tumor resection, an endoloop was anchored onto the circumferential margin of the gastric defect with a grasping forceps assistant and tightened gently (with videos). Patient characteristics, tumor size, en bloc resection, and post-operative complications were evaluated. Results: Of the 13 lesions in the stomach, 2 were located in the greater curvature of the stomach. The endoscopic GAL closure method was successfully performed after EFR in all 13 patients without laparoscopic assistance. The mean procedure time was 43.5 min (range 20–80 min), while the GAL closure procedure took a mean of 9.4 min (range 3–18 min). The endoscopic GAL closure method was feasible, effective and safe for closing the gastric defect after EFR in patients. 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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OP0087 LONG-TERM OUTCOMES OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION: FOCUS ON METASTACHRONOUS AND NON-CURATIVE RESECTION MANAGEMENT
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1Gastroenterology Department, Portuguese Oncology Institute of Porto, Porto/Portugal
2Pathology Department, Portuguese Oncology Institute of Porto, Porto/Portugal

Aims & Methods: The current curative criteria for ESD and additionally underwent radical surgery. The inclusion criteria were: patients with non-curative resection and with tumors located in the mid-upper body, 11 were located in the fundus. The endoscopic GAL closure method was feasible, effective and safe for closing the gastric defect after EFR in patients. Disclosure of Interest: All authors have declared no conflicts of interest.

References
K. Kawaura1, T. Kosaka2

Gastric cancer, because it was possible to incise all-layer of the stomach while
without collapse of the stomach by covering the serosa using silicon sheet and
Results:
Seven patients (78%) were negative for sentinel node metastasis, and
defect of gastric wall is closed laparoscopically using hand-sewn sutures. Finally, the
tumor, silicon sheet and polyglycolic acid (PGA) sheet are removed through oral cavity. Finally, the
manner as ESD. Continuously, silicon sheet and polyglycolic acid (PGA) sheet
submucosal layer around the lesion. Using an infrared fluorescence laparoscope,
Laparoscopic sentinel node biopsy. On the day before surgery, indocyanine green
obtained from each patient. All procedures were conducted in accordance with
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
inhibitory effects of non-caloric sweeteners on gastric emptying and plasma motilin levels in healthy volunteers
A.C. Meyer-Gerschap, E. Deloose, J. Biesiekierski, I. Depoortere, L. Van Oudenhove, J. Tack
Targard, KU Leuven, Leuven/Belgium
Contact E-mail Address: ac.meyergerschap@gmail.com
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 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

Reference

Monday, October 17, 2016
14:00 - 15:30
Gastric Function in Health and Disease – Room BU
OP191 Caloric and Non-Caloric Artificial Sweeteners Have Dissociable Effects on Antral Motility and Plasma Motilin Levels in Healthy Volunteers
A.C. Meyer-Gerschap, E. Deloose, J. Biesiekierski, I. Depoortere, L. Van Oudenhove, J. Tack
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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 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 analyzing using mixed model analysis. Post-hoc analyses were corrected using Bonferroni.

Results: Antral motility was significantly reduced in response to the caloric sweeteners glucose: p = 0.004 and fructose: p = 0.006 and ace-K: p = 0.006 and ace-K administration did not differ significantly from placebo. Glucose induced a significant reduction in antral motility compared to ace-K (p = 0.010). In contrast, duodenal motility was significantly reduced by both the caloric as well as non-caloric sweeteners compared to placebo (glucose: p = 0.043, fructose: p = 0.006 and ace-K: p = 0.032, respectively). The change over time of plasma glucose concentrations was significantly increased after glucose and fructose administration, but not after ace-K administration (p < 0.026 and p = 0.002, respectively); ace-K had no effect on plasma motilin concentrations. The change over time of plasma motilin concentrations was significantly decreased after fructose (p = 0.001) administration; ace-K administration induced no difference compared to placebo. Plasma motilin levels were significantly decreased after the caloric sweeteners compared to the non-caloric sweetener ace-K (glucose: p = 0.005 and fructose: p = 0.008, respectively). The time course of satiation scores differed significantly between glucose and ace-K (p = 0.041) with a slower decrease in satiation scores after glucose compared to ace-K administration.

Conclusion: Caloric and non-caloric sweeteners have dissociable effects on antral but not duodenal motility; the reduction in antral motility after glucose and fructose administration parallels changes in motilin secretion. These findings provide an important contribution to the current discussion about possible physiological effects of non-caloric sweeteners on appetite metabolism.

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

OP192 Xylitol and Erythritol Induce Satiation Peptide Secretions and Retardation in Gastric Emptying in Healthy Humans
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Introduction: With the increasing prevalence of obesity and its possible association with increasing sucrose consumption, non-nutritive sweeteners are gaining popularity. Artificial sweeteners might have adverse effects and alternative solutions are sought. Polysaccharides such as xylitol and erythritol have not been studied.
Aims & Methods: We measured gastric emptying and meal-induced satiety scores in healthy volunteers. The study was a randomized, double-blind, cross-over trial. 12 healthy volunteers were included. Participants underwent gastroduodenal manometry recording for the occurrence of one phase III contraction followed by the intragastric administration of 250 mL tap water (control), or equisweet caloric (50 g/kg, 25 g/kg) and non-caloric sweeteners (220 mg acesulfame-K (ace-K)) dissolved in 250 mL tap water. Measurement was continued until at least one subsequent phase III occurred. Recording of motility showed a profound duodenal pressure increase, blood samples were collected for determination of plasma glucose and motilin concentrations. Visual analogue scales were used to rate satiation scores and satiety feelings. Data were analyzed using mixed model analysis.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aim & 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. Ligatured (Victozza®), 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 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 as the number of contractions/average amplitude contractions/average duration contractions)×5/min. Average MI was calculated by averaging 6 consecutive antral or duodenal channels. Occurrence of antral or duodenal phase III contractions was evaluated. Protocol 2: After a stabilization period, LG ingestion of a liquid test meal (200 ml, 300 kcal: 89% carbohydrate, 11% protein) labeled with 100 µCi 14C-sodium octanoate. GA was measured as the intragastric pressure (IOP) drop in the first 30 min after the drink and was calculated as the average pressure over 5 channels in the fundus compared to baseline 5 minutes before the drink. GE rates were determined from breath test samples collected before the meal and at 15-min intervals for 4 hours. Occurrence of antral or duodenal contractions, both first and second phase III contractions was significantly lower after LG (p = 0.002 and p = 0.005 respectively). Similarly, the duodenal MI was also 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 it significantly delayed the GE t1/2 (p = 0.005). As far as the antioxidant system is concerned, mean serum levels of LPS and IL-6 did not show any statistical difference between PDS vs HV. IL-6 and insulin were significantly higher in PDS patients (1.62 ± 0.21, 3.73 ± 0.24, 15.4 ± 10.24, respectively) compared to HV (0.26 ± 0.15, 0.13 ± 0.11 and 7.45 ± 0.08, respectively; p < 0.05 for all). Similarly, postprandial values of TNFα, IL-1 and insulin were significantly higher in PDS (2.0 ± 0.70, 0.64 ± 0.59, 30.39 ± 12.60, respectively) than in HV (0.23 ± 0.17, 0.19 ± 0.11, 21.04 ± 7.02 respectively (p < 0.05 for all). In FD but not in HV, mean postprandial levels of TNFα were significantly higher than fasting values (p < 0.05). As far as the antioxidant system is concerned, postprandial values of UA were significantly higher in PDS (52.94 ± 19.16) than in HV (34.46 ± 5.61) (p < 0.05). Serum levels of LPS and IL-6 did not show any statistical differences between PDS vs HV. As expected, not only IL-6 but also in HV was not there a significant increase of postprandial symptoms. Finally, the severity of symptoms was significantly correlated with the postprandial serum levels of both inflammatory and antioxidant markers.

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

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

References

OP095 A DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSS-OVER STUDY USING BACLOFEN IN THE TREATMENT OF RUMINATION SYNDROME
A. Pauwels1, C. Broers1, B. Van Houtte1, N. Rommel2, T. Vanuytsel1, J. Tack1
1Clinical and Experimental Medicine, Translational Research Center For Gastrointestinal Disorders (targi), KU Leuven, Leuven/Belgium
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Introduction: Rumination syndrome and supra-gastric belching are two conditions with limited treatment options. Baclofen, a γ-aminobutyric acid agonist, decreases lower oesophageal sphincter (LOS) pressure. We previously demonstrated, in an open-label study, that baclofen reduces pressure flow events in patients with clinically suspected rumination and/or supra-gastric belching.

Aim & Methods: To study the effect of baclofen in a placebo-controlled, double-blind, cross-over study in patients with clinically suspected rumination and/or supra-gastric belching. Consecutive patients with clinically suspected rumination and/or supra-gastric belching were randomized in a double-blind fashion to receive baclofen (10 mg, 3 t.i.d) or placebo for 2 weeks with cross-over to the alternative intervention after 1 week wash-out. At the end of each treatment period, patients underwent a solid state high resolution impedance manometry (HRM) measurement. After positioning of the probe, 10 wet swallows were performed to assess oesophageal function. After 30 min recording, patients received a 1000 kcal solid meal and recordings continued for 1 hour. Patients filled in daily diaries, daily diary reported end of treatment. A 5-point overall treatment evaluation (OTE) on a 3-to +3 scale) and registered symptoms during the HRM using an event marker. The number of symptoms registered and number and type of flow events during the HRM were compared between placebo and baclofen.

Results: A total of 15 patients were randomized to baclofen or placebo. 11 patients completed the trial and were included in the intention-to-treat analysis. 

Conclusion: Our trial confirmed the positive effects of baclofen treatment in patients with rumination and/or supra-gastric belching, which is a condition with limited treatment options. Further studies are needed to confirm the pathogenetic role of the inflammatory antioxidant response in a condition characterized by low-grade inflammatory alterations.

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

References
1. Farre, Gastroenterology 2013.
Disclosure of Interest: An effective GES reduced significantly the frequency of refractory vomiting, was not associated with a better QoL.

Results: We enrolled 20 patients (mean age 42y (range 18–61), 13f). Lower oesophageal sphincter pressure was significantly higher in the baclofen treatment arm compared to the placebo arm (17.8±1.4 vs. 12.8±1.4mmHg, p = 0.001). The number of transient LOS relaxations was lower (6 ±1 vs. 8 ±2, p = 0.015), and the number of transient relaxation episodes was significantly faster during the “ON” period. The greater symptomatic effect with an effective GES was not activated. Then each subject was randomized in a masked fashion to one of 2 treatment arms: 4 months “ON” then 4 months “OFF” or 4 months “OFF” then 4 months “ON”. Both in diabetic and non diabetic patients and was more important in case of patients with rumination syndrome, probably through its effect on LOS pressure.

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Introduction: Despite numerous efforts to develop novel therapies, pancreatic ductal adenocarcinoma (PDAC) has remained one of the most devastating and lethal malignancies worldwide. Despite chemotherapy, 5-year survival rate of PDAC patients is still less than 5%.

Results: In human patient tumor samples, a total of 85% and 66% of patients harbored activating mutations in BRAF and KRAS, respectively. These data were confirmed in a large human patient cohort. In vitro, we observed that the expression of ITGA5 in PSCs using shRNA-ITGA5. We investigated the paracrine effect of TGF-

Contact E-mail Address: j.prakash@utwente.nl

Introduction: Pancreatic cancer is the deadliest tumor type with less than 5% survival rate, characterized by the presence of abundant stroma. Pancreatic stellate cells (PSCs) are the main precursor of myofibroblasts (cancer-associated fibroblasts (CAFs)) in tumor stroma and therefore become key target in pancreatic cancer therapy. CAFs’ secreted growth factors, extracellular matrix (ECM) and thereby aggravate tumor growth and metastasis. This is of paramount importance to find out new targets in stromal myofibroblasts which have been used for developing novel prognostic, diagnostic and therapeutic strategies.

Aims & Methods: In this study, we investigated integrin α5 (ITGA5), a receptor for ECM protein fibronectin, as a potential new target in pancreatic tumor stroma.

Results: We show that Bcl-3 is highly expressed in human PDACs and in a KC mouse model of pancreatic cancer. In vivo, in mice carrying a KC pancreas tumor model, Bcl-3 promotes cell growth and cell survival in vivo and in vitro. Further, Bcl-3 leads to acceleration in PanIN progression, tumor development and metastasis in a KC mouse model of pancreatic cancer.

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 ITGA5 as a novel prognostic and therapeutic target in pancreatic tumor stroma. These data make a strong base to utilize this target for developing novel diagnostic and therapeutic strategies against pancreatic tumor.

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

References

OP999 MICRORNA-622 INHIBITS EPITHELIAL-MESENCHYMAL TRANSITION BY TARGETING LONG NON-CODING RNA HULC IN HUMAN PANCREATIC CANCER
K. Takahashi, Y. Ota, Y. Suzuki, H. Iwamoto, K. Yamakita, Y. Kitano, Y. Makino
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Introduction: Transforming growth factor (TGF)-b-induced epithelial-mesenchymal transition (EMT) is a trigger of invasion and metastasis in pancreatic cancer. Although long non-coding RNAs (lncRNAs), which are defined as non-coding RNAs (ncRNAs) more than 200 nucleotides in length, have been implicated in disease pathogenesis, their contributions to pancreatic cancer are not well understood. Recently, the inter-relationship between two classes of ncRNA, microRNAs (miRNAs) and lncRNAs, has been reported to contribute to the epigenetic regulation of gene expression in several cancers.

Aims & Methods: Our aims were to investigate the involvement and functional roles of TGF-b-induced lncRNA during EMT and reveal contributions of the inter-relationship between the TGF-b-induced lncRNA and miRNA to the regulatory mechanisms of EMT in human pancreatic cancer. We used human pancreatic cancer cells (Panc-1, BxPC-3, MiaPaCa-2, QGP-1 and KP-3) and non-malignant pancreatic ductal epithelial (hTERT-HPNE) cells. Expression profiling of 90 lncRNAs and 2565 miRNAs were performed using qPCR and miRNA microarray. miRNA targets were predicted by miRanda. Cells were treated with 10 ng/ml of TGF-b for 72 hours to induce EMT. siRNA or miRNA mimic were used to modulate RNA expression. Cell viability was assessed by MTS assay and trypan blue. Cell invasion and migration were examined by transwell and wound healing assay. Expression of RNA was assessed by qPCR and of protein by Western blot.

Results: LncRNA expression profiling identified 22 lncRNAs that were induced by TGF-b in Panc-1 cells by >1.4-fold. Of these, HULC was amongst the top most significantly up-regulated. HULC expression was induced by TGF-b by 1.5 to 2.7-fold in a panel of pancreatic cancer cells and up-regulated by 2.4 to 8.9-fold in pancreatic cancer cells compared to hTERT-HPNE cells. In Panc-1 cells, knockdown of HULC by siRNA significantly increased expression of E-cadherin and decreased expression of N-cadherin, Snail and Vimentin (p < 0.05). Moreover, siRNA to HULC decreased cell viability, invasion and migration. Furthermore, to identify miRNAs that can target HULC and suppress EMT, miRNA microarray and bioinformatics analysis were performed. Microarray identified 187 miRNAs that were decreased by < 0.87-fold in Panc-1 cells treated with TGF-b compared to control. Of these, miR-622 was predicted to target HULC by miRanda. miR-622 expression was reduced by TGF-b by 0.5 to 0.9-fold in a panel of pancreatic cancer cells. Overexpression of miR-622 using miRNA mimetic significantly decreased expression of HULC, increased expression of E-cadherin and decreased expression of Snail, N-cadherin and Vimentin (p < 0.05). In addition, miR-622 overexpression significantly reduced cell invasion and migration.

Conclusion: These findings provide mechanistic insights into EMT in pancreatic cancer by (a) identifying HULC as a highly induced lncRNA 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.

OP100 ESSENTIAL ROLE OF THE NON-RECEPTOR TYROSINE-PHOSPHATASE PTPN11/SHP-2 IN ORGAN DEVELOPMENT AND HOMEOSTASIS OF THE MURINE EXOCRINE PANCREAS
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Introduction: The Src-homology-2 (SH2) domain containing protein tyrosine phosphatase SHP-2 is expressed ubiquitously and is involved in an array of intracellular signal transduction processes (Ras-Raf-MAPK, JAK-STAT, P3k-Akt-mTOR, NF toilets). Thus, for instance, SHP-2 plays a role in cellular growth factor signaling (IGF, EGF, FGF, PDGF), cytokines (IL5, GM-CSF, ...), and extracellular matrix (via integrins, focal adhesion complex). Via these pathways SHP2 mediates transcriptional regulation of mitogenic activation, cell proliferation, survival, differentiation, migration and metabolism. The role of SHP-2 in organ development and homeostasis of the pancreas has so far not been explored.

Aims & Methods: Mouse models with pancreas specific deletion of SHP-2 (Ptf1aCrePtpn11fl/fl) [1] with or without BAC (LSL-KrasG12D) and/or lineage tracing allele (ACTB-TdTomato;EGFP) were used for analysis.

Results: Early embryologic Deletion of SHP-2 in the pancreas via Ptf1a-Cre (OP100) results in complete pancreatic agenesis. In adult mice, organ weight is reduced by about 50%, compared to unrecombined litter-mate-controls. In the organ growth phase, (centro-)acinar cells display enhanced expression of the exocrine compartment in the growing pancreas is impaired. In adult mice, organ weight is the first of SHP-2 (Ptf1aCrePtpn11fl/fl) with or without Kras (LSL-KrasG12D) and/or lineage tracing allele (ACTB-TdTomato;EGFP) were used for analysis. Results: Early embryologic Deletion of SHP-2 in the pancreas via Ptf1a-Cre(CrePtf1a) leads to complete pancreatic agenesis. In adult mice, organ weight is reduced by about 50%, compared to unrecombined litter-mate-controls. In the organ growth phase, (centro-)acinar cells display enhanced expression of the exocrine compartment in the growing pancreas is impaired. In adult mice, organ weight is reduced by about 50%, compared to unrecombined litter-mate-controls. In the organ growth phase, (centro-)acinar cells display enhanced expression of the exocrine compartment in the growing pancreas is impaired. In adult mice, organ weight is reduced by about 50%, compared to unrecombined litter-mate-controls.

Disclosure of Interest: All authors have declared no conflicts of interest.
**OP10 RELA CONTROLS KRAS-DRIVEN PANCREATIC CARCINOGENESIS BY MEDIATING 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 possesses these opposite activities during tumour development remains elusive.

**Aims & Methods:** To study the invasion of tumour cells along neurites and how NF-κB can modulate senescence and enhance cancer progression in mice.

**Results:** We have previously shown that NF-κB is involved in the regulation of tumour growth and senescence via the SERK2/NF-κB-mediated expression of senescence-associated cytokines.

**Conclusion:** Our data clearly demonstrate a dual role of NF-κB/RelA activation in pancreatic carcinogenesis. In early stages of tumorigenesis, the tumour-suppressive function of NF-κB is beneficial because it controls oncogene-induced senescence (OIS) by regulating the CXCL1/KC/CXCR2 axis. However, as soon as OIS is bypassed due to the development of tumours, NF-κB supports tumour progression by enhancing proliferation of the transformed pancreatic cancer cells.

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

**References:**

4. All authors have declared no conflicts of interest.

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

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

**References:**

OP104 EFFICACY OF USTEKINUMAB FOR INDUCTION AND MAINTENANCE OF ENDOSCOPIC HEALING IN PATIENTS WITH CROHN'S DISEASE
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Introduction: Usteekinumab (UST) has been shown to induce & maintain clinical response & remission in 2 induction (UNITI-I &2) & 1 maintenance trial (IM-UNITI) in moderate-severe Crohn's disease (CD). A substudy evaluated the efficacy of UST in the induction & maintenance of endoscopic healing.

Aims & Methods: Patients in the substudy had up to 3 colonoscopy evaluations (i.e. at UNITI-I or 2 baseline [BL] and wk8, and IM-UNITI wk44) in 5 ileocolonic segments (i.e. ileum, right colon, transverse colon, left colon, rectum) within the 52-wk study period. A single central reader blindly scored all video endoscopies for ulcerations and simplified endoscopic activity score for CD (SES-CD). At induction wk0, patients received a single IV dose (UST 130 mg, UST 90 mg, or 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 12 wks (q12w), or UST 90 mg every 8 wks (q8w). For the 3 non-randomized maintenance groups: (1) UST induction non-responders received SC UST 90 mg, then continued SC UST 90 mg q8w if CDAI decreased ≥100 after 10 wks; (2) PBO induction non-responders received UST IV 130 mg, then continued SC UST 90 mg q8w if CDAI decreased ≥100 after 8 wks; and (3) PBO induction responders received PBO for an additional 10 weeks. Patients who demonstrated clinical response (CDAI-100) underwent corticosteroid tapering after Week 10. Anti-TNF naïve patients were included. Immunosuppressants were to be discontinued prior to treatment initiation. Final data for the primary endpoint of the study was met: Filgotinib induced clinical remission in 47% of patients, which has demonstrated 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, Placebo: n = 116, Filgotinib: n = 58) were enrolled. Patients with SES-CD ≥5 (i.e. ulceration in any segment) at induction BL were eligible for analysis. The primary endpoint was change in SES-CD from BL at induction wk8 in the integrated UST group (data across induction studies & dose groups) vs PBO. Efficacy at IM-UNITI wk44 was evaluated in the primary randomized maintenance population and the post-hoc pooled maintenance population (i.e. randomized & nonrandomized IM-UNITI populations combined). Additional induction & maintenance endpoints included clinically meaningful endoscopic improvement, endoscopic evidence of active disease, endoscopic remission & mucosal healing; in both combined and individual treatment groups.

Results: The substudy primary endpoint was met, as UST induced significantly greater reduction in SES-CD from BL at wk8 vs PBO. Results were similar by induction study & UST dose. Other induction endoscopic endpoints also consistently favored UST vs PBO (Table 1a). At IM-UNITI wk44, trends for greater efficacy with UST vs PBO, maintenance, especially UST 90 mg q8w, was observed in the primary randomized maintenance population, but small sample sizes (UST n = 46; PBO n = 24) precluded definitive conclusions. In the larger post-hoc pooled maintenance population (Table 1b), consistent trends in support of UST maintenance, especially UST 90 mg q8w, were observed across endoscopic endpoints at wk44.

Conclusion: The endoscopic substudy primary endpoint was met; a single IV dose of UST induced significantly greater reduction in endoscopic disease activity vs PBO, despite a relatively early evaluation at wk8. Results in the small primary randomized maintenance population were supported by the larger post-hoc pooled maintenance population; greater proportions of subjects receiving UST maintenance, especially UST 90 mg q8w, achieved maintenance endoscopic endpoints vs PBO. Together, these data support the efficacy of UST in inducing & maintaining endoscopic healing of the mucosa in CD.

Disclosure of Interest: P. Rutgeerts: Investigator for Janssen Research and Development, LLC
C. Gasink: Employee of Janssen Research and Development, LLC
D. Chan: Employee of Janssen Research and Development, LLC
Y. Lang: Employee of Janssen Research and Development, LLC
P. Pollack: Employee of Janssen Research and Development, LLC
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D. Jacobstein: Employee of Janssen Research and Development, LLC
J. Johanns: Investigators for Janssen Research and Development, LLC
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B.G. Feagan: Investigator for Janssen Research and Development, LLC
W. Sandborn: Investigator for Janssen Research and Development, LLC

OP105 FILGOTINIB, A SELECTIVE JAK1 INHIBITOR, INDUCES CLINICAL REMISSION IN PATIENTS WITH MODERATE-TO-SEVERE CROHN’S DISEASE: FINAL ANALYSIS OF THE PHASE 2 FILGOTINIB STUDY
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Introduction: Filgotinib is an oral, selective Janus kinase 1 (JAK1) inhibitor, which has demonstrated high efficacy in patients with rheumatoid arthritis. This 20-week Phase 2 study was designed to evaluate the efficacy and safety of filgotinib in patients with active Crohn’s disease (CD).

Aims & Methods: 174 patients with moderate-to-severe CD (CDAI 220 to 450, Placebo: n = 116, Filgotinib: n = 58) were enrolled. Patients with SES-CD ≥5 (i.e. ulceration in any segment) at induction BL were eligible for analysis. The primary endpoint of the study was met: Filgotinib induced clinical remission in 47% of patients, which has demonstrated efficacy and safety of filgotinib in patients with active Crohn’s disease (CD).

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 patients, compared to placebo (p = 0.0077), 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). Filgotinib was well tolerated with only minor treatment-related side effects.

Table 1: Key efficacy parameters

<table>
<thead>
<tr>
<th>Variable/unit/population</th>
<th>Placebo</th>
<th>Filgotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical remission (CDAI &lt; 150), %, 95%-NRI</td>
<td>23</td>
<td>47</td>
</tr>
<tr>
<td>p-value</td>
<td>0.0077</td>
<td></td>
</tr>
<tr>
<td>PRO2, mean change from baseline, ITT-LOCF</td>
<td>0.0321</td>
<td></td>
</tr>
<tr>
<td>17.6</td>
<td>33.8</td>
<td></td>
</tr>
<tr>
<td>0.0045 (continued)</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (N=97)</th>
<th>Filgotinib (N=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES-CD Change from BL, mean (SD)</td>
<td>−0.7 (4.97)</td>
<td>−2.8 (10.8)</td>
</tr>
<tr>
<td>Clinically meaningful endoscopic improvement1</td>
<td>29.9%</td>
<td>47.7%</td>
</tr>
<tr>
<td>Endoscopic Response2</td>
<td>13.4%</td>
<td>20.6%</td>
</tr>
<tr>
<td>Endoscopic Remission3</td>
<td>4.1%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Mucosal Healing4</td>
<td>4.1%</td>
<td>9.0%</td>
</tr>
</tbody>
</table>

*Primary endpoint: SES-CD reduction ≥3 from induction BL
**SES-CD reduction ≥50% from induction BL
†SES-CD total score ≥7
‡Complete absence of ulcers

Table 1: Maintenance Week 44 (IM-MUNITI)"
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 IBDQ score, mean change from baseline, ITT-LOCF</td>
<td>13.6</td>
<td>25</td>
<td>NS</td>
</tr>
<tr>
<td>SES-CD improvement at least 50%, %, ITT-LOCF</td>
<td>-0.6</td>
<td>3.5</td>
<td>0.0359</td>
</tr>
</tbody>
</table>

CDAI: Crohn’s Disease Activity Index; ITT: Intent-to-treat; NRI: Non-responder imputation; LOCF: Last observation carried forward; PRO2: Patient Reported Outcome 2 (mean daily number of liquid or very soft stools) + 7x (mean daily abdominal pain score); IBDQ: Inflammatory Bowel Disease Questionnaire; SF: Simple Endoscopic 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.

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


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


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Introduction: Tofacitinib is an oral, small molecular JAK inhibitor that is being investigated for ulcerative colitis (UC). Two Phase 3 randomised placebo (PBO)-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01458951) demonstrated efficacy of tofacitinib 10 mg twice daily (BID) vs PBO as induction therapy for patients (pts) with moderate to severe UC. We investigated the effect of prior tumour necrosis factor inhibitor (TNFi) therapies or disease activity (baseline Mayo score) on clinical endpoints, the comparison of tofacitinib 10 mg BID vs 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 read centrally. PROs at Wk 8 included Inflammatory Bowel Disease Questionnaire (IBDQ) remission (total score ≤170) and IBDQ response (≥16-point increase from baseline). For binary endpoints, the comparison of tofacitinib 10 mg BID vs PBO was assessed using the Cochran-Mantel-Haenszel (CMH) chi-square test stratified by study, prior TNFi treatment, corticosteroid use at baseline and geographic region. Within each subgroup, the CMH chi-square test stratified by study was used. Results: At Wk 8, significantly more pts achieved remission, mucosal healing and clinical response with tofacitinib 10 mg BID vs PBO (all p < 0.0001, Table). The difference generally remained significant regardless of prior TNFi exposure, prior TNFi failure, reason for TNFi failure (primary or secondary) or disease severity (based on baseline Mayo score ≥9 or < 9; Table). For all three endpoints, greater effects were observed when comparing secondary vs primary TNFi failure subpopulations and baseline Mayo score <9 vs baseline Mayo score ≥9. IBDQ remission and response were significantly greater with tofacitinib 10 mg BID vs PBO at Wk 8 regardless of prior TNFi exposure/prior TNFi failure.

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

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

<table>
<thead>
<tr>
<th>10 mg BID N = 905</th>
<th>Tofacitinib Placebo N = 234</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission, n (%)1</td>
<td>159 (17.6) 14 (6.0)</td>
<td>11.7 (7.5, 15.9)**</td>
</tr>
<tr>
<td>Prior TNFi exposure2</td>
<td>99 (23.7) 13 (12.5)</td>
<td>11.2 (5.7, 18.8)**</td>
</tr>
<tr>
<td>Prior TNFi failure3</td>
<td>106 (24.1) 13 (11.8)</td>
<td>12.3 (5.0, 19.5)**</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)4</td>
<td>19 (7.5) 1 (1.4)</td>
<td>6.2 (2.0, 10.3)**</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)4</td>
<td>31 (16.6) 0 (0.0)</td>
<td>16.6 (11.2, 21.9)**</td>
</tr>
</tbody>
</table>

Comparison of prior TNFi exposure/prior TNFi failure subpopulations and baseline Mayo score ≥9 vs baseline Mayo score <9. IBDQ remission and response were significantly greater with tofacitinib 10 mg BID vs PBO at Wk 8 regardless of prior TNFi exposure/prior TNFi failure.

Disclosure of Interest: G.R. Daheens: Study-related disclosures: Dr Daheens received speaker fee from and is an advisor for Pfizer Inc B.E. Sands: Grant(G), Personal Fee(P), NonFinancial/Pfizer G, P.Amgen, MedImmune, Celgene, Millennium, Prometheus, Abbvie, Takeda, Janssen, Hospira, Ferring, Alvogen, Abbvie Personal fees: Eizai, Takeda Pharma, MedImmune, Celgene, Millennium, Prometheus, Abbvie, Takeda, Hospira, Ferring, Alvogen, Abbvie Personal fees and non-financial support from MedImmune, Celgene, Millennium, Prometheus, Abbvie, Takeda, Hospira, Ferring, Alvogen, Abbvie Personal fees and non-financial support from Takeda; non-responder imputation NSNot significant; *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 = 82 for tofacitinib 10 mg BID and N = 151 for placebo; statistical significance based on the Cochran-Mantel-Haenszel chi-squared test stratified by study, prior treatment with tumour necrosis factor inhibitors, corticosteroid use at baseline and geographic region BID, twice daily; CI, confidence interval; TNFi, tumour necrosis factor inhibitor; Wk, week.
Patients were randomly assigned to receive two single doses of cobitolimod (30 mg and 1 mg groups. At the Week 44 visit in the OLE, 119/131 (90.9%) had little or no blood in their stools (rectal bleeding subscore [RBS] 0 or 1), 105/131 (80.2%) had little or no increase in their number of stools (Stool Frequency subscore of 0 or 1), 111/131 (84.7%) had no blood in the stools (RBS 0), and 105/131 (80.2%) had little or no increase in their number of stools (Stool Frequency subscore of 0 or 1). The most common adverse events (AEs) (>2.0%) 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 > 3 x upper limit of normal occurred in 4 (2.4%) of the 170 patients in the OLE. All elevations were asymptomatic, <5xULN, transient, and resolving while receiving continued treatment.

Conclusion: The results of the COLLECT study demonstrate that the TLR-9 agonist cobitolimod is able to induce clinical remission in UC patients both with moderate and severe disease activity. The concept of TLR-9 activation represents a promising and well-tolerated novel therapeutic option for ulcerative colitis patients with active disease and warrants further trials.

Disclosure of Interest: W.J. Knittel: Consultancy for Index Pharmaceuticals; L. Peyrin-Biroulet: Consultancy for Index Pharmaceuticals; W. Renisch: Consultancy for Index Pharmaceuticals; F. Scaldalferri: Consultancy for Index Pharmaceuticals; C. Admyre: Consultancy for and stock options of Index Pharmaceuticals; T. Knitell: Consultancy for and share holding of Index Pharmaceuticals; J. Kowalski: Consultancy for and share holding of Index Pharmaceuticals; M.F. Neurath: Consultancy for Index Pharmaceuticals; C.J. Hawkey: Consultancy for Index Pharmaceuticals.
We assessed a recently developed self-assembling peptide matrix as a wound dressing after endoscopic resection for the prevention of esophageal stricture. 

Aims & Methods: Ten pigs were randomly assigned to the self-assembling peptide RADA-16 (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 esophageogram, weight variation, and histological measurements of fibrosis, granulation tissue, and neoeithelium were assessed in each animal.

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

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

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

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

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

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

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.

Disclosure of Interest: All authors have declared no conflicts of interest.
### Table (OP114)

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<td>No</td>
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### OPI15 PREVENTION OF POST-SPHINCTERO TOMY 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 40 mg bid from Day 2 to 10. Standard care arm would receive usual care without any acid suppressive therapy. Endoscopists were unaware of the treatment allocation of the patients. Primary outcome was the proportion of patients with immediate or delayed post-EST bleeding. Immediate bleeding was defined as bleeding that occurred during the procedure and required endoscopic hemostasis. Delayed bleeding was defined as bleeding after the completion of ERCP and EST, and 24 hours of observation. Secondary outcomes included hospitalization, procedures, and costs. The primary outcome measure was the incidence of bleeding (defined as epigastric pain plus either amylase or lipase levels > 3 times the upper limit of normal at 24h). Secondary 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).

**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. The baseline characteristics of the two groups included patients with immediate or delayed post-EST bleeding. Immediate bleeding was defined as bleeding that occurred during the procedure and required endoscopic hemostasis. Delayed bleeding was defined as bleeding after the completion of ERCP and EST, and 24 hours of observation. Secondary outcomes included hospitalization, procedures, and costs. The primary outcome measure was the incidence of bleeding (defined as epigastric pain plus either amylase or lipase levels > 3 times the upper limit of normal at 24h). Secondary outcome was the incidence 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 standard hydration arm, two patients presented with moderate and severe PEP, respectively. Contrast injection of the Wirsung was significantly associated with PEP (28.6% versus 71.4%, 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

**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.

### OPI16 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 standard hydration arm, two patients presented with moderate and severe PEP, respectively. Contrast injection of the Wirsung was significantly associated with PEP (28.6% versus 71.4%, 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 in the control group, with a negative predictive value of 100%.

Conclusion: In our series, the incidence of PEP was 9.3%, and a non-significant negative predictive value of 100% for the development of PEP. No complication was observed in the control group, with 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 OCTANOLATED 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 pathway) control of feeding.

Aims & Methods: The aim of this project was to study the effect of intragastric administration of the bitter tastant Quinicine Hydrochloride (QHC) on brain activity in homeostatic and hedonic regions and on circulating ghrelin plasma levels. Furthermore, to test the hypothesis that reduced hunger and prospective food consumption ratings, and lower hedonic food intake after QHC administration compared to placebo. Fifteen healthy women were studied after an overnight fast. Brain activity before and up to 50 minutes after infusion of QHC (10mmol/kg; 30 min before sacrifice) was recorded using functional magnetic resonance imaging (MRI). Hunger and prospective food consumption scores were assessed every 10 min using Visual Analogue Scales. Blood samples were taken at the same time points. Hedonic food intake was measured immediately after scanning using an ad libium chocolate milkshake drink test. MRI preprocessing and analysis was conducted using SPM12. Brain responses to QHC versus placebo infusion were compared in a priori defined regions of interest (ROI) at both voxel- and cluster-level threshold of pFWEcorrected < 0.05. The interaction effect was tested on hunger and prospective food consumption scores with mixed models. Hedonic food intake was compared between infusions using a one-tailed paired T-test. Blood plasma was analysed for circulating ghrelin levels using radioimmunoassays.

Result: Compared to placebo, intragastric QHC infusion significantly increased neural activity in 5 different clusters within the ROIs, with local maxima in the putamen, insula, caudate, amygdala, anterior cingulate cortex, medial prefrontal cortex, medial orbitofrontal cortex and hippocampus. A decrease of neural activity was observed in the lower system. Significantly lower prospective food consumption scores were observed after QHC administration compared to placebo (p = 0.02), but no significant differences were observed for hunger scores. Milkshake intake significantly lower after QHC administration, compared to placebo (p = 0.04; Cohen’s d = 0.50). A significant decrease of octanoylated ghrelin plasma levels was observed post-infusion after bitter administration compared to placebo (p = 0.05).

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

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

OP118 TRANSDIAGNOSTIC COGNITIVE BEHAVIOUR THERAPY SHOW PROMISE FOR BOTH MOOD AND GASTROINTESTINAL SYMPTOMS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS
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Introduction: Irritable Bowel Syndrome (IBS) is a heterogeneous disorder characterized 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 IBS show improvement in abdominal symptoms with antidepresants [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 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, referred to as iCBT. Based on this model, a transdiagnostic iCBT program developed specifically for gastrointestinal disorders shows considerable promise with improvements in both gastrointestinal symptoms as well as psychological functioning. The correlation between change in both mood scores and catastrophizing with change in abdominal symptoms opens avenues for further understanding of the mechanisms of change. Lessons from the program 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

OP119 DYSGOBIOSES INDUCES GUT INFLAMMATION AND DEPRESSIVE-LIKE BEHAVIOR ASSOCIATED WITH BRAIN BIOCHEMICAL AND FUNCTIONAL ALTERATIONS WHICH ARE RESTORED BY PROBIOTIC TREATMENT
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Introduction: The gut-brain axis has been indicated as major substrate of pathophysiological mechanisms in psychiatric comorbidities associated with chronic inflammatory bowel disorders. In particular, intestinal microbiota alterations observed in chronic inflammatory bowel diseases suggest that alterations of gut microbiota may play a role in psychiatric disorders. However, this relationship is difficult to understand and probably involves multiple mechanisms.

Aims & Methods: In this study we examined the presence of gut inflammation and depressive-like behavior associated with brain biochemical and functional alterations in an antibiotic-induced dysbiosis animal model. Young male mice received a mixture of nonabsorbable antimicrobials (ampicillin, streptomycin and clyndamycin), which has been associated to the microbiota composition alteration2, for 2 weeks. Afterwards, mice were treated with probiotic (Lactobacillus Casei DG, 109 cells) or vehicle up to 7 days. Whereupon, various behavioral testing were performed. After sacrifice, mice intestine was cut in segments (duodenum, jejunum, ileum, colon) and proximal and distal segments were collected for measurement of inflammatory cytokines, and mRNA expression of pro-inflammatory markers (IL-1β,
TNFα and iNOS) was evaluated by Western Blot analysis. Extracellular recording from CA3 region of dorsal hippocampus was performed. Astrocytes and microglial cells markers (GFAP and Iba-1, respectively) expression was evaluated by immunohistochemistry.

**Results:** Biochemical evaluations indicated that dysbiosis induced an overall gut inflammation characterized by significant increases in IL-1β, TNFα and iNOS expression, associated with a depressive-like behavior and a reduced social interaction. Altered behavior was accompanied by significant changes CA3 pyramidal neurons firing activity. Moreover, the number of GFAP and Iba-1 positive cells was significantly dysbiotic. Very interestingly, probiotic treatment significantly decreased IL-1β, TNFα and iNOS expression, normalized mice behavior, restored the spontaneous ongoing activity of CA3 pyramidal neurons and reduced the GFAP and Iba-1 positive cells number.

**Conclusion:** We found that, in mice, dysbiosis induced gut inflammation and sickness behaviors associated with biochemical and electrophysiological alterations in hippocampus. Probiotic treatment counteracted the gut inflammation and restored the behavioural phenotype as well as the biochemical and functional changes occurring in the brain of diabetic mice. These data suggest that intestinal dysbiosis, via the gut-brain axis, might contribute to the psychiatric comorbidity in patients with bowel disorders associated with an altered microflora and that probiotic treatment may improve this condition.

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

**References**

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**OP120 QUORUM SENSING MOLECULES OF GUT MICROBIOTA AFFECT INTESTINAL TASTE RECEPTORS AND ANOREXIC PEPTIDES TO CONTROL SATIETY IN THE HOST**

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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 submitted to swallowing and pharyngeal water stimulation (PWS) (Mittal, 2013) and animals were submitted to a 6 week baseline period followed by 3 weeks of oral 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. Moreover, PQS and AHL-12 significantly reduced hypothalamus. Intraperitoneal administration of AHL-12 or PQS had no effects, altered body weight gain, oral glucose tolerance test. Orexigenic peptides by qRT-PCR on colon and hypothalamus; d) food intake, body weight gain, oral glucose tolerance test.

**Results:** In mice, dysbiosis induced gut inflammation and sickness behaviors associated with biochemical and electrophysiological alterations in hippocampus. Probiotic treatment counteracted the gut inflammation and restored the behavioural phenotype as well as the biochemical and functional changes occurring in the brain of diabetic mice. These data suggest that intestinal dysbiosis, via the gut-brain axis, might contribute to the psychiatric comorbidity in patients with bowel disorders associated with an altered microflora and that probiotic treatment may improve this condition.

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

**References**

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**OP122 ACOTIAMIDE-SENSITIVE IMPAIRED RECEPTECTIC RELAXATION OF LOWER ESOPHAGEAL SPHINCTER IN PATIENTS WITH ESOPHAGO Gastric JUNCTION OUTFLOW OBSTRUCTION**

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**Introduction:** The pathogenesis and treatment of esophagogastroduodenal junction outflow obstruction (EGJOO) are not fully understood. The lower esophageal sphincter (LES) reportedly exhibits accommodation responses, and LES pressure is suppressed by swallowing and pharyngeal water stimulation (PWS) (Mittal, 2013). We have previously reported that acotiamide was effective for patients with EGJOO. High-resolution manometry was performed according to a standard protocol with the participant in the supine position, while swallowing ten 5-ml liquid boluses. 13 patients with EGJOO (mean age 65.5 ± standard deviation 4.1 years, eight of whom were women) and 19 participants with normal esophageal pressures (mean age 50.0 ± 3.0 years, 11 of whom were women) were enrolled. Basal LES pressure (BLES) and the integrated relaxation pressure (IRP) were measured. The extent of PWS-induced LES relaxation (mmHg) was calculated as the difference between BLES and the mean LES pressure in the 5-s period before PWS.

**Results:** There was no difference in BLES between normal subjects (34.6 ± 2.1 mmHg) and patients with EGJOO (32.7 ± 1.8 mmHg), but IRP was significantly higher in patients with EGJOO (20.3 ± 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 12.7 ± 5.9 mmHg in normal subjects, but was absent in patients with EGJOO.
The mean LES pressure induced by PWS was 33.0±1.6 mmHg, and did not differ between all SMTs (HPS 52.7±15.6 mmHg). Acetazolamide normalized impaired receptive LES relaxation and substantially improved symptoms.

Conclusion: This study demonstrates that receptive LES relaxation is impaired at the cervical esophagus. Although the mechanism is not clear, these findings should be considered in the management of GERD in patients with symptoms at the cervical esophagus.

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

Reference

Monday, October 17, 2016

15:45-17:15

ENDOSCOPIC MANAGEMENT OF UPPER GASTRO INTESTINAL CANCER – ROOM U

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 lumen. It is also 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 safety and efficacy of ESD for superficial cancer located at the cervical esophagus. Patients who met the following criteria (case group) were enrolled in this retrospective study: 1) ESD was performed from January 2006 to December 2015; 2) the lesion was located at the cervical esophagus; and 3) squamous cell carcinoma (SCC) was proven histologically. Forty-five patients met those criteria. As a control group, 379 patients with 405 lesions of SCC which were located at the middle thoracic esophagus were enrolled. The lesions with entire circumferential mucosal defect, recurrent lesions after radiotherapy, and the lesions located near the scar were excluded in both groups. We evaluated adverse events including strictures and pneumonitis, 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 3:2 (73.3%). The average maximum size of lesions was 20.7 mm, and the histological depth of invasion was EP/LPM, MM, and SM2 in 39, 5, and 1 cases, respectively. The en bloc resection rate and R0 resection rate was 100% and 96%, respectively, and the mean procedure time was 57 min. ESD was performed for under general anesthesia in 32 patients. Damage of the muscle layer during treatment was observed in 5 patients, for which clipping was performed in 2 patients. Esophageal stricture was observed in 9 patients (41%), for which local injection of steroid was administered in 6 patients. No post-ESD bleeding was observed. Although perforation was identified in one patient, he recovered with conservative treatment. Chemoradiation therapy as additional treatments were conducted in 17 patients. No local recurrence was observed during an average duration of follow-up of 34.1 months. In the control group, the average age was 64.0 ± 11.2 years old, and the male-to-female ratio was 3:2 (57.9%). 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 97%, respectively, and the mean procedure time was 54 min. ESD was performed under general anesthesia in 45 patients (11.1%). Damage of the muscle layer during treatment was observed in 91 patients (22.5%), for which clipping was performed in 38 patients. Esophageal stricture was observed in 14 patients (6.6%) of 213 patients with more than half of mucosal defect, for which local injection of steroid or PGA sheet were administered in 38 patients. No post-ESD bleeding was observed. Although perforation was identified in three patients, they recovered with conservative treatment. Surgery or chemoradiotherapy as additional treatments were conducted in 19 or 49 patients respectively. Local recurrence was observed in one patient during an average duration of follow-up of 41.8 months.

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

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

OP124 SUBMUCOSAL TUNNELING ENDOSCOPIC RESECTION VS. THORACOSCOPIC SURGERY FOR LARGE SYMPTOMATIC SUBMUCOUS TUMORS IN THE ESOPHAGUS AND ESOPHAGOGRASTIC 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) has been recommended for the resection of upper gastrointestinal SMTs. Recently, reports about STER are increasing. However, it is unclear whether STER is feasible for large SMTs. Moreover, studies about comparison of STER and surgery for upper gastrointestinal SMTs are still little.

Aims & Methods: The aim of this study is to compare the clinical outcomes of STER and thoracoscopic surgery for large symptomatic SMTs in esophagus and esophagogastric junction, as well as to analyze the clinicopathological factors that affect the feasibility of STER. Patients with large SMTs of the esophagus and the MP layer in esophagus and EJG were enrolled in this retrospective study between May 2011 and December 2013. The clinicopathological data of a total of 145 patients were collected and analyzed.

Results: Among the 145 patients, 39 patients (26.9%) complained specific symptoms, while 106 patients (73.1%) had non-specific complaints. In the STER group, the mean tumor long and transverse diameters were 5.8 cm and 2.2 cm. Meanwhile, in the TS group, the mean tumor long and transverse diameters were 6.5 cm and 3.1 cm, respectively. In all SMTs, 64 lesions were classified as SM1, 49 lesions as SM2, and 81 had irregular shapes (55.9%). All of the tumors were located in esophagus (84, 57.9%), and EJG (61, 42.1%). There was no significant difference between the two groups in age, gender, symptom, tumor size, tumor location, tumor shape, tumor histopathology, and tumor infiltrative-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 3 patients (11.1%), and indeterminate in 7 patients (33.3%). On H. pylori eradication therapy after initial ESD, 17 patients 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 (range, 12.4–83.8) months. The locations of the lesions were classified as 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-Ia in one lesion (3.4%), 0-IIa in 15 lesions (51.7%), 0-IIc in 12 lesions (41.4%), and 0-IVa in one lesion (3.4%). The mean tumor size was 10 (range, 6.5–16) mm. In 67 lesions, en bloc resection was performed for 28 lesions (96.6%). Aspiration pneumonitis 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, 8 were tubulovillous adenomas, and 5 were villous adenomas. Histologically, curative resection was obtained in 27 lesions (93.1%). In contrast, the location of 31 metachronous lesions was U in 9 lesions (29%), M in 8 lesions (25.8%), and 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-Ia-HB 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 pneumonitis occurred in one patient. The patient was successfully treated by intravenous therapies.

Disclosure of Interest: All authors have declared no conflicts of interest.
antibiotics. There were no treatment-related deaths. On pathological examina-
tion, 20 were tubular adenocarcinoma, and 11 were tubular adenoma. Histologically, curative resection was obtained in 26 of the 31 lesions (83.9%). There were no differences in gross type (elevated type/flattened depressed type), tumor size, or histology between primary and metachronous lesions. However, local recurrence (4 lesions) was significantly different (P = 0.029). Furthermore, there were significant differences in U/P (M = 0.016) and U/L (P = 0.014). Therefore, there was a slightly higher frequency of 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 endoscopy after ESD for gastric neoplasms.

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

Aim & Methods: The aim of this study is to find the best method for treating early gastrointestinal neoplasia. Fifty-one patients (mean patient age 71, range 32–92 years, male: female ratio 25/26) including 19 involved adenoma with low-grade dysplasia, 21 intraepithelial cancer with high-grade dysplasia, 3 minute submucosal cancers, 6 submucosal deep cancers and 2 carcinoid tumors submitted to ESD, were compared to 98 patients (mean patient age 62.7, range 20–88 years, male: female ratio 52/46) who underwent EMR (20 involved adenoma with low grade dysplasia, 42 intraepithelial cancers with high-grade dysplasia, 24 minute submucosal cancers, 3 submucosal deep cancers, 4 carcinoid tumors, 3 granular cell tumors and 2 Brunner’s adenoma). In ESD group, the mean operation time was 1.6 hrs and the mean size of resected specimen was 25.5 mm (range 10–80 mm); in EMR group, the mean operation time was 0.5 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, post-operative bleeding and perforation rate were compared with the use of chi-square test.

Results: En-bloc resection rate (ESD: 82.4%, 42/51 vs EMR: 51%, 50/98; p < 0.001) 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. Piecemeal resection was significantly lower in ESD (17.7%, 9/51) when compared to EMR group (49.9%, 48/98) (p < 0.01). In the EMR group, 6 patients developed local recurrences (6.1%) five were successfully treated by additional EMR and one by surgical resection; in contrast, there was no recurrence in the ESD group (p = NS). The post-operative bleeding rate was 3.9%/2.5% in ESD and 3.1%/3.9% 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 resection methods from the perspectives of en-bloc and curative resection rates. Based on these aspects, an ESD was found to be the best method for early gastrointestinal cancers; EMR would be a good alternative to an ESD, especially for low-risk patients or when performed by less experienced endoscopists.

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

Reference

Aim & Methods: This multicenter study aimed to establish a scoring system (eCurA system) for deciding the potential risk of LNM after ESD with pathological factors related with LNM. However, as LNM occurs in only 5–10% of patients who undergo radical surgery, this recommendation may be overestimated.

Aim & Methods: This scoring system predicted cancer-specific survival, which may be helpful to evaluate 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.

Reference
Aims & Methods: Aspiration sclerotherapy is a therapeutic option for large symptomatic hepatic cysts. However, inadequate cyst reduction is frequently reported. Somatostatin analogues are able to curtail cyst volume. We hypothesized that combining 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, symptoms assessment (QoL), and efficacy in cysts with low cyst fluid/plasma somatostatin ratio.

Results: Thirty-four patients (32 females (94%); mean age 53.6 years) were randomized to pasireotide or placebo (n = 17 per arm). Baseline characteristics were well balanced between the arms. Baseline ultrasound assessment showed adequate cyst fluid/plasma somatostatin ratio (> 1). Primary endpoint was met in both groups: 6-week cyst diameter reduction among pasireotide group was 35% (range 17–50%; n = 17) and placebo group was 23% (range 12–30%; n = 17); P = 0.004. Baseline QoL scores were well balanced between the arms: 6-week QoL improvement was 28% (range 12–53%; n = 17) and placebo group was 18% (range 0–48%; n = 17); P = 0.018. Mean PCL-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: All authors have declared no conflicts of interest.
MUC3A is high expression in tumor tissue of ECC, and related to diagnostic accuracies (86.6%, 63%, 80.4%) and less false positive rates (10%, much higher sensitivity (84.6%, 38.5%, 76.9%), specificity (90%, 95%, 85%)).

ECC were significant higher than patients with SOD (57.8/C6).

Using isobaric tags for relative and absolute quantitation (iTRAQ) in 20 patients (MUC3A) was the main differential protein in bile with proteomics technology.

**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 ECC specimens by quantitative real-time PCR. (2) The preoperative serum values of MUC3A in patients with ECC were compared preoperative with postoperative. (3) The clinicopathological data on the prevalence of gallbladder polyps and attribution of neoplastic and nonneoplastic polyps.

**Aims & Methods:**

1. The positive cells rates of MUC3A in ECC specimens were significantly higher than in normal bile duct tissues specimens (83.3% vs. 35.0%, P < 0.01). The expression of MUC3A was significant correlated with metastasis of lymph node infiltration and peritoneal distant metastasis. (The stage of carcinoma (P < 0.05). (2) The preoperative serum values of MUC3A in patients with ECC were significantly higher than with patients with SOD (57.8 ± 19.6 vs. 25.1 ± 9.2 ng/ml, P < 0.01). Compared with the preoperative results, postoperative serum MUC3A in patients with ECC was 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% sensitivity, 90% specificity). (3) The serum MUC3A has more significant and early changes over the period of 2 months (90%, 38.5%, 76.9%). (4) The serum 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 excerpt was classified as neoplastic. Prevalence of gallbladder...
polyps and the attribution of neoplastic polyps and nonneoplastic polyps was calculated. To examine 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 4539 patients. A total of 337 patients were excluded due to primary non-gallbladder surgery, leaving 4012 unique cholecystectomies. In 2083 cholecystectomies (0.9%), a polyp was identified.

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

References


MONDAY, OCTOBER 17, 2016 15:45:17:15 MECHANISMS OF LIVER CANCER AND PORTAL HYPERTENSION – ROOM 1.86

**OP135 CHANGES IN CIRCULATING MICRORNAs AFTER TREATMENT: MICRONARa SIGNATURES TO PREDICT THERAPY RESPONSE AND DISEASE FREE SURVIVAL IN HEPATOCELLULAR CARCINOMA**

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

**Aims & Methods:** To identify potential circulating miRNA signatures for the prediction of therapy response and patient follow-up. Methods: 1337 patients with advanced stages of HCC were enrolled and treated according to the ECOG/ASLELD practice guidelines. Patients were staged (CT scan and/or MRI) at 0 time (T0, before treatment), 1 month (T1) and 6 months (T6) from therapy. Serum blood RNA samples were isolated and hybridized on Affymetrix GeneChip miRNA arrays 3.0. qRT-PCR was used for miRNA validation in an independent cohort of 15 matched patients. The Kaplan–Meier model was used to estimate disease-free survival (DFS).

**Results:** Six single miRNA profiles have been analyzed using a microarray approach. We analyzed 1733 miRNAs over the 6 months period. The analysis yielded different profiles in serum and blood identifying the two biofluids as two distinctive sources of miRNA carrying the same message. Only a small portion of the circulating miRNA remained significant in all time points indicating a dynamic variation in the miRNA expression. Blood-miR-3179, 373, 4773 significantly increased from T0 to T6 while miR-2277-5p, 106b, 202 decreased. In serum, miR-6469-3p, 3148, 371 increase while miR-103b decrease. The hierarchical clustering revealed stable miRNAs on log scale clearly differentiated T0 profiles from T1 and T6 both in blood and serum. Interestingly at T1 two main clusters distinguished patient with a complete response from whose having only a partial response to therapy. Further validation of miR-106b showed a correlation between miR-106b levels and treatment response (P < 0.0001), and the longer DFS (P < 0.0038). MiRNA-106b was also significantly correlated with the with BCLC staging A1 and A2 (P = 0.001).

Conclusion: This study underlines the importance of the different information provided by miRNA profiles during the follow-up of a single patient. Circulating miR-106b detection offers a promising non-invasive analysis tool to identify patients with the longest disease-free survival in response to anticancer therapies. Disclosure of Interest: All authors have declared no conflicts of interest.
clarify the mechanisms responsible for liver atrophy, pathological analysis showed the liver carried out within the limits of our knowledge. 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, 4 or 6 (d0, w2, w4 and w6, respectively). In specimens of embolized lobe (E) and non-embolized lobe (control, Cont), we measured the distance between portal vein and central vein (PV-CV), area and hepatocyte number per lobule and apoptotic activity. Immunohistochemical reactivities of microtubule-associated protein-light chain 3 beta (LC3) as autophagy and glutamine synthetase (GS) and cytochrome 2E1 (CYP2E1) as zonation were evaluated.

**Results:** PV-CV and lobule area showed no significant difference between E and Cont at d0, but were lower in E than in Cont at w2, w4 or w6 (P < 0.001). Hepatocyte number was not significantly reduced in E at d0 and w2 but was reduced 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 staining in E and 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 lobular 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**


**OP138 RIGOROUS, A STIMULATOR OF THE GUANYLYL CYCLASE, REDUCES LIVER FIBROSIS AND PORTAL PRESSURE IN CIRRHOTIC RATS**

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**Introduction:** Intrahepatic nitric oxide (NO) signaling including activation of its receptor guanylyl cyclase (GC) is impaired in cirrhosis. The GC stimulator rigor (RIO) is approved for treatment of pulmonary hypertension. Experimental studies suggest antifibrotic effects of RIO. We investigated the effects of RIO in cirrhotic rats with portal hypertension (PHT).

**Aims & Methods:** In 54 rats (BMI 16.5±2.2 g/kg) the rats were randomized into early and advanced grade cirrhotic rat models were used to assess changes in hemodynamics and fibrosis after RIO treatment. Cirrhosis was induced by i.p. carbon tetracloridrute (‘early’; 1 mL/kg - ‘advanced’: 2 mL/kg 50% CCl4, 8 weeks) or bile duct ligation (BDL, ‘early’: 3 weeks; or ‘advanced’: 5 weeks) in 100 male Sprague Dawley rats. Controls received olive-oil (OO) or underwent sham operation (SO), respectively. RIO (1 mg/kg) or vehicle was gavaged from weeks 5–8 in CCl4/OO and weeks from 2–3 to 4 [or 4–5] in BDL/SA0. Systemic hemodynamics, portal pressure (PP), superior mesenteric blood flow (SMABF) and portal- systemic shunting (PSS) were measured.

**Results:** BDL and CCl4 rats presented with cirrhosis, elevated PP, SMABF and PSS, which was more pronounced in the advanced stage. In early BDL cirrho-

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T. Reiberger: received payments for lectures from AbbVie, Gilead, Jansen and Roche

M. Trauner: received grants from MSD, honoraria for consulting from AbbVie, Gilead, Jansen, and MSD, and payments for lectures from Gilead, and Roche, as well as travel support from Gilead.

M. Peck-Radosavljevic: grants from Gilead, MSD, and Roche, and financial support from Roche.

All other authors have declared no conflicts of interest.

**References**


**OP139 MECHANISM OF LIVER ATROPHY DUE TO PORTAL VEIN EMBOLIZATION - ASSOCIATION WITH AUTOPHAGY AND APOPTOSIS**

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**Introduction:** The mechanism of liver atrophy due to portal vein embolization was still unclear. With regard to the liver, autophagy has been reported to be caused by starvation and related to hepatocellular atrophy. Using pig models of portal vein ligation and balloon catheter portal vein embolization (PTPE) with absolute etha-

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

**References**


**OP140 EFFECT OF CHRONIC THIOACETAMIDE TREATMENT ON HEPATIC HEMODYNAMIC PARAMETERS IN RATS**

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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 (0.03% TAA / 100 ml H2O). The TAA dosage was given 5 days a week 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 predichnial MR scanner: portal vein area, portal blood flow velocity, portal blood flow volume and aortal blood flow volume. Specific 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 cirrhosis. Median score of 1–3 (group 12w/flb). From the rats which
TUESDAY, OCTOBER 18, 2016
08:30–10:00
OPTIMISING ANTI-TNF THERAPY – ROOM G

OP141 CORRELATION OF ENDOSCOPIC FINDINGS WITH SERUM DRUG CONCENTRATIONS AND NEED FOR RESCUE THERAPY: SUBANALYSIS OF THE TROUGH CONCENTRATION ADAPTED INFliximab TREATMENT (TAXIT) TRIAL
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Introduction: The Trough Concentration Adapted Infliximab Treatment (TAXIT) randomized controlled trial [1] showed that targeting patients’ infliximab trough concentrations to a 3–7 μg/mL window resulted in a more efficient use of the drug in patients with inflammatory bowel disease. Following dose optimization, continued concentration-based dosing was not superior to clinic-based dosing and therefore continue with the use of supplementary intervention. Previous anti-TNF exposure was predictive factor for infusion reaction.

Aims & Methods: This was a retrospective analysis of all endoscopies performed at the end of TAXIT. For Crohn’s disease (CD), mucosal healing was defined as absence of ulcerations (complete mucosal healing) or clear improvement in ulcerations (partial mucosal healing) when compared to baseline. For ulcerative colitis (UC), healing was defined as a Mayo endoscopic subscore of 0 or 1. Rates of mucosal healing were 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 (n=70 in arm 1 and n=55 in arm 2). Patients in arm 1 had a mucosal healing rate of 42.6% (55/129) compared to 38.9% (38/96) in arm 2 (p=0.09). Interestingly, 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 (9/113 or 8%) (p=0.02). Numerically more patients who reached 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).

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

Reference

OP142 FREQUENCY AND CHARACTERISTICS OF INFUSION REACTIONS DURING BIOSIMILAR INFliximab TREATMENT IN INFLAMMATORY BOWEL DISEASE PATIENTS: RESULTS FROM CENTRAL EUROPEAN NATIONWIDE COHORT
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12. Janus Hospital, Budapest/Hungary
13. University of Pecs, Pecs/Hungary
14. 1IBD Clinical and Research Center, Icaarusa., Prague/Czech Republic
15. Medica, A.S., PharmaSwiss-Czech Republic, Praha/Czech Republic
16. Institute of Medical Biochemistry and Laboratory Diagnostics, 1st Medical Faculty and General Teaching Hospital, Charles University, Prague/Czech Republic
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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 was strongly associated with occurrence of infusion reaction. Concomitant azathioprine therapy showed borderline protective effect on infusion reaction.

Conclusion: Patients 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
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Introduction: Combination therapy with infliximab (IFX) and azathioprine (AZA) is the most effective strategy in patients with Crohn’s disease (CD) and ulcerative colitis (UC) naive to both therapies. However the optimal dose of AZA which is frequently used during the induction phase of IFX in inflammatory bowel disease (IBD) patients on combination therapy.

Aims & Methods: This prospective study included three cohorts of IBD patients treated with IFX-AZA and being in deep remission (clinical

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

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

<table>
<thead>
<tr>
<th>COHORT</th>
<th>T-1 (n = 33)</th>
<th>T0 (n = 43)</th>
<th>T1 (n = 43)</th>
<th>T2 (n = 26)</th>
</tr>
</thead>
<tbody>
<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>
<td></td>
</tr>
<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 (5.8–9.8) 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>
</tr>
<tr>
<td>Median (IQR) PRO2 serum albumin</td>
<td>44.5 g/L (42.6–47.0)</td>
<td>44.1 g/L (42.2–47.0)</td>
<td>43.7 g/L (41.6–47.2)</td>
<td>43.7 g/L (41.6–47.2) p = 0.893</td>
</tr>
</tbody>
</table>

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

**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, as 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, Tillotts, Ferring, Centocor, Takeda, Hospira; consultancy for Ferring, Abbvie, Shire, Genentech/Roche, Celgene, Janssen, MSD, Takeda, Galapagos, Hospira, Mundipharma, Pfizer.

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

**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, as 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, Tillotts, Ferring, Centocor, Takeda, Hospira; consultancy for Ferring, Abbvie, Shire, Genentech/Roche, Celgene, Janssen, MSD, Takeda, Galapagos, Hospira, Mundipharma, Pfizer.
results were most sensitive to changes in the perspective of the analysis, utility values and time horizon (10-year).

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

Disclosure of Interest: J. Aisenberg has received consulting fees from Boehringer Ingelheim, Janssen, Medimmune and Pfizer. P. Reilly has received honoraria from Pfizer, Boehringer Ingelheim, Janssen, Lilly and Medimmune. P. Baji has received fees for speaking from Boehringer Ingelheim, Janssen, Medimmune and Pfizer. S. Glund and J. Van Ryn have received grants and fees for speaking from Boehringer Ingelheim, Janssen and MedImmune. L. Gulacsi has received speaker’s fees from Pfizer, Hospira and Hospira.

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8:30:10 AM

DABIGATRAN-RELATED ANTICOAGULATION DURING SEVERE GASTROINTESTINAL HEMORRHAGE: INTERIM RESULTS (N = 123) FROM THE REVERSE-ADTM STUDY
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Introduction: Gastrointestinal bleeding (GIB) is a feared complication of anticoagulant therapy. Idarucizumab (IDA) is a rapid-acting, human monoclonal antibody directed against the direct thrombin inhibitor dabigatran. IDA should benefit management of dabigatran users experiencing severe GIB.

Aims & Methods: The on-going REVERSE-AD™ study evaluates the safety and efficacy of IDA 5 grams intravenously in dabigatran users with (A) life-threatening haemorrhage or (B) requirement for emergency surgery. Here, we analyze the clinical characteristics and outcomes of REVERSE-AD™ enrollees presenting with severe GIB. Our study is performed on an interim analysis cohort of 123 patients: centralized laboratory coagulation data are available for 90/123 (72%) patients with major GIB.

Results: Of the 66 patients enrolled in REVERSE-AD™ due to severe bleeding, 27 (41%) bled in the GI tract. The mean age of GIB patients was 77.5 years (range, 20–93), 15 (56%) were male and renal impairment was present in 22 of 23 the patients with creatinine clearance measurements (96%). Atrial fibrillation was the indication for anticoagulation in 93%; 74% took their most recent dabigatran dose <24 hours before presentation. Ten patients (37%) bled from the upper GI tract, 8 (30%) from the lower GI tract, and 9 (33%) from an unknown level of the GI tract. IDA achieved immediate reversal of dabigatran-related anticoagulation, and its effect lasted for up to 24 hours in the majority of patients. Hospital admission was required for 25 patients (93%, median length of stay = 6.0 nights); 8 patients required ≥1 day in intensive care unit (ICU) (30%; median length of ICU stay = 3.5 days). Patients with lower GI bleeding had shorter time to cessation of bleeding (median 1.5 hours vs. 7.3 hours). No adverse events attributable to IDA were reported. A total of 24 patients received ≥1 unit packed red cells (mean 4.5 units); 9 received fresh frozen plasma (mean 2.6 units); 2 received platelets (mean 1.5 units); and 1 received prothrombin complex concentrate prior to dabigatran therapy. There were no deaths by 90 days, but 1 patient died directly attributable to GIB. Antithrombotic therapy was resumed in 20 patients (74%) prior to study termination, with a median of 6.1 days (range 0–41 days) after IDA administration. Dabigatran was resumed in 6 patients (22%).

Conclusion: The GI tract is the most common site of anticoagulant-associated haemorrhage meeting clinical criteria for emergent reversal. IDA achieves immediate reversal of dabigatran-induced anticoagulation, an effect that is sustained for up to 1 day in the majority of patients. Overall, GIB outcomes in this cohort were favourable; antithrombotic therapy can be resumed promptly in most patients.

Disclosure of Interest: J. Aisenberg: James has provided consultancy to Boehringer Ingelheim.

P. Reilly: Paul Reilly is an employee of Boehringer Ingelheim Pharmaceuticals

E. Kleine: Eva Kleine is an employee of Boehringer Ingelheim GmbH & Co KG

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Introduction: Biosimilar infliximab CT-P13 received positive CHMP recommendation in June 2013 for all indications of the originator product. It has been previously shown that CT-P13 is effective and safe in inducing remission in inflammatory bowel diseases (IBD). However, prospective, long-term data on the efficacy and safety of the biosimilar infliximab in IBD are lacking.

Aims & Methods: A prospective, nationwide, multicentre, observational cohort was designed to examine the efficacy and safety of CT-P13/infliximab biosimilar in luminal Crohn’s disease (Crohn’s disease of the ileum or ilio-caecal tract) and ulcerative colitis (UC). Demographic data were collected and a harmonized monitoring strategy was applied. Clinical remission, response and biochemical response was evaluated at week 14, 30 and 54. None of the patients had received infliximab within 12 months prior to initiation of the biosimilar infliximab. Safety data was registered.

Results: 291 consecutive IBD (184 CD and 107 UC) patients were included in the present cohort, of which 100 patients reached the week 54 endpoint. The age at disease onset was 28 years (range, 0–72) in CD and 22–39 in UC patients, respectively. 32/49% of CD patients had colonic/ileocolonic disease location, 41% had complicated disease behaviour, 35% had perianal disease and 23% had gone through previous surgery. 33/59% of UC patients had proctitis/anal-sided colitis/extension to rectosigmoid. 25/14% of patients had received previous anti-TNF therapy in CD and UC, respectively. 60/52% of CD/UC patients received concomitant immunosuppressives at baseline. 55, 57 and 47% of CD patients reached clinical remission by week 14, 30 and 54. Clinical response was 83, 77 and 58%, respectively. 59, 46 and 53% of UC patients reached clinical remission by week 14, 30 and 54. Clinical response was 78, 69 and 64%, respectively. Previous anti-TNF exposure was associated with lower response and remission rates (p < 0.001). AUC14/0.05 and p > 0.001, 0.1, 0.0, 0.048) at weeks 14, 30 and 54. Mean CRP decreased significantly both in CD and UC patients by week 14, which was maintained throughout the 1-year follow-up. (CRP level decreased from 20.5 to W14: 8, W30: 8.7 and W54: 12.1 mg/ L in CD and from 29.5 to W14: 8.5, W30: 13 and W54: 12.3 mg/L in UC). 21 (6.6%) patients had infusion reactions, 23 (7.9%) patients had infections and 1 death occurred.

Conclusion: This prospective nationwide cohort shows that CT-P13 is effective and safe in inducing and maintaining remission in both CD and UC. Efficacy was influenced by previous anti-TNF exposure.

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

OP146 COST-UTILITY OF BIOSIMILAR INFILXIMAB (INFLECTRA®) FOR THE TREATMENT OF LUMINAL CROHN’S DISEASE IN NINE EUROPEAN COUNTRIES
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Introduction: Biosimilar infliximab (Inflectra®) has been approved by the European Medicines Agency for the treatment of luminal Crohn’s disease (CD). The biosimilar offers a more competitive price reduction in most European countries. Nevertheless, no study has yet compared the cost-effectiveness of originator and biosimilar agents in luminal CD patients. (Furthermore, there are no published studies reporting between-biologicals cost-effectiveness for luminal Crohn’s disease).

Aims & Methods: We aim to compare cost-effectiveness of adalimumab, infliximab, vedolizumab and biosimilar infliximab for the treatment of luminal CD in nine European countries (Belgium, France, Germany, Hungary, Italy, the Netherlands, Spain, Sweden 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 five-year time horizon. Discount rates for both costs and benefits complied with the national pharmacoeconomic guidelines.

Results: The incremental cost-utility ratio (ICUR) of the biosimilar infliximab-standard care treatment sequence vs. standard care varied between £35,170/QALY in Portugal and £62,640/QALY in Sweden. Over the five years, the average undiscounted health gain was 0.3 QALY per patient. In all countries, biosimilar infliximab was dominant relative to originator infliximab-standard care strategy.

The inclusion of additional biologicals to the treatment sequence resulted in a higher cost-utility ratio. ICURs of biosimilar infliximab-adalimumab-vedolizumab sequences ranged from £77,305/QALY to £125,643/QALY compared to the standard care. The biosimilar infliximab-adalimumab-vedolizumab sequence dominated the originator infliximab-adalimumab-vedolizumab sequence.
OP18 ROLE OF MELATONIN RECEPTORS, SURVIVIN, INSULIN GROWTH FACTOR-1 AND ITS RECEPTOR IN PROTECTIVE ACTION OF MELATONIN AGAINST INDOMETHACIN DAMAGE OF GASTRIC EPITHELIAL CELLS

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Introduction: Melatonin is a major pineal gland hormone involved in the control of sleep and circadian rhythm but present also in large quantities in the gut. This indoleamine is a potent free radical scavenger and exerts protective action against mucosal injury induced by gastric corrosive substances (ethanol, bile) and stress but the possibility that melatonin directly protects in vitro gastric epithelial cells (cytoprotection) against injury under conditions independent of systemic (endogenous) melatonin has not been explored before. Likewise, the expression of melatonin receptors (MT1 & MT2) in gastric epithelial cells; and, their spatial relation to factors promoting cell survival such as survivin, insulin like growth factor (IGF-1) and its receptor 1 p (IGFR-1b) has not been so far elucidated.

Aims & Methods: We studied whether the pretreatment with melatonin results in protection of cultured rat gastric epithelial cells against indomethacin-induced gastric mucosal injury and whether it affects the expression of MT1 & 2, survivin, IGF-1 and IGFIR-1b in these cells. In in vitro study, the cultured normal rat gastric mucosal epithelial cells (RGM1) were pretreated with vehicle or melatonin (10 μM) for 24 hrs and then exposed to: medium alone (controls), or indomethacin (IND 0.25 mM) for 4 hrs. In these cells the following were assessed: 1) cell injury under confocal microscopy, 2) survival and apoptosis using Calcein AM live cell tracking dye and MTT assay; 3) cell proliferation using BrdU assay; 4) quantitative expression of MT1 & 2, and survivin, IGF-1 and IGFIR-1b by Western blotting and immunostaining.

Results: Indomethacin induced injury in cultured gastric epithelial and submucosal structures from full thickness wall specimens of a normal rat stomach was evaluated.

Conclusion: 1) Melatonin directly protects the gastric mucosal epithelial cells against IND-induced injury and this effect is independent of systemic and neural factors, 2) rat gastric epithelial cells express melatonin receptors MT1 and MT2 that are co-localized with survivin, IGF-1 and IGFIR-1b indicating both systemic and local effects of melatonin derived from pineal gland, this indoleamine can protect the gastric epithelial cells possibly due to its local autocrine and paracrine actions and interactions with survivin, IGF-1 and its receptor.

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

OP19 RISK OF BLEEDING, 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 anti- coagulant (AC) and/or antiplatelet (AP) therapy represent a clinical challenge. Constitute of either a long-term or short-term indication 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: Method(s): 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 regarding the follow-up period, which ended on December 31st 2013 were obtained from databases of 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: A total of patients included were (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, bleeding was interrupted in 302/774 (39.4%), resumption period was 40.1% (313/774) of patients and 80.1% (572/ 714) resumed afterwards (median time 6 days (1–370). Resumption of therapy was associated with higher risk of rebleeding (3.5% vs 24/gp < 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 a higher rate of ischemic events. Resumption of AP or AC treatments later than 7 days is associated with significant higher risk of ischemic events.

Disclosure of Interest: A. Lanas: Professor Lanas has been advisor for Astra-Zeneca, Bayer and Pfizer.

All other 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. Thus, 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 [5S,3S,5-Di-tert-butyl-4-hydroxy-benzylidene)-2-thioxo-thiazolidin-4-one] and Les-5055 [3-[3,5-Di-tertbutyl-4-hydroxy-phenyl]-2-mercapto-acrylic acylid] as a novel H2S donors in promoting the resolution of inflammation and injury in small intestine. The studies were 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 hr; III, 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 NOS increased more than threefold (P < 0.01) as well as the content of nitrite enhanced in two times while arginase activity decrease more than 4 fold (P < 0.01); enhanced activity of lipid peroxidation manifested by rise of MDA concentration (P < 0.01), MPO activity enhanced more than 4 fold (P < 0.01) and catalase activity – by 32% (P < 0.01). Compound Les-5054 displayed significant cytoprotective effect and decreased the total area of hemorrhagic lesions for 63% (P < 0.01). The administration of Les-5054 on the background of IM decreased the activity of iNOS for 35% (P < 0.01), and activity of eNOS increased for 52% (P < 0.01), MPO activity enhanced more than 4 fold (P < 0.01) as compared with indices of the second group.

Conclusion: Administration of 4-thiazolidinone derivatives on the background of indomethacin induced injury reduce the activity of iNOS, myeloperoxidase, intensity of lipid peroxidation and increase generation of H2S, that may be linked with the structure of this compounds. However compound Les-5054 showed more efficacious effect and antioxidant properties than compound Les-5055. Thus, the novel 4-thiazolidinone derivatives, particularly compound

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Aspirin is a potent anti-platelet agent used for the prevention of cardiovascular and cerebro-vascular diseases. In this study, we 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 non-users in a ratio of 1:2 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 mortality rates. Subgroup analyses were performed for those with ulcer bleeding, or for those with regular aspirin prescribed.

Results: A total of 4,564,100 subjects were identified in the system between year 2000 and 2004, and 254,887 of them (5.6%) were prescribed aspirin for at least one 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 prescribed 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 = 0.76, 95% CI = 0.73 to 0.80). Women in aspirin group showed significantly higher incidence of GI bleeding (OR = 1.77; 95% CI = 1.74 to 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 even after multivariable adjustments.

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 incidence 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 intensive analysis of 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. Method: Patients who underwent POEM were compared for the treatment of achalasia and SEDs at 12 tertiary-care centers (5 US, 4 Europe, 2 Asia and 1 Australia) between 2011 and 2015 were used in a case-control study. Cases were defined by the occurrence of any AEs related to POEM procedure. Control patients were selected for each AE case by matching for age, gender, disease classification (type IIH vs. type IIIH/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. Over 137 patients (7.5%) had one or more 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 102 (74.5%), 26 (19%) and 9 (6.5%) patients, respectively. Among the 9 severe AEs, 2 were related to endoscopy (with vasoconstrictor, 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 Charlson comorbidity index/ASA class, prior pneumatic dilatation, AEs related to POEM procedure. Control patients were selected for each AE by preparing the index patient for POEM as a safe therapeutic modality with an overall safety of 99.8%

Conclusion:

A total of 1826 patients underwent POEM during the study period. Overall, 153 AEs occurred in 137 patients (7.5%). 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 102 (74.5%), 26 (19%) and 9 (6.5%) patients, respectively. Among the 9 severe AEs, 2 were related to endoscopy (with vasoconstrictor, 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 Charlson comorbidity index/ASA class, prior therapy, sigmoid esophagus, operator specialty, direction of myotomy (anterior vs. posterior), type of used knife, extent and length of myotomy, and operator endoscopy training. The rate of procedure was significantly longer in cases as compared to controls (123 ± 49 vs. 103 ± 38, p = 0.002). Length of stay was significantly higher in patients who experienced AEs (4.9d vs. 2.7d, p < 0.001).

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

References


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

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

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

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

Results: A total of 347 patients underwent POEM (mean age 47 years, 48% males). Seventy-eight patients (22.5%) had type I achalasia, 174 type II (50.1%), 40 type III (11.5%), 2 Jackhammer esophagus (0.6%), 4 distal esophageal spasm (1.1%), 1 nutcracker esophagus (0.3%); in 48 patients (13.8%) achalasia type was not classified (ie: standard manometry or incomplete examination). Before POEM, 52 patients had undergone pneumatic dilation (PD), 8 surgical myotomy and 1 Heller myotomy. All the above mentioned complications were treated conservatively. Four patients were lost at follow-up. A minimum 6-month follow-up was available for 274 patients (mean follow-up 19 months). Clinical success was achieved in 95% of patients. Thirteen patients had symptoms recurrence: 7 underwent successful PD, 3 surgery, 3 received no treatment because of mild symptoms. Clinical success slightly decreased with time, being 97%, 97%, 93%, 85%, 72% and 67% after 6, 12, 24, 36, 48 and 60 months, respectively. 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 effectively controlled with PPI in all the patients but 2 who complained with heartburn and regurgitations.

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

Disclosure of Interest: All authors have declared no conflicts of interest.
In this large multicenter study, POEM was safe and effective for treatment of achalasia. Technical success, clinical success and safety of POEM in achalasia patients with and without prior HM are comparable to those in patients with no prior HM. The safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is comparable to that of patients with no prior HM, the safety profile of POEM is compar
**OP160 EXPRESSION OF CD161 ON CD4+ T CELLS PROMOTES HEPA-VIRUS-RELATED 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+ 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 experiments.

**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 IFN-γ production, TNF-α, 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 CD1 and using imipramine to inhibit aSM could down-regulate CD4+ T cell-proliferation and production of IFN-γ and IL-17, especially for IL-17. HSCs express lectin-like transcript-1 (LTL1), the only ligand of human CD161. HBV-stimulated HSCs upregulated LTL1 expression in the co-culture system of HSCs and CD4+ CD161+ T cells. CD161-LTL1 interaction not only promoted the proliferation and activation of HSCs, but increased IL-17 and IFN-γ production of CD4+ CD161+ T cells as well. Knocking down of CD1 on CD4+ CD161+ T cells or LTL1 on HSCs could partly reverse the aforementioned effects. In HSCs-CD4+ CD161+ T cells co-culture system, expression of pro-fibrotic genes in HSCs were inhibited. However, when CD161 was overexpressed on CD4+ CD161+ T cells, we detected a reactivated HSCs phenotype.

**Conclusion:** Our data revealed that the expression of CD161 on CD4+ T cells, we detected a reactivated HSCs phenotype. CD161 and using imipramine to inhibit aSM could down-regulate CD4+ T cell-proliferation and production of IFN-γ and IL-17, especially for IL-17. HSCs express lectin-like transcript-1 (LTL1), the only ligand of human CD161. HBV-stimulated HSCs upregulated LTL1 expression in the co-culture system of HSCs and CD4+ CD161+ T cells. CD161-LTL1 interaction not only promoted the proliferation and activation of HSCs, but increased IL-17 and IFN-γ production of CD4+ CD161+ T cells as well. Knocking down of CD1 on CD4+ CD161+ T cells or LTL1 on HSCs could partly reverse the aforementioned effects. In HSCs-CD4+ CD161+ T cells co-culture system, expression of pro-fibrotic genes in HSCs were inhibited. However, when CD161 was overexpressed on CD4+ CD161+ T cells, we detected a reactivated HSCs phenotype.

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

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**OP162 The Accuracy of WAVSTAT Version 4 Optical Biopsy Forceps in Characterizing Colorectal Polyps Less Than 10 mm: A Prospective Blinded Study**

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

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

**Disclosure of Interest:** R. W. Leong: Endochoice USA investigator-initiated grant All other authors have declared no conflicts of interest.

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

<table>
<thead>
<tr>
<th>WAVSTAT alone</th>
<th>WLE+NBI assessment</th>
<th>Combination of WAVSTAT + endoscopic assessment (algorithmic approach)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>97.6% (95% CI 0.88-0.95)</td>
<td>85.0% (95% CI 0.77-0.89)</td>
</tr>
<tr>
<td>Specificity</td>
<td>46.9% (95% CI 0.44-0.88)</td>
<td>77.2% (95% CI 0.61-0.82)</td>
</tr>
<tr>
<td>NPV</td>
<td>96.8% (95% CI 0.85-0.91)</td>
<td>91% (95% CI 0.75-0.84)</td>
</tr>
<tr>
<td>PPV</td>
<td>54.7% (95% CI 0.28-0.77)</td>
<td>66% (95% CI 0.44-0.79)</td>
</tr>
<tr>
<td>Surveillance interval (% of patients celled 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>

**References:**

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Patients known to have inflammatory bowel disease or colorectal cancer were excluded from the study. Polyps sized <10 mm were assessed in real time by high definition white light, NBI and WavSTAT version 4 optical biopsy forceps. Standard techniques were used for polypectomy. Histopathological specimens were read separately by two expert GI pathologists blinded to the results of the NBI/Wavstat4 endoscopy. 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: Of 126 polyps <10 mm in size but only predicts surveillance intervals correctly in 81.2% of patients. An algorithmic approach combining Wavstat4 and endoscopic assessment is detailed in the table. Wavstat4 had a NPV of 95.8% and predicted 100% of surveillance intervals correctly.

Conclusion: Wavstat4 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.

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

OPIO DEEPER AND DEEPER INTO THE SMALL BOWEL IN PEDIATRIC CROHN'S DISEASE: PROSPECTIVE COMPARATIVE STUDY BETWEEN SMALL INTESTINE CONTRAST ULTRASONOGRAPHY (SICUS) AND MAGNETIC RESONANCE IMAGING

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Introduction: Small bowel (SB) assessment is essential for the proper management of pediatric Crohn's disease (CD). Magnetic resonance imaging (MRI) is considered the gold-standard for the evaluation of small bowel (SB). However, MRI is expensive, it requires a strong compliance and a considerable amount of oral contrast to adequately digest the intestinal lumen. Small intestine contrast ultrasonography (SICUS) is non-invasive, low cost and generally well-tolerated by pediatric patients (pts).

Aims & Methods: We aimed to compare the diagnostic accuracy of SICUS and MRI in detecting presence and site of SB disease and in assessing strictures and SB lesions. Children with suspected CD or relapse of SB known CD were prospectively enrolled. All underwent SICUS, MRI and ileocolonoscopy, performed by different operators blinded to other results. The SB was subdivided into 5 segments: jejunum, ileum, ileocolic junction, ileo-transverse and transverse colon. The concordance (k) between the two techniques for presence and site of lesions was calculated according to Landis and Koch criteria. For the TI, sensitivity (SE) and specificity (SP) were also assessed, with ileocolonoscopy as reference standard. One-way ANOVA with Kruskal-Wallis post-test was applied to compare the extension (cm) of disease in the different segments.

Results: 66 pts (median age 13 years; range 7–18), 23 suspected, 43 known CD were included. The overall concordance (k) between SICUS and MRI for presence of SB lesions was 0.94 (ES 0.66; 95% CI 0.91–0.97). The k for segments was: jejunum 0.67 (ES 0.1, 95% CI 0.40–0.8), ileum 0.91 (ES 0.06; 95% CI 0.76–1), TI 0.91 (ES 0.06; 95% CI 0.8–0.9). SE and SP (%)? 0.80) of SICUS and MRI for TI lesions were 98, 100 and 93, respectively. There was no difference in the assessment of disease extension between SICUS and MRI (p ns). The overall k for strictures was 0.62 (ES 0.1, 95% CI 0.40–0.8). SE and SP (%)? 0.80) of SICUS and MRI for TI strictures were 100, 100 and 92, respectively. MRI provided 7 false positive results, not detected at SICUS nor confirmed at endoscopy.

Conclusion: The diagnostic performance of SICUS is comparable to that of MRI in pediatric CD. SICUS is useful in assessing SB strictures, probably with higher accuracy than MRI. SICUS might represent a first-line tool in pediatric CD, able to reduce costs and to post-pone or even avoid more invasive and expensive investigations.

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

Reference

OPI64 A ROLE FOR T CELL CLONAL EXPANSIONS IN THE POST-OPERATIVE RECURRENCE IN CROWN'S DISEASE: A STUDY FROM THE REMIND GROUP

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

The aim of the study was to explore the impact of the presence of T cell clonal expansions in the inflamed tissue at time of surgery on the risk of post-operative endoscopic recurrence, and to analyse the correlation between the persistence of these T cell clones in the neoterminal ileum and inflammation. The REMIND Post-Operative study has been performed in 9 centers, collecting data at time of surgery (M0) and of endoscopy (performed at M6), associated with an extensive bio-banking. Clinical, endoscopic and histological 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 month 6. 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. Remission post seven patients were included in the REMIND cohort; the analysis of 33 (88%) 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, and at M6, T cells with persistent clonal expansions were more frequent in patients with endoscopic 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 persistent T cell clonal expansions in the neoterminal ileum 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

OPI65 TARGETED CHEMICAL ANALYSIS OF THE COLON CANCER MICROBIOME USING DESORPTION ELECTROSPRAY IONISATION MASS SPECTROMETRY IMAGING (DESI-MSI)

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Introduction: The gut microbiome is an important modulator of colorectal (CRC) cancer risk. Here we describe a novel methodology for the targeted analysis of the
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 post-operative 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 Mohur and Stamp), target bacteria including Fusobacterium spp., E.Coli and Bifidobacteria were identified. A chemical database was then constructed using Rapid Evaporative Ionisation Mass Spectrometry (REIMS) from pure cultures of the target microbes. Desorption Electrospray Ionisation Imaging Mass Spectrometry (DESI-MSI) was then performed to provide a spatially resolved map of the mucosal microbial lipidome. This approach compared masses for 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 disease specific regions based on co-segmentation 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 = 0.75. Increased long chain fatty acids were seen in malignant tissue and phosphatidylcholines 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 Firmicutes, 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.

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

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Introduction: Heterogeneity in IBD patient populations is widely cited as the main barrier to efficient clinical trials and development of therapies with high clinical efficacy. We and others hypothesize that phenotypic heterogeneity is a direct result of molecular heterogeneity in disease-driving molecular pathways. We have calculated that not extending our methodology for defining molecular heterogeneity in a manner independent of known biology.

Aims & Methods: Whole-genome transcriptomic data was generated for colonic biopsies from 266 ulcerative colitis patients and 108 healthy normal controls. Subjects were scored based on enrichment of 113 co-expression modules, or lists of correlated genes, derived from colonic biopsies from both UC and CD biopsies. Scores for each subject and co-expression module were computed using the gene set variation analysis algorithm. Co-expression modules were then hierarchically clustered into 4 module clusters and annotated with pathways using the union of genes within each of the 4 module clusters. Each subject was then reclassified based on the 4 module clusters by taking the median enrichment score of the modules within each module cluster. IBD subjects and normal controls were then hierarchically clustered into 4 subgroups using the 4 module clusters and assessed for relationship to anti-TNF response.

Results: The 4 module clusters represented distinct pathway sets which we summarized as inflammation/monoocytes, mucosa/pro-regulatory, T cells/metabolism and mitochondria/metabolism. Patients belonging to the subgroup characterized by the highest enrichment for the inflammation/monoocyte module cluster trended towards lower expression levels to anti-TNF therapy. Conversely, the highest relative response rates to anti-TNF therapy were observed in the subgroup characterized by the lowest enrichment for the inflammation/monoocyte module cluster. These subgroups also contained normal healthy controls. Enrichment values for the 113 co-expression modules were calculated (r = 0.49) with enrichment values for the inflammation/monoocyte module cluster.

Conclusion: We find that there is pronounced molecular heterogeneity in the pathways present in colonic biopsies from UC patients. We also show that this hyperlink can be used to determine the ability of patients to respond to anti-TNF therapy. This suggests that molecular stratification may be a key step towards designing smaller clinical trials and identifying meaningful personalized medicine approaches for IBD patients.

Disclosure of Interest: C. Monast: Employee of Janssen Research and Development, LLC
A. Stojsimirovic: Employee of Janssen Research and Development, LLC
R. Dobrin: Employee of Janssen Research and Development, LLC
C. Brodmerkel: Employee of Janssen Research and Development, LLC
F. Baribaud: Employee of Janssen Research and Development, LLC

OP167: COMPREHENSIVE CIRCULATORY TRANSCRIPTOMINE AND PROTEOMIC PROFILING IN NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASES: A MULTI-CENTER COHORT STUDY

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

Aims & Methods: Gene expression patterns from whole blood RNA and proteomic profiles from serum were assessed from patients using targeted RNA-seq (IEx AmpSeq Transcriptional Profiling 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 567 genes were differentially expressed between IBD and controls. Using hsCRP to adjust for inflammatory status, 1440 remained significant. The most differentially expressed genes were CD-177 (Bonferroni corrected p = 2.3x10⁻⁸), VBP1 (p = 2.9x10⁻⁷) and S100 proteins (S100A9, p = 7.5x10⁻⁹ and S100A1 p = 10⁻⁸). 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 = 4.1x10⁻⁹) and IL6 (4.1x10⁻⁹ and p = 1.7x10⁻⁹). Protein expression profiles were available and correlated with RNA expression. 39 proteins showed significant correlation with gene expression including OSM (rho = 0.51, Hs00920789s_m1, p = 9.1x10⁻⁴) and MMP12 (rho = 3.4x10⁻²) while other markers such as CXCL9 show poor correlation (rho = 0.16, p = 0.04). As biomarkers, top 2 serum markers were able to discriminate IBD from controls with a similar area under the receiver operator characteristics curve (AUC) of 0.75 and 0.74 respectively. Individually these markers outperformed hsCRP (n = 619, AUC 0.64, p for comparison = 2.7x10⁻⁴ vs. MMP12) and albumin (AUC 0.66, p = 0.004 vs MMP12). 6 proteins differentially UC from CD including MMP12 (p = 4.6x10⁻⁵). In CD, MMP12 levels were lower in those with small bowel involvement/Montreal Classification L1, L3 and L4 vs L2 (p = 0.009) while in UC, MMP12 levels were significantly higher in extensive disease (Paris classification E1 and E2 vs. E3, p = 5.8x10⁻⁵).

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 Characterurer Speaker Fees J. Jahnsen: J has served as a speaker, and a advisory board member for MSD, Tilott, Ferring, AbbVie, Celtrion, Orion Pharma, Takeda, Napp Pharm, Meda, AstroPharma, Hikma and Pfizer.
F. Gomollon: Advisor: Grifols, Abbvie, MSD. Travel Grants: Abbvie, MSD. Research Grants (Department) MSD
J. Satsangi: JS has served as a speaker, and 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></td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>224 (54.9)</td>
<td>223 (54.7)</td>
<td>225 (55.1)</td>
<td></td>
</tr>
<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>26.6 (4.4)</td>
<td>0.751</td>
</tr>
</tbody>
</table>

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

| Screening FIT+ | 242 (59.3) | 242 (59.3) | 222 (54.4) | p = 0.0007 |
| Screening FOBT+ | 18 (4.4) | 19 (4.7) | 19 (4.7) | p = 0.865  |

**Family history of colorectal cancer**

| 47 (11.5) | 47 (11.5) | 45 (11.0) | 0.128  |

**Primary colonoscopy**

| 101 (24.8) | 100 (24.5) | 116 (29.2) | p = 0.870  |

**Procedural outcomes**

| Cecal intubation time (final), n (min) | 402 (98.5) | 400 (98.0) | 399 (97.8) | p = 0.098  |
| Cecal intubation time, mean (SD), min | 10.1 (5.4) | 9.4 (5.7) | 9.7 (6.7) | p = 0.364  |
| Withdrawal time without polypectomy, mean (SD), min | 9.5 (3.2) | 9.5 (3.6) | 8.9 (3.1) | p = 0.145  |

**Overall advanced adenoma detection rate, n (%)**

| 79 (19.4) | 70 (17.2) | 58 (14.2) | p = 0.413  |

**Overall ADR, n (%)**

| 201 (49.3) | 177 (43.4) | 165 (40.4) | p = 0.395  |

**Infused water during insertion, median (range), mL**

| 550 (50–6500) | 400 (50–2000) | 0 (0–1000) | p = 0.145  |

**Procedural outcomes**

| Right colon BBPS score (SD) | 2.6 (0.6) | 2.4 (0.6) | 2.4 (0.7) | p = 0.870  |
| Cecal intubation rate (final), n (%) | 402 (98.5) | 400 (98.0) | 399 (97.8) | p = 0.870  |
| Right colon BBPS score (SD) | 2.6 (0.6) | 2.4 (0.6) | 2.4 (0.7) | p = 0.870  |

**Aims & Methods:**

In a prospective, multi-site randomized controlled trial we

**Limitations of these studies were their retrospective analysis and/or investigators**

To assess adequacy of blinding the withdrawal, the second endoscopist was asked to guess the insertion technique.

**Results:** All results are reported in Table 1. Demographics, clinical features, indications, cecal intubation rates and procedure times were comparable.

**Conclusions:** The current study shows that in European screening patients, WE

**References**


SD, standard deviation; FIT+, positive at fecal immunochromatographic test; FOBT+, fecal occult (guaiac-based) blood testing; Advanced adenomas: adenomas ≥10 mm in diameter, or high grade dysplasia, or with ≥20% villous components. 1 Chi-squared; 1 t test; ANOVA, analysis of variance.
OP169 EFFICACY OF ENDOCUFF-ASSISTED COLONOSCOPY IN THE DETECTION OF COLORECTAL POLYPS USING THE NEWLY INTRODUCED OPTICAL ENHANCEMENT (OE) TECHNOLOGY

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Introduction: Colonoscopy is the gold standard for detecting colorectal adenomas and cancers. Endoscopic surveillance has been shown to be effective for preventing colorectal cancer. Although the detection of colorectal polyps at an early stage is important, the endoscopic visualization of early neoplasia can be difficult.

Aims & Methods: The EndoCuff is a new device that can be attached to the tip of the colonoscope to hold the colon fold away from the field of view during withdrawal. The aim of this study was to compare the polyp and adenoma detection rates between EndoCuff-assisted colonoscopy and standard colonoscopy. This randomized prospective study was conducted at two academic endoscopy departments in Japan. The subjects were 446 patients who underwent a complete colonoscopic examination from April 2015 to September 2015. The EndoCuff group included 239 patients. Cecal intubation rate, insertion time, withdrawal time, pain score, complications, polyp detection rate, and adenoma detection rate were assessed.

Results: There were no differences between the groups in cecal intubation rate, insertion time, withdrawal time, pain score. Cecal intubation was achieved in 235 patients (98.8%) in the EndoCuff group. In four patients, the EndoCuff-assisted examination had to be stopped in the sigmoid colon due to severe stenosis caused by diverticula or cancers. These examinations were completed with a standard colonoscope. Superficial mucosal erosions occurred in 54 patients (23.0%) during withdrawal in the EndoCuff group but no major complication occurred. The polyp detection rate in patients increased by 12% (62% vs. 50%, P = 0.013) and the adenoma detection rate increased by 15% (55% vs. 40%, P = 0.001) with the use of EndoCuff. The advanced adenoma detection rate was higher in the EndoCuff group but no statistically significant difference was found (6.1% vs. 3.2%, P = 0.17).

Conclusion: EndoCuff-assisted colonoscopy enabled a significantly higher polyp and adenoma detection rate than standard colonoscopy. This attachment improved important quality measures used for screening colonoscopy.

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

OP170 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 allowing differentiation of hyperplastic and adenomatous colorectal polyps in vivo. 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, nurses and GI fellows. At least, a pilot clinical evaluation was performed during real-time colonoscopy.

Results: A simple classification system for differentiating hyperplastic and adenomatous colorectal lesions by using OE was developed and validated. Diagnosis was made in 85% to 99% of polyps with high-confidence. Sensitivity ranged from 92% to 96% and specificity ranged from 86% to 93%, respectively. During real-time colonoscopy, diagnosis was made with high-confidence in 90% of polyps with sensitivity of 96%, specificity of 92%, and accuracy of 95%. Positive and negative predictive values were 96% and 93%, respectively.

Conclusion: We developed and validated for the first time a simple and effective classification system for differentiating hyperplastic and adenomatous colorectal lesions by using the newly introduced OE-technology during real-time colonoscopy. These findings need to be evaluated in future prospective, controlled, and blinded clinical trials.

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

OP171 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 (LNPCPs) is challenging, with a significant proportion of them containing malignancy. The potential to improve the diagnostic work-up and treatment might imply higher mortality, effect on the quality of life of the diagnosed individuals, and association with extra costs for health services.

Aims & Methods: We previously trained all endoscopists (9 faculty and 14 trainees) at Maastricht UMC+ 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-polypoid (flat and depressed) colorectal neoplasms using lectures, videos and individual feedback. Phase 2: Training in endoscopic resection techniques using video-training 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 (cecal intubation rate, adenoma and polyp detection 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 histopathology. We defined LNPCPs as large (>20 mm non-pedunculated (i.e. sessile, flat, depressed, combinations) colorectal neoplasms (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 downward. 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 59.9 years, 46% male), of which 1768 in 176 (1.9%) patients (mean age 68.3 years, 56.3% male) were LNPCPs. The majority (65.9%) of LNPCPs were located in the proximal colon. Mean size was 30 mm (20-100 mm). Ninety-six LNPCPs (46.8%) were sessile and 109 (55.2%) LSTs. LNPCPs contained advanced histopathology more often than sessile hyperplasia adenoma (29.2%), 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-LNPCPs more often contained advanced histopathology than LST-LNPCPs (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 LNPCP ≥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 mortality rate to surgery increased from 0% in the first half of the study period to 16.7%. Delayed bleeding occurred in 6 (0.6%) 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 LNPCP. Lesion size, sessile shape and distal location were independent predictors of advanced histology. Careful case selection which considers both patient-related factors and endoscopic prediction of advanced histopathology is critical to optimize the outcomes of endotherapy for LNPCP.

Disclosure of Interest: S. Sanduleanu: Consultancy: Pentax Europe All other authors have declared no conflicts of interest.

Reference

OP172 HEALTH EFFECTS AND COSTS DUE TO POST-COLONOSCOPY COLORECTAL CANCER

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Introduction: Colorectal cancers (CRC) detected shortly after a colonoscopy are referred to as a post-colonoscopy colorectal cancer (PCCRC), and has been reported to represent 2-9% of all CRCS, depending on the definition, setting and methods for estimating its incidence. The delay in detection of the CRC might imply higher mortality, effect on the quality of life of the diagnosed individuals, and association with extra costs for health services.

Aims & Methods: The aim of this study was to estimate the loss of health and costs due to CRC-diagnosis in PCCRC in Sweden.

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

Reference
Aims & Methods: The DY of multiple rounds of FIT-screening to one-time screening by sigmoidoscopy 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 simulations 3% of the PCCRC was expected to be at an adenoma stage at the time of the prior colonoscopy. The extra cost per case is estimated to be €1,922. 000 less if the patients had been diagnosed at the time of the prior colonoscopy. The extra cost per case is €1,305.

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

Recent register study of colonoscopies in Sweden during 2001–2010 revealed that 18,244 individuals were diagnosed with CRC within 0–36 months after a colonoscopy. A CRC was defined as a PCCRC if it was detected within 6–36 months after a colonoscopy in which no cancer was detected. A total of 1,473 (8.1%) PCCRCs were found in the register study and included in this study. A lifelong mathematical Markov model was employed to calculate the lifelong health effects and resource usage for PCCRC. The effects were calculated by simulating the hypothetical lives of the individuals diagnosed with PCCRC if their condition had instead been diagnosed at the time of colonoscopy. These lives were then compared with simulated lives of individuals diagnosed with PCCRC, in terms of life expectancy, quality of life and costs. The simulation model was constructed by using Swedish registry data, supplemented with data from the published scientific literature and databases.

Results: Our simulation indicated that if the CRC of the individuals diagnosed with PCCRC had been diagnosed at the prior colonoscopy, there would have been a down-staging of the cancer. The proportion of patients at each cancer stage shifted from 53% in stage I-II, 35% in stage III and 9% in stage IV at the time of the index colonoscopy, to 47% in stage I-II, 31% in stage III and 22% in stage IV, respectively, when diagnosed as a PCCRC. Additionally, based on our simulations 3% of the 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 1,511 life-years or, expressed differently, 1,275 quality-adjusted life-years, compared to being ones detected at colonoscopy. Additionally, the delay in detection was also associated with higher lifetime costs due to an increased need of health care services related to CRC. The cumulative cost was estimated to be €1,922. 000 less if the patients had been diagnosed at the time of the prior colonoscopy. The extra cost per case is €1,305.

Conclusion: Our simulation results imply that false negative colonoscopies cause significant loss of life-years and quality of life in the affected individuals. This, together with higher costs, motivates further efforts to improve the quality of colonoscopies.

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

OP174 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, comparisons between these screening methods was mainly focused on one-time endoscopic screening to one-time FIT screening. A fair comparison of diagnostic yield (DY) of FIT would comprise cumulative DY after multiple rounds of FIT screening. The aim of our study is to compare the DY of multiple rounds of FIT-screening to one-time screening by sigmoidoscopy and colonoscopy.

Aims & Methods: Demographic data of 30,007 randomly chosen individuals aged 50–74 were obtained from municipal population lists of the municipality of Rotterdam (18% of the Dutch population aged 50–74) in 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 invites 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 invites was highest for colonoscopy (24%) compared to FIT (13%; p < 0.001) and sigmoidoscopy (3%; p < 0.001). For invites 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 endoscopic screening: 4.7% for 2 rounds of FIT compared to 7.3% for sigmoidoscopy (p < 0.001), and 6.1% for 4 rounds of FIT compared to 9.1% colonoscopy (p < 0.001).

Conclusion: In this population-based CRC screening cohort, we demonstrated that multiple rounds of FIT screening detects significantly more advanced neoplasia per invite compared to one-time sigmoidoscopy and colonoscopy screening, and with significantly fewer colonoscopies needed. Colonoscopy detected more advanced neoplasia per participant. However, due to low participation in colonoscopy screening, FIT seems most effective in population-based CRC screening.

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

TUESDAY, OCTOBER 18, 2016 08:30–10:00
SURGERY IN IBD – ROOM L7

OP174 OUTCOMES OF EMERGENCY ADMISSIONS WITH CROHN’S DISEASE IN ADULTS IN ENGLAND BETWEEN 2004 AND 2014
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Introduction: Between 2006 and 2010, the UK national audit of adult inflammatory bowel disease admissions revealed a small but non-significant fall in mortality. John’s disease (CD) fell from 1.3% to 0.8%, an 18% fall in the rate of prescription of anti-TNF therapy on admission from 3.9 to 0.8% and a fall in mortality in Crohn’s disease (CD) from 1.3 to 0.8%, an 18% fall in the rate of prescription of anti-TNF therapy on admission from 3.9 to 0.8% and a fall in mortality in Crohn’s disease (CD) from 1.3 to 0.8%, an 18% fall in the rate of prescription of anti-TNF therapy on admission from 3.9 to 0.8% and a fall in mortality in Crohn’s disease (CD) from 1.3 to 0.8%, an 18% fall in the rate of prescription of anti-TNF therapy on admission from 3.9 to 0.8% and a fall in mortality in Crohn’s disease (CD) from 1.3 to 0.8%, an 18% fall in the rate of prescription of anti-TNF therapy on admission from 3.9 to 0.8% and a fall in mortality in Crohn’s disease (CD) from 1.3 to 0.8%, an 18% fall in the rate of prescription of anti-TNF therapy on admission from 3.9 to 0.8% and a fall in mortality in Crohn’s disease (CD) from 1.3 to 0.8%, an 18% fall in the rate of prescription of anti-TNF therapy on admission from 3.9 to 0.8% and a fall in mortality in Crohn’s disease (CD) from 1.3 to 0.8%, an 18% fall in the rate of prescription of anti-TNF therapy on admission from 3.9 to 0.8% and a fall in mortality in Crohn’s disease (CD) from 1.3 to 0.8%...
OP75 IS THE ‘RESET’ SURGERY EFFECTIVE FOR CROHN’S DISEASE PATIENTS REFRACTORY TO ANTI-TNF THERAPY?

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Introduction: Anti TNF-alfa agents (anti-TNFα) are currently the most effective therapeutics for Crohn’s disease (CD). Some of CD patients under anti-TNFα therapy, however, need surgery because of disease progression. Surgical resection (‘Reset’) usually leads to the elimination of the intestinal regions with disease activity. The aim of the 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 after surgery. 29 refractory to 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-refractory treatment 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. All analyses were performed as an intention to treat, anti-TNFα therapy, hospitalization, or surgery due to worsening of abdominal symptoms, CRP elevation with the evidence of endoscopic recurrence.

Results: Patients of the TNFα-naïve group showed significantly higher rate of remission than those of the TNFα-refractory 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, et al. was significantly associated with relapse after surgery: 19 refractory to preoperative anti-TNFα therapy after preoperative surgical treatment 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. All analyses were performed as an intention to treat, anti-TNFα therapy, hospitalization, or surgery due to worsening of abdominal symptoms, CRP elevation with the evidence of endoscopic recurrence.

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 anti-TNFα treatment after preoperative surgery tend to relapse after surgery. Those patients may need additional treatment besides anti-TNFα therapy or increase in the dosage amount of the anti-TNFα agent.

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

OP76 IMPACT OF MINIMALLY INVASIVE 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 this study is to assess the impact of minimally invasive surgery on quality of life after surgery for Crohn’s disease terminal ileitis. From June 2010 to December 2015, one surgeon interviewed by telephone and responded to the generic European Glacial Global Quality of Life (CQGOL) 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 CQGOL 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 CQGOL score was directly correlated with minimally invasive surgery. Anti-TNF therapy during admission was 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.

Conclusion: Minimally invasive surgery was associated to a better quality of life and body image perception. This results is probably due in part to the beneficial effect of minimally invasive surgery on body image but also by the less severe disease of these patients (less recurrent Cd as indication for surgery or simpler surgery). Quality of life is essentially predicted by current disease activity and minimally invasive surgery. Finally, minimally invasive surgery tends to be associated to a less frequent CD recurrence.

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: Pelvic exenteration encompasses all the available surgical techniques for treating locally advanced or recurrent disease of the pelvis that cannot be managed by conventional surgery. However, the extent of pelvic dissection may vary widely depending on the surgeon’s experience and preference. The term ‘close rectal dissection’ (CRD) has been used to describe a surgical technique that leaves around 3–5 cm of rectal remnant, with the rationale that it could reduce this complication by leaving the rectal mesentery in situ to minimize dead space cavity compared to total mesorectal excision (TME).

Aims & Methods: The aim of this study was to compare perineal wound healing in UC and CD patients who underwent close rectal dissection (CRD) or TME. Since it has been suggested that Crohn’s mesenteric adipose tissue is involved in CD pathology with reduced regulatory potential of wound healing and immune cells in CD patients with the balance between CD3 lymphoid and CD16+ myeloid cells skewed significantly towards the myeloid popu-

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 27 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 63.4%, p = 0.066) were seen. No significant differences in outcome between the techniques in UC. Perineal complications occurred significantly more frequently in CRD 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 CD1+ 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.

Discussion: In UC, significantly less perineal complications were seen after proctocolectomy or completion proctectomy, compared to CD with higher healing rates. >50% of CD patients had perineal complications and impaired healing, which was seen more frequently after CRD. These findings can probably be explained by the increased pro-inflammatory myeloid cell population with decreased wound healing macrophages, irrespective of the presence of a deferred stoma.
Evidence has been accumulating indicating that the appendix has an limited and the therapeutic mechanism is not yet understood. The objective of endpoints were remission, improvement in IBDQ score and failure. Results performed after 2004, a longer duration of disease at the time of IRA and having spondyloarthropathy. Univariate analysis identified factors associated with IRA failure: IRA proctectomies were performed for refractory proctitis, and 20% for rectal neo-

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.

TUESDAY, OCTOBER 18, 2016
08:30-10:00
GI INFECTIONS FROM MECHANISMS TO TREATMENT – ROOM LB

OP110 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 acid 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 this 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 clinical (Clinical Practice Research Datalink) and secondary (Hospital Episode Statistics) care 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 Clostridium difficile infection was 3.3/1000 person-years for those with pernicious anaemia while it was 1.7/ 1000 person-years for controls. Patients with pernicious anaemia had a 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. Ohman: 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.

Reference:

OP109 CONSISTENT AND REPRODUCIBLE PRODUCTION OF A MICROBIOTA-BASED DRUG FOR RECURRENT C. DIFFICILE INFECTION: APPLICATION OF A NOVEL DIAGNOSTIC FOR DYSBIOSIS
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Introduction: Antibiotics are the first-line treatment for C. difficile infection (CDI). However, the most commonly prescribed antibiotics for CDI are associated with high recurrence rates. Antibiotics have been shown to disrupt the intestinal microbiota to its pre-disease state protects against recurrence. There is an unmet need for a standardised, reproducible and affordable therapy for recurrent CDI. RBX2600, a
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 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 for 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 allows the calculation of the faecal bacterial abundance profile as well as potentially clinically relevant alterations in the microbiome over time. These capabilities of the GA-test were used to assess the production processes for RBX2660. The differences in bacterial abundance between the DP and DS were calculated from log2fold 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.

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

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Signal Strength in DP vs. DS</th>
<th>Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteroidetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>Increased 0.07 (0.03, 0.11)</td>
<td></td>
</tr>
<tr>
<td>Parabacteroides</td>
<td>Increased 0.12 (0.07, 0.17)</td>
<td></td>
</tr>
<tr>
<td>Alitiges</td>
<td>Increased 0.17 (0.11, 0.23)</td>
<td></td>
</tr>
<tr>
<td>Firmicutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lachnospirae</td>
<td>Decreased −0.13 (−0.15, −0.11)</td>
<td></td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Decreased −0.16 (−0.20, −0.13)</td>
<td></td>
</tr>
<tr>
<td>Negativicutes</td>
<td>Increased 0.03 (0.01, 0.06)</td>
<td></td>
</tr>
<tr>
<td>Clostridia</td>
<td>Decreased −0.18 (−0.20, −0.16)</td>
<td></td>
</tr>
<tr>
<td>Actinobacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bifidobacterium</td>
<td>Decreased −0.33 (−0.38, −0.28)</td>
<td></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:**


**OP182 A METHYL DONOR MOLECULES-SUPPLEMENTED DIET ERADICATES E. coli POPULATION AND METHYLATES CEACAM6 PROMOTER DECREASING ITS EXPRESSION IN COLON EPITHELIAL CELLS IN MICE**

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**Introduction:** Adhesion-invasive *E. coli* are clearly involved in triggering and maintaining ileal CD. AIEC bacteria adhere to the enterocytes through high affinity interaction between their variant type one pili and abnormally expressed CEACAM6 protein on host cells. We previously reported an original mechanism of CEACAM6 regulation depending on DNA methylation factors HIF-1 binding site (HRE, Hypoxia responsive element) in the promoter of the gene. We observed that an unmethylated HRE site allows HIF-1 to bind the promoter and to induce CEACM6 expression in intestinal epithelial cells (IEC). Decreasing CEACAM6 expression in CD intestinal cells is one strategy that could prevent AIEC bacteria colonization of the intestinal mucosa and subsequent inflammation. This work aims at studying the effect of a methyl donor enriched diet (HMD: High Methyl Diet) on microbial composition, on DNA methylation and on genes expression on microbiota.

**Aims & Methods:** CEABAC10 female mice were fed a HMD (supplemented in folate, biotin, B12 vitamin, zinc, methionine) for 2 weeks before pregnancy. After weaning, the colonic epithelial cells from offspring were purified using EDTA. We used different parameters such as: i) qPCR to compare the *E. coli* population was quantified using a qPCR approach. DNA methylation was measured at a global level and on the CEACAM6 promoter using bisulfite-sequencing. qPCR was used to quantify CEACAM6 mRNA. RNA-seq data was also used to highlight transcriptomic changes in colonic cells in the both conditions tested.

**Results:** We observed that mice fed a HMD show a significant decrease in basal lipocalin-2 level in stools compared to mice receiving a conventional diet suggesting a global effect on gut inflammation. No significant differences 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. As expected, global DNA methylation revealed a global increase in DNA methylation in mice fed a HMD compared to mice fed 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 immunity.

**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 gene expression such as a decrease in CEACAM6 and modify microbial 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**

**C. Campbru,** **M. Lopez-Siles,** **M. Ferrer-Guixeras,** **L. Niubo-Carulla,** **C. Abellá-Ametller,** **J. García-Gil,** **M. Martinez-Medina**

**Biologia, University of Girona, Girona/Spain**

**Contact E-mail Address:** c.campbru@gmail.com

**Introduction:** The molecular basis of Adherence-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 a 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 using M2ise; ii) SPAdes for assembly and compara-tive genomics between pairs in relation to a genome of reference (*AIEC UM146*) with Mauve. Only non-synonymous Single Nucleotide Polymorphisms (SNPs) in coding regions were selected. Sanger sequencing was performed to confirm the presence of SNPs and to evaluate the distribution of the SNPs in a collection of 22 AIEC and 29 non-AIEC isolates. Nucleotides for each SNP were analysed taking into account AIEC phenotype, adhesion and invasion indices of isolates by *χ*² 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 O6:H1-B2 and O22:H7-B1 were 4.86, 5.16 and 4.79Mb respectively. 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 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 was implicated 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.
Aims & Methods: The objective of this study was to evaluate 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 or gastrointestinal tract and large intestine. To investigate the involvement of Lpf in the ability of EDL933 to target Peyer’s patches, we generated a ΔlpfA1/ΔlpfA2 mutant and trans-complemented them with lpf genes. Lpf interaction with M cells was assayed using an in vitro model of specialized M cells. In vivo interactions of EHEC with murine Peyer’s patches were analyzed in ileal loop assays. Mice were infected with a mixture of two bacterial strains, and the numbers of Peyer’s patches-interacting bacteria were determined using a competitive index analysis. 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 epithelial cells compared with 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. This restoration of expression that expressing lpfA1 or lpfA2 genes is required for interactions with Peyer’s patches. Bloodshot Peyer’s patches were macroscopically observed following EHEC infection of murine ileal loops. We showed that pre-treatment with yeasts significantly inhibited O157:H7 interaction with Peyer’s patches and reduced the number of hemopoietic 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 interaction of EHEC with Peyer’s Patches.

Conclusion: We conclude that Lpf are involved in the interactions of EHEC with murine Peyer’s patches and are needed for an active translocation across M cell monolayer. Tropism of EHEC to Peyer’s patches can be limited by probiotic yeasts and carbohydrates.

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

OPI58 CURRENT OR PAST CLOSTRIDIOID DIFFICILE INFECTION IS ASSOCIATED WITH INCREASED MORTALITY, MORBIDITY AND RESOURCE UTILIZATION AMONG PATIENTS HOSPITALIZED FOR CROHN’S DISEASE: RESULTS OF A NATIONWIDE ANALYSIS

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2Catalyst Medical Consulting, Baltimore/United States of America/MD

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Introduction: Multiple factors have been associated with an acute flare of Crohn’s disease, including cigarette smoking and non-steroidal anti-inflammatory drug use. Recently, Clostridium difficile infection (CDI) has been added to this list. CDI can become chronic or recurrent in 20% of patients. To date, the impact of CDI on patients’ mortality and other outcomes among patients with Crohn’s disease has not been investigated.

Aims & Methods: The aim of this study is to explore the impact of past or current CDI on mortality, morbidity and resource utilization among patients hospitalized for Crohn’s disease. This was a retrospective cohort study using the 2012 National inpatient sample, the largest publically available inpatient database in the United States. The inclusion criteria were: 1– a principal diagnosis of Crohn’s disease 2– A principal diagnosis of intestinal hemorrhage, obstruction, fistula, or abdominal abscess with a secondary diagnosis of Crohn’s disease. There were no exclusion criteria. The primary outcome was in-hospital mortality. The secondary outcomes were morbidity as measured by shock, intensive care unit (ICU) admission, colectomy or intestinal resection rate and resource utilization as measured for CDI patients and TDT patients during their hospital stay. The comparison was done between patients with and without CDI.

Results: Of the 4,277,245 patients with ICD-9 diagnoses for IBD, 74,515 patients with Crohn’s disease were included in the study, 1,465 (2%) of whom had CDI. The mean age was 43 years (SD: 13 years). Female patients with CDI had a higher mortality rate (adjusted odds Ratio (OR): 1.25; 95% confidence interval (CI): 1.19–1.30; p < 0.0001) compared with patients without CDI. Looking at morbidity, patients with CDI had a similar colectomy rate (OR: 1.16, CI: 0.93–1.44, p = 0.25) and similar mortality rate compared with patients without CDI. When resource utilization was examined, patients with CDI had a lower LOS (adjusted mean (mean): 5.4 days, CI: 1.78–3.30, p < 0.01), higher TPN use (OR: 2.71, CI: 1.92–3.82, p = 0.02), higher total hospital charges (mean: $14,259, CI: $8,473–$20,926, p < 0.01) and similar abdominal CT scan use (OR: 1.41, CI: 0.78–2.59, p = 0.25) compared with patients without CDI.

Conclusion: Current or past CDI is associated with increased mortality among hospitalized patients with Crohn’s disease. However, patients with CDI have similar colectomy rates, shock or ICU admission rate compared with patients without CDI. Finally, CDI has a profound effect on resource utilization with longer length of stay, increased TPN use and substantially higher total hospitalization charges.

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

TUESDAY, OCTOBER 18, 2016
08:30–10:00
COLON CANCER: FROM SCREENING TO PALLIATION – ROOM 1B6

OPI56 SELF-EXPANDABLE METALLIC STENT AS BRIDGE TO SURGERY IS MORE SUPERIOR THAN TRANSDUCTION TUBE AT QUALITY OF LIFE FOR THE PATIENTS WITH PRIMARY MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: Self-expandable metallic stents (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 (±17.0years) and 42 patients in TDT group (male 54.8%, median age 65 (±15.2 years). Technical success rate was 100% of SEMS group and 95.2% of TDT group (p = 0.15). The endoscopic decompression as BTS for primary colorectal cancer was performed in 57.1% of SEMS group and 85.7% of TDT group (p = 0.02). Among these patients, the duration for surgery after decompression was longer in SEMS group (19.2 days vs 12.3 days) (p = 0.036). The 15.2 oral intake (at least soft solids) was significantly higher in SEMS group (89.2% vs 25.0%, p < 0.001). The Colonc Stent Safe Procedure Research Group Colorectal Obstruction Scoring System (CROSS) score before decompression was no significant difference in both group (1.1 (±0.9) vs 1.4 (±0.7), p = 0.49), but CROSS score after decompression was significantly improved in SEMS group (3.7 (±0.8 vs 2.3 (±0.9), p < 0.001). The complications after procedure, such as perforation, migration, re-obstruction, had no significant difference in both group.

Table: Patients characteristics and results

<table>
<thead>
<tr>
<th>SEMS (n = 27)</th>
<th>TDT (n = 42)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>10 (37.0%)</td>
<td>23 (54.8%)</td>
</tr>
<tr>
<td>Age (median, years)</td>
<td>73 ±17.0</td>
<td>±65 ±15.2</td>
</tr>
<tr>
<td>Age &gt; 85years</td>
<td>9 (33.3%)</td>
<td>31 (7.1%)</td>
</tr>
<tr>
<td>Obstructed location (left side)</td>
<td>23 (85.2%)</td>
<td>38 (90.5%)</td>
</tr>
<tr>
<td>Primary colorectal cancer</td>
<td>21 (77.8%)</td>
<td>28 (70.0%)</td>
</tr>
<tr>
<td>Metastatic colorectal cancer</td>
<td>12 (44.4%)</td>
<td>24 (57.1%)</td>
</tr>
<tr>
<td>-Bridge to SEMS insertion</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>-Palliation</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>-Emergent surgery</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>-Mortality</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>-Total Success</td>
<td>27 (100%)</td>
<td>40 (95.2%)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>SEMS (n = 27)</th>
<th>TDT (n = 42)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-obstruction</td>
<td>5 (18.5%)</td>
<td>1 (2.4%)</td>
</tr>
<tr>
<td>Migration</td>
<td>2 (7.4%)</td>
<td>4 (8.8%)</td>
</tr>
</tbody>
</table>

QOLs
- Temporary discharge: 5/12 (41.7%) vs. 24/0.0% (p < 0.001)
- Duration for surgery (days): 14.9 ± 7.0 vs. 10.5 ± 6.6 (N.S.)
- Hospitalization (days): 36.1 ± 23.5 vs. 46.4 ± 36.0 (p = 0.36)
- Oral intake (at least soft solids): 11/12 (88.9%) vs. 24/25.0% (p < 0.001)
- CROSS score (before procedure): 1.1 ± 0.9 vs. 1.2 ± 0.7 (N.S.)
- CROSS score (after procedure): 3.7 ± 0.8 vs. 2.3 ± 0.5 (p < 0.001)

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

Conclusion: SEMS has the equivalent safety, clinical efficiency and is more superior at QOLs for the patients with malignant colorectal obstruction, comparing TDT.

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

OP187 EVALUATION OF CLINICAL FACTORS ASSOCIATED WITH THE TECHNICAL DIFFICULTY OF SELF-EXPANDABLE METALLIC STENT PLACEMENT FOR MALIGNANT COLONIC OBSTRUCTION

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Introduction: In January 2012, the National Health Insurance began covering endoscopic self-expandable metallic stent (SEMS) placement for malignant colorectal 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 colorectal 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. Of these, 289 were men (57%), and the mean age was 70.6 years. Three hundred eleven patients (61%) underwent stenting as a bridge to surgery, and 501 patients (98%) were metastasis of peritoneal carcinomatosis (odds ratio [OR], 2.24; 95% confidence interval [CI], 1.58–3.16; p < 0.01), a Colorectal Obstruction 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 associated with technical difficulty were a history of chemo/chemoradiation 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 colorectal 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 as a single stent.

Disclosure of Interest: M. Shimada: personal fees:Century Medical Inc., Boston Scientific Japan
T. Kuwai: personal fees: Boston Scientific Japan
T. Matsuzawa: personal fees: Boston Scientific Japan
K. Koizumi: Lecture fee: Century medical inc,personal fees: Olympus Medical System

Reference

OP188 17 YEARS OF SINGLE CENTER EXPERIENCE WITH SELF-EXPANDABLE METAL STENTS IN COLONIC OBSTRUCTION

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Introduction: Since 1991, self-expandable metal stents (SEMS) has been used in the treatment of malignant colonic obstruction (1). In 1997, Bispebjerg Hospital was the first hospital in Denmark to initiate the use of SEMS in the treatment of malignant colonic obstruction. This study represents the largest material from a single centre ever published.

Aims & Methods: This is a prospective registration of all patients who underwent SEMS at our institution, in the period from January 1st 1997 to October 1st 2014. No patients were excluded. The indications were predominantly malignant, but a few were performed at benign indications. All procedures were performed with a combined endoscopic and fluoroscopic technique. Relevant patient characteristics, the postoperative course, complications and follow-up data, were gathered by retrospective patient chart review.

Results: In the period, 521 SEMS procedures was performed in 455 patients, 402 of these had colorectal cancer. Mean age was 74 ± 13 years, and 50.3% were male. The indications for SEMS placement were malignant colonic obstruction in 339 patients, including 158 as bridge to surgery (BTS), 237 as palliation, three with malignant anastomotic stricture and 20 patients with obstruction due to external tumor compression. The benign indications in 37 patients were respectively diverticulitis stricture in 15, diverticulitis fistula in two and benign anastomotic stricture in two. Two hundred and seventy-two patients had manifest total colonic obstruction and 121 had small bowel dilatation at the time of the procedure. The placement of the SEMS was in 111 in rectum, 221 in sigmoid colon, 52 in descending colon, 30 in splenic flexure, 30 in transverse colon, 6 in hepatic flexure and 5 in ascending colon. Median length of stenosis was 4.5 ± 1.9 cm and mean days of obstruction was 5.2 ± 3.4 days. There was an overall technical success rate at 90.3% and clinical success rate at 87.7%. Stent procedure related complications was 4.2%, mainly guidewire perforations, and none of these patients died within 30 days. A second stent intervention was performed in 53% in the BTS group, 11.9% in the palliative group and in 27.3% in the group of benign indications, external tumor compression and malignant anastomotic stricture. Very few patients required additional re-interventions. The overall all 30-day mortality rate was 13.4%, 5.8% for BTS group and 17% for palliative group. Follow up time for BTS group was mean 79 ± 70 months and at last follow up 35.3% (36/102) showed clinical signs of recurrence. 5-year survival in BTS group was 32.3% and 25% in the palliative group.

Conclusion: Our data shows that routine use of SEMS insertion is a safe and effective technique for colonic decompression in the setting of malignant large bowel obstruction, as either a palliative measure or as a bridge to subsequent resection. SEMS for benign conditions is feasible but with less favourable outcome.

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

Reference

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

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Introduction: Self-expandable metallic stents are increasingly used in the treat-ment of obstructive colorectal cancer. Although endoscopic stenting is widely accepted in a palliative setting, disagreement exists about its role in a curative setting. It offers the opportunity for an adequate pre-operative assessment of the patient and a good preparation of the colon.

Aims & Methods: This study aims to describe the long-term survival data in a large patient cohort, 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 survival in Belgian colorectal cancer patients in the same period (p = 0.14). One-, five- and ten-year survival was not statistically different in both groups (95.9% vs 79.0%; 54.7% vs 51.2%; 41.0% vs 35.6% respectively). Additionally, for tumour stage II, III and IV no statistical differences between both cohorts were found (p = 0.21, p = 0.58, p = 0.10 respectively). Technical success rate was 94.8%. Seventy patients did not experience any complication. Stent migration occurred in 9 patients, whereas stent-related micro- and macro perforations were observed in 14 patients, without influencing survival. Incidence rates of peritoneal 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 per cent of the patients got only primary surgery. In 5.2% of the patients a laparoscopic procedure was converted to laparotomy, because of adhesions or peritonitis. Stoma rates were low (5.2%).

Conclusion: In this study we demonstrated that stenting before surgery is effective and safe in the treatment with curative intent of patients with obstructive colorectal cancer and reinforce the debate on stenting as a BTS.

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

References

OP191 IMPACT OF MORTALITY FROM SURGICAL ADENOMA REMOVAL ON THE EFFECTIVENESS OF COLORECTAL CANCER SCREENING

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2Dept. Of Gastroenterology, Netherlands Cancer Institute, Amsterdam
3Gastroenterology & Hepatology, Erasmus Medical Center Gastroenterology and Hepatology, Rotterdam/Netherlands
4Erasmus MC, Rotterdam/Netherlands
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Introduction: Implementation of colorectal cancer (CRC) screening programs results in an increase in the number of adenoma diagnoses. Some of the advanced adenomas (AADs) cannot be endoscopically removed and patients may then be referred for surgery. However these surgical reactions have an associated mortality. We assume that AADs without perioperative mortality have a negative impact on the effectiveness of CRC screening. So far, the size of this impact is unknown. Therefore the objective of this study is to estimate the size of this perioperative mortality in relation to AAD removal on the effectiveness of CRC screening.

Aims & Methods: We used the MISCAN-Colon microsimulation model to simulate the Dutch population, aged 50 years and older in 2013 and followed them lifetime. The population was offered biennial FIT (FOB-Gold at a cut-off of 46 μg/g) screening from ages 55 and over. Screening was calculated from 2014 to 2020 according to implementation. To assess the impact of perioperative mortality in relation to AAD removal, we simulated a scenario with and without perioperative mortality with and without ADR. The impact on costs of the screening program was evaluated. There were significantly more neoplasias (ADR), advanced neoplasias (advanced adenoma and carcinoma) and carcinomas in older group and also adenoma per colorectal cancer (APCR) was higher in seniors. Caeal intubation rate was significantly lower. The numer of colonoscopies after positive FOB was significantly higher than primary colonoscopies in seniors. See the table. There were no bleeding complications or perforations during screening examinations in both groups.

Results: So far, the size of this impact is unknown. Therefore the objective of this study is to estimate the size of this perioperative mortality in relation to AAD removal on the effectiveness of CRC screening.

Conclusion: Screening colonoscopies in population over 70 years of age in our study were safe, with higher detection of neoplasias, but with lower completion rate. There was higher number of colonoscopies after positive FOBT than primary colonoscopies among seniors.

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

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

COMPLICATIONS IN IBD – ROOM F2

OP192 THE OCCURRENCE OF ANAEMIA AND ANAEIMIA SUBTYPES DURING THE FIRST YEAR OF DISEASE IN AN EAST-WEST EUROPEAN INCLUSION COHORT – AN EECO-EPICOMIC PHOSTUDY

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Disclosure of Interest: All authors have declared no conflicts of interest.
Table 1: Prevalence of anaemia at diagnosis and at 1-year follow up.

<table>
<thead>
<tr>
<th>Country</th>
<th>At Diagnosis</th>
<th>At 1-year Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Czech Republic</td>
<td>43%</td>
<td>26%</td>
</tr>
<tr>
<td>Romania</td>
<td>29%</td>
<td>13%</td>
</tr>
<tr>
<td>Vigo/Spain</td>
<td>58%</td>
<td>25%</td>
</tr>
<tr>
<td>Moscow/Russian Federation</td>
<td>45%</td>
<td>12%</td>
</tr>
<tr>
<td>Oporto Medical School and Institute for molecular and cell biology, University of Porto, Porto/Portugal</td>
<td>25%</td>
<td>12%</td>
</tr>
</tbody>
</table>

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Introduction: The EpCom-cohort is a European prospective population-based cohort study of unselected patients uniformly diagnosed with inflammatory bowel disease (IBD) in 2010 in 31 Western and Eastern European centres. Previously, this cohort has demonstrated differences in the treatment strategy of IBD patients between Eastern and Western European centres including that significantly more patients in Western Europe receive biological therapy. 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 guideline.

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 than in Western Europe (16.4% UC, 19.1% CD) compared to Western Europe (8% UC 9% CD), while a similar proportion in both regions changed from the anaemic state to normal (20% UC and 35% CD in both regions) during follow-up. More IBD patients receiving biological therapy during the first year of disease changed status from anaemia at diagnosis to no anaemia at follow-up (83%) compared to patients not having received biological therapy (70%), while fewer patients receiving biological therapy remained anaemic during follow-up (17% vs 30%). These differences did, however, not reach statistical significance (p = 0.09).

Table 1: Prevalence of anaemia at diagnosis and 1-year follow up.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>At Diagnosis</th>
<th>At 1-year Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcerative colitis</td>
<td>43%</td>
<td>26%</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>29%</td>
<td>13%</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>58%</td>
<td>25%</td>
</tr>
<tr>
<td>Western Europe</td>
<td>45%</td>
<td>12%</td>
</tr>
<tr>
<td>At Follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Anemia - overall</td>
<td>26%</td>
<td>29%</td>
</tr>
<tr>
<td>Mediterranean</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>North Europe</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>9%</td>
<td>3%</td>
</tr>
<tr>
<td>Mixed anaemia</td>
<td>6%</td>
<td>1%</td>
</tr>
<tr>
<td>Other anaemia</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>Unclassified</td>
<td>14%</td>
<td>16%</td>
</tr>
</tbody>
</table>

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.
since most available studies are small and cover a relatively short follow-up period. We established a nationwide cohort of IBD patients with a history of LGD to 1) determine the cumulative CRC incidence, and 2) identify risk factors for developing CRC.

Aims & Methods: Using the Dutch National Pathology Registry (PALGA) we identified all consecutive patients diagnosed with LGD between 1991 and 2005 in the Netherlands. Subsequently, follow-up data were extracted until 2016. We determined the cumulative CRC incidence with Kaplan Meier curves 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), was performed to identify risk factors for developing CRC. Demographic data, including gender, IBD type, age at diagnosis, age and duration, and LGD age and recurrence, were extracted from PALGA. Subsequently, multivariable Cox regression analyses with backward elimination were used to identify independent risk factors.

Results: We identified 1177 IBD patients with colonic LGD with a median follow-up time of 9.8 years per patient after LGD diagnosis (total follow-up time: 11741 patient-years). 825 (70.1%) patients had ulcerative colitis, 216 (18.4%) Crohn’s disease and 136 (11.6%) indeterminate colitis. Hundred nine out of 1177 (9.3%) patients underwent colectomy. CRC developed in 86 out of 1177 patients resulting in a cumulative incidence of 2.9%, 5.8%, 11.1%, and 18.7% after respectively 5, 10, 15 and 20 years. Patients with an IBD duration of more than 5 years before LGD development had a significantly higher cumulative CRC incidence (14.7% after 15 years) compared to those with a shorter IBD median (9.4% after 15 years; log rank p = 0.006). Furthermore, patients with recurrent LGD had a higher CRC risk compared to patients with single LGD (10.5% after 15 years versus 4.5% after 15 years; log rank p = 0.026). Multivariable Cox regression identified both a longer IBD duration (hazard ratio, 2.5; 95% confidence interval 1.5-4.3) and recurrent LGD (hazard ratio 1.9, 95% confidence interval 1.1-3.4) as independent factors associated with increased CRC risk.

Conclusion: We showed a cumulative CRC risk of 18.7% after 20 years in a large national cohort of IBD patients with a history of LGD. Both a longer IBD duration and recurrent LGD were identified as independent risk factors for CRC development following LGD. These findings may aid in risk stratification following a diagnosis of LGD in IBD patients.

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

OP195 ROLE OF DIFFUSION-WEIGHTED IMAGING (DWI) IN MRI-ENTEROGRAPHY FOR THE EVALUATION OF SURGICAL RISK IN PATIENTS WITH CROHN’S DISEASE

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Introduction: In Crohn’s disease (CD) it’s useful to discriminate inflammatory from fibrotic lesions, as MRI-Diffusion Weighted Imaging (DWI) is able to identify active inflammation in most pathological tissues.

Aims & Methods: We aimed to define the role of DWI in evaluating the risk of surgery in CD. We performed an observational prospective study including all consecutive patients with active CD undergoing MRI. MRI study included: measurement of bowel wall thickness (BWT), CD extension, enhancement patterns, endoscopic and histologic inflammation was collected. The identified CRN risk factors were used to build a predictive score that was then tested in a nested case-control study.

Results: Among 404 patients who underwent 1236 colonoscopies, 38 patients who developed CRN in inflamed mucosa and 92 matched controls were included in a nested case-control study. Independent factors significantly associated with CRN were primary sclerosing cholangitis (PSC) (Odds ratio (OR), 6.26; CI 95% 1.07–37.3; p = 0.032), presence of neutrophils, crypt abscess or histological ulceration (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, 0.047-0.608, p=0.01) and 5-aminosalicylates (OR, 0.27; CI 95% 0.084-0.876, p=0.03) at the time of neoplasia or last colonoscopy. We developed a score based on these five items at the time of the surveillance colonoscopy negative for neoplasia. Among patients with a score of 0, the negative predictive value in predicting any CRN was 100% in patients with 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-aminosalicylates. The use of a predictive score derived from these factors could be considered for making decisions on optimal intervals between two surveillance colonoscopies.

Disclosure of Interest: A. Bourrier: Anne Bourrier has received lecture fees from UCB
H. Sokol: Harry Sokol received consulting fees from Enterome, Astellas, Roche, Merck, Maat and Danone.
P. Sekis: Philippe Sekis had consulting fees from Abbvie, Merck-MSD and Biocodex and grants from Biocodex.
J. Cosnes: Jacques Cosnes has received lecture fees from Abbvie, consulting fees from Vifor Pharma
L. Beaugerie: Laurent Beaugerie has received consulting fees from Abbott, lecture fees from 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

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 who underwent at least two colonoscopies at Saint-Antoine Hospital between 01/01/1996 and 01/03/2015 and whose first procedure was a surveillance colonoscopy were included. A nested case-control study was performed to assess risk factors of CRN in inflamed mucosa. Information on treatment, endoscopic and histologic inflammation was collected. The identified CRN risk factors were used to build a predictive score that was then tested in the whole study population.

Results: Among 404 patients who underwent 1236 colonoscopies, 38 patients who developed CRN in inflamed mucosa and 92 matched controls were included in a nested case-control study. Independent factors significantly associated with CRN were primary sclerosing cholangitis (PSC) (Odds ratio (OR), 6.26; CI 95% 1.07–37.3; p = 0.032), presence of neutrophils, crypt abscess or histological ulceration (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, 0.047-0.608, p=0.01) and 5-aminosalicylates (OR, 0.27; CI 95% 0.084-0.876, p=0.03) at the time of neoplasia or last colonoscopy. We developed a score based on these five items at the time of the surveillance colonoscopy negative for neoplasia. Among patients with a score of 0, the negative predictive value in predicting any CRN was 100% in patients with colonoscopies performed 1 and 3 years after the first surveillance colonoscopy.

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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.
Time-dependent Cox-regression analysis of baseline FIT of advanced neoplasia.

| Table 1: Time-dependent cox-regression analysis of baseline FIT of advanced neoplasia. |
|---------------------------------|------------------|------------------|
| Advanced neoplasms              | Univariate HR    | Multivariate HR  |
| Univariate HR                  | 95% CI p-value   | 95% CI p-value   |
| Gender (male)                   | 1.7              | 1.3–2.3          | <0.001 1.6   | 1.2–2.1          | <0.001 1.1   | 1.0–1.1          | <0.001 1.36   | 1.2–2.0          | <0.001 1.0   |
| Age (years)                     | 1.1              | 1.0–1.1          | <0.001 1.1   | 1.0–1.1          | <0.001 1.0   | 1.0–1.0          | <0.001 0.99   | 1.0–1.0          | <0.001 0.99   |
| Baseline Hb conc.               |                 |                  |               |                  |               |                  |               |                  |               |
| 0–5 g Hb/g                      |                 |                  |               |                  |               |                  |               |                  |               |
| Ref.                            |                 |                  |               |                  |               |                  |               |                  |               |
| >0–5 g Hb/g                     | 1.8              | 1.3–2.4          | 1.7            | 1.2–2.2          | <0.001 1.0   | 1.0–1.0          | <0.001 0.99   | 1.0–1.0          | <0.001 0.99   |
| >5–10 g Hb/g                    | 7.0              | 4.6–10.5         | 6.0            | 4.0–9.0          |               |                  |               |                  |               |
| Socioeconomic status            |                 |                  |               |                  |               |                  |               |                  |               |
| High                            |                 |                  |               |                  |               |                  |               |                  |               |
| Ref.                            |                 |                  |               |                  |               |                  |               |                  |               |
| Average                         | 1.1              | 0.7–1.3          | 1.0            | 0.6–1.4          | 0.08          |                  |               |                  |               |
| Low                             | 0.6              | 0.4–1.0          | 1.0            | 0.6–1.0          | 0.08          |                  |               |                  |               |

Conclusion: Among FIT negative screeners, baseline Hb concentration is an independent predictor for the risk of future AN. Moreover, Hb concentrations of at least 4 g Hb/g are a strong predictor of the risk of AN with up to a 14-fold risk increase. These findings suggest a role for Hb in personalized screening strategies in population-based screening policies. In addition, the use of Hb of negative FITs may permit alteration of screening intervals. Such strategies could decrease unnecessary burden for screeners and optimize the use of program related resources.

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

References
The present study does not suggest unfavorable short-term consequences in health behavior after getting a negative CRC screening test result. Conclusion:

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 two different screening modalities and controls not invited to screening. Participants of both gender, aged 50–74, were invited to complete a self-reported lifestyle questionnaire (LSQ), 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 glass/week, 95%CI; −0.54 to −0.04) during one-year follow-up. Body weight decreased more in participants with a negative screening test result in the FIT 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 impact of colorectal cancer screening on CRC incidence and mortality, number of colonoscopies per detected CRC, life-years saved and costs per individual in the lifetime of 20,000,000 individuals.

Table (OP202)

<table>
<thead>
<tr>
<th>Stage–I–II–III–IV–Missing</th>
<th>Total CRCs</th>
<th>Screen-detected cancer</th>
<th>FIT interval cancer</th>
<th>Colonoscopy interval cancer</th>
<th>CRC in non-participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>51.7 (60)</td>
<td>116</td>
<td>27</td>
<td>13</td>
<td>7.7 (1)</td>
<td>30.8 (4)</td>
</tr>
<tr>
<td>59.3 (16)</td>
<td>2.2 (60)</td>
<td>40.7 (11)</td>
<td>37 (10)</td>
<td>7.1 (61.5)</td>
<td>30.8 (3)</td>
</tr>
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<td>53.8 (7)</td>
<td>6.29 (73)</td>
<td>59.3 (16)</td>
<td>15.4 (2)</td>
<td>7.7 (1)</td>
<td>1.8 (2)</td>
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<tr>
<td>63.3 (69)</td>
<td>69.2 (9)</td>
<td>23.1 (3)</td>
<td>13.8 (16)</td>
<td>55.7 (71)</td>
<td>7.1 (71)</td>
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<tr>
<td>p = 0.803</td>
<td>3.49 (38)</td>
<td>61.5 (67)</td>
<td>36.4 (4)</td>
<td>15.6 (17)</td>
<td>28.5 (31)</td>
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<tr>
<td>p = 0.001</td>
<td>0.010</td>
<td>0.001</td>
<td>0.001</td>
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</table>

Aims & Methods: The aim of our study was to compare patient demographics, tumor site, stage and survival between patients with screen-detected CRCs (SD-CRC) and non-screen-detected CRCs (non-SD-CRC). Between 2006 and 2014, asymptomatic persons aged 50 to 74 were invited to take part in four consecutive biennial FIT-screening rounds. CRC cases were identified through linkage with the Netherlands Cancer Registry and were classified into four groups: SD-CRC, FIT interval cancers (diagnosed between screening rounds after negative FIT), colonoscopy interval cancers (diagnosed after negative colonoscopy 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 46.4 months (IQR 18.5–72.8). Among participants, 3,009 (16%) had a positive FIT in one of the 4 screening rounds. In total, 265 patients were diagnosed with CRC: 116 were SD-CRCs, 27 FIT interval CRCs, 13 colonoscopy interval CRCs and 109 CRCs detected in non-participants. There were no differences between the groups regarding age, gender and SES distribution. Screen-detected CRCs, FIT interval cancers and CRCs in non-participants were mostly located in the distal colon (70.7%, 63%, 61.5% of cases, respectively), whereas colonoscopy interval CRCs were mainly located in the proximal colon (69.2%) (p = 0.010). Stage distribution was significantly different between the four groups, with more favorable stages in patients with SD-CRCs (p < 0.001). Stage distribution in patients with FIT interval CRC and CRCs in non-participants was similar (p = 0.361). Survival rates were significantly higher among patients with SD-CRCs and FIT interval cancers compared to non-participants and patients with colonoscopy interval cancers.

Conclusion: In this population-based CRC screening cohort, 0.14% of all participants were diagnosed with a 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. Outcomes were CRC incidence and mortality, number of colonoscopies per detected CRC.
Result: FIT screening without a surveillance programme reduced CRC incidence and mortality by respectively 25.4% and 39.6% compared to FIT screening alone 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. Prolonged surveillance intervals slightly reduced surveillance efficiency by respectively 26.6%–27.2%, mortality reductions 39.6% to 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. Prolonged surveillance intervals decreased this burden to 129–366 colonoscopies per surveillance-detected CRC. All screening plus surveillance strategies were equally or more effective (0.0011 life-years gained) and less costly (~2.45€–8.24€ than screening only. The surveillance intervals were set at five years, dominating 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 that incurred in a surveillance 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
VIRAL HEPATITIS: NATURAL HISTORY AND TREATMENT – ROOM M

OP204 SUSTAINED ViroLOGIC RESPONSE TO INTERFERON-FREE THERAPIES AMELIORATES HCV-INDUCED Portal hypertension
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Introduction: Portal pressure, assessed by hepatic venous pressure gradient (HVPG) measurement, drives the development of liver-related complications and mortality in patients with advanced chronic liver disease. Since a decrease in HVPG translates into a clinically meaningful benefit, it is an acceptable surrogate endpoint.

Aims & Methods: We aimed to investigate the impact of sustained 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 measurement and transient elastography (TE) before IFN-free therapy (baseline [BL]) were retrospectively studied. The effect of SVR on portal pressure was investigated in patients with SVR who also underwent follow-up (FU)-HVPG and TE after IFN-free therapy (group A; n = 60). To demonstrate the generalizability of our results, we included a second group (group B; n = 40), comprising all patients who achieved SVR and were available for the FU-HVPG measurement. In these patients only information on FU-TE was available. Moreover, we also included 4 patients who did not achieve SVR.

Results: SVR to IFN-free therapies significantly decreased HVPG across all BL-HVPG strata. HVPG decreased from 6–9 mmHg (BL:7.3±0.28 vs. FU: 5.1±0.38 mmHg; 72.6–0.42 mmHg; P < 0.001), 10–15 mmHg (BL:12.2±0.4 vs. FU: 8.91±0.62 mmHg; 13.0–0.59 mmHg; P < 0.001) and >16 mmHg (BL:18.0±0.5 vs. FU: 13.4±0.89 mmHg; 18.0–0.59 mmHg; P < 0.001). In the subgroup of patients with BL-HVPG of >6-9 mmHg, portal hypertension resolved in 63% (±12%) during BL-HVPG ≥ 6–9 mmHg at FU. Among patients with a BL-HVPG of 10–15 mmHg, portal hypertension resolved in 14% (±32%), 29% (±62%) (HR, 1.0 vs. 0.4; 95% CI, 1.01–0.99; P = 0.044) was a predictor of a HVPG decrease ≥ 10%. The area under the receiver operating characteristic curve for the diagnosis of FU-HVPG ≥ 10 mmHg by FU liver stiffness was 0.931 (95% CI:0.865–0.997). The liver stiffness values at FU for ruling-in and ruling-out FU-HVPG ≥ 10 mmHg were 12.4 (negative predictive value:100%) and 25.3 kPa (positive predictive value:94%), respectively. Changes in liver stiffness, platelet count, and liver function tests were comparable between patients with and without SVR. SVR increased FU-HVPG and TE (group B), providing an argument for the generalizability of our results. Among the 4 patients without SVR, one patient underwent FU-HVPG and TE (HVPG increased from 18 to 20 mmHg; liver stiffness increased from 45 to 75 kPa), while 3 patients only underwent FU-HVPG and TE (HVPG remained stable in 2 patients and decreased in 1 patient). P = 0.102 to 15.5 kPa).

Conclusion: SVR to IFN-free therapies ameliorates portal hypertension across all BL-HVPG strata. However, amelioration of portal hypertension was less likely in patients with more advanced liver dysfunction. TE might be useful for the non-invasive evaluation of portal hypertension after SVR. In contrast, patients who did not achieve SVR showed either no significant improvement or even worsening of liver disease.

Disclosure of Interest: M. Manderfor: M.M. received honoraria for consulting from AbbVie, Bristol-Myers Squibb and 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. S. Beinhard: S.B. received honoraria for consulting from AbbVie, payments for lectures from Bristol-Myers Squibb, Janssen and Roche. T. Reiberger: T.R. received payments for lectures from Roche, as well as travel support from Gilead, MSD and Roche. M. Trauner: M.T. received grants from MSD, honoraria for consulting from AbbVie, Gilead, Janssen and MSD, payments for lectures from Gilead, MSD and Roche, as well as travel support from Gilead, MSD and Roche. H. Hofer: H.H. received payments for lectures from AbbVie, Gilead, Janssen, MSD and Roche. A. Feilitz: A.F. received grants from Janssen and payments for lectures from Gilead, MSD 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/TIDE ANALOGUE THERAPY
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Introduction: Clinical hepatitis may follow virological relapse in chronic hepatitis B (CHB) patients after discontinuing nucleos/tide analogues (NA), but the incidence and risk predictors remained elusive.

Aims & Methods: Between July 1, 2011 and July 1, 2015, this multicenter study prospectively enrolled 140 consecutive CHB patients with negative HBeAg and detectable viral DNA at the cessation of NAs after a minimum of 3 years on therapy. In those who experienced virological relapse (viral DNA > 2.000 IU/mL), the incidence of clinical relapse (virological relapse plus ALT > 80 IU/mL) and persistent/severe hepatitis (clinical relapse lasting for 3 months or accompanied by jaundice) was 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], 1.71; 95% CI, 1.41–2.00), ALT (HR, 1.005; 95% CI, 1.001–1.009), and alanine aminotransferase (ALT) at virological relapse (HR, 1.003 per IU/L; 95% CI, 1.001–1.004), as well as ALT at NA cessation (HR, 1.008; 95% CI, 1.002–1.010), whereas persistent/severe hepatitis was associated with viral DNA (HR, 1.71; 95% CI, 1.16–2.71), ALT (HR, 1.004; 95% CI, 1.001–1.007), and afoldetopir (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 DNA, ALT, and persistent/severe hepatitis (clinical relapse lasting for 3 months or accompanied by jaundice). Predictors were explored by the Cox proportional hazard modelling.

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

OP207 COMBINATION THERAPY WITH DACLATASVIR AND ASV IN CHRONIC HEPATITIS C PATIENTS WITH HEPATITIS C VIRUS GENOTYPE 1B IN JAPAN
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Introduction: Combination therapy with direct-acting antivirals (DAA; VSV 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 not approved for IFN-free therapy. The objective was to assess the efficacy and tolerability of DCV/ASV combination therapy in patients with hepatic cirrhosis.

Aims & Methods: In total, 153 consecutive patients with HCV 1 b initiating DCV/ASV therapy were enrolled. The cohort comprised 52 patients with compensated cirrhosis and 101 patients without cirrhosis. On the other hand, those with cirrhosis showed significantly higher baseline, ALT level, creatinine level, or NS5A RAVs between patients with and without cirrhosis. Only 10 (6.5%) patients had L31M or Y93H RAVs. There was no statistical difference in incidence of adverse effects, were recorded at baseline and during follow-up.

Results: Only 10 (6.5%) patients had L31M or Y93H RAVs. There was no statistical difference in incidence of adverse effects, were recorded at baseline and during follow-up. Clinical, biological, and virological data, including adverse effects, were recorded at baseline and during follow-up.

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.

OP208 EXPERIENCE IN THE MANAGEMENT OF DECOMPENSATED HCV CIRRHOTIC PATIENTS WITH LOW DOSE SOFOSBUVIR AND RIBAVIRIN COMBINED WITH DACLATASVIR
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Introduction: Decompensated viral 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 compensation that necessitates liver transplantation. The observed remission of reduced rates of sustained virological response in decompensated cirrhosis was explained by extensive portosystemic collaterals, advanced fibrotic parenchyma which are difficult to be penetrated, and provide dormant foci for viral reactivation. It was claimed that achieving SVR with MELD- and EASL scores in patients with baseline decompensated cirrhosis was explained by sustained virological response in decompensated cirrhosis which was explained by extensive portosystemic collaterals, advanced fibrotic parenchyma which are difficult to be penetrated, and provide dormant foci for viral reactivation.

Aims & Methods: Evaluation of the efficacy and safety of managing chronic active HCV in patients with decompensated cirrhosis and if SVR will improve clinical status of these patients. Two stages, two progressed to decompensated cirrhosis with a level (T3), one developed interstitial pneumonia, one had severe bronchitis, one had arterial fibrillation, two had gastrointestinal bleeding, and two developed edema. Of the patients without cirrhosis (9%), ALT elevation was observed in one, edema occurred in one, and high 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:

OP209 INTERFERON-FREE DAA TREATMENTS DECREASE PORTAL PRESSURE AND HALT HISTOLOGICAL NEOCROINFLAMMATION IN HIV/HCV - CONNECTED PATIENTS WITH PORTAL HYPERTENSION
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Introduction: Patients with HIV/HCV coinfection show increased fibrosis progression and are at risk for complications of portal hypertension (PHT). We measured changes in liver stiffness and portal pressure and evaluated liver histology after successful interferon (IFN)-free DAA therapy.

Aims & Methods: HCV/HIV patients undergoing IFN-free DAA treatment and had paired hepatic venous pressure gradient (HVPG) and liver stiffness measured at baseline and three months after end of treatment (SVR12) were included. LS and HVPG were measured in a fasted, non-sedated state. Concomitant beta-blocker treatment was stopped for all measurements. Post-treatment liver biopsies were assessed by METAVIR score.

Results: Of 19 patients (56% male, age: 53.4 ± 6.7 years, 95% concomitant antiretroviral therapy), 16 received SOF/DCV, 2 SOF/RBV, and 1 SOF/LDV. Seven (37%) patients were treatment experienced and HCV genotype (GT) distribution was GT1a: 12, GT1b: 2 and GT3a: 5. All patients had portal hypertension (HVPG > 5 mmHg) and 14 patients (74%) presented with liver cirrhosis (LS > 12 kPa). DAA treatment resulted in 100% SVR12. LS decreased significantly from 23.0 ± 16.5 to 16.9 ± 16.1 kPa (mean change (Δ): −6.1 ± 5.2 kPa; p < 0.0001). Also, HVPG decreased from 10.4 ± 4.0 to 7.6 ± 4.3 mmHg (Δ: −2.8 ± 2.4 mmHg; p < 0.0001). In patients with clinically significant portal hypertension (HVPG ≥ 10 mmHg, n = 9), HVPG decreased from 13.8 ± 3.0 to 10.9 ± 3.8 mmHg (Δ: −2.9 ± 2.8 mmHg; p = 0.015) – resulting in a hemodynamic improvement of 7±0% in 6/9 (66%) patients. In the subgroup of patients with baseline HVPG < 10 mmHg (n = 10), a reduction from 7.3 ± 1.3 to 4.6 ± 1.8 mmHg (Δ: −2.7 ± 2.2 mmHg; p = 0.003) was noted – resulting in cure of PHT (<5 mmHg) in 6/10 (60%). Posttreatment liver biopsies were available in 15 patients. A significant reduction in hepatic necroinflammation and bilirocytic activity (METAVIR A0). 8 of 14 (57%) patients with cirrhosis at baseline, presented a post-treatment histological METAVIR ≤ F3. Serum transaminases were normalized after therapy (AST: 66 ± 34 vs. 33 ± 20, p = 0.0001; ALT: 103 ± 24 vs. 15 ± 15, p < 0.0001), while hemoglobin, WBC and CD4 cell counts remained stable.

Conclusion: Virological response to IFN-free DAA therapies decreases LS and ameliorates portal hypertension. SVR12 seems to abolish histological necroinflammation and activity in most HIV/HCV coinfected patients. It remains to be explored if these improvements result in decreased liver-related mortality in the setting of HIV/HCV coinfection.

Disclosure of Interest: P. Schwabl: received payments for lectures from Roche and Böhringer Ingelheim, and travel support from AbbVie, Gilead, Janssen, and Roche
Conclusion: New generation of NBI (HQ290) may reduce polyp miss rates and be more effective in reducing polyp miss rates of flat type.

Disclosure of Interest:
K. Katagiri, T. Baba, F. Ishida received payments for lectures from Roche, as well as travel support from Bristol-Myers Squibb, Gilead, and GlaxoSmithKline. A. Atsumi received grants from MSD, honoraria for consultation 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 and travel support from AbbVie and Gilead.

T. Reiberger: received payments for lectures from Roche, as well as travel support from AbbVie, Gilead, Janssen, and MSD.

All other authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 10:30–12:00

OP210 RANDOMIZED, BACK-TO-BACK TRIAL OF NEW GENERATION OF NBI (HQ 290) FOR THE DETECTION OF COLORECTAL POLyps — ROOM N2

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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 detection of colorectal polyps compared to the previous generation.

Methods: From June 2015 to September 2015, 102 patients were randomized to undergo either 290-NBI and high-resolution white light endoscopy (HR-WLE). The aim of this study was to compare polyp miss rates between 290-NBI and HR-WLE.

Results: In 290-NBI group, colonoscopic examination were performed with NBI. In 290-NBI group, colonoscopic examination were performed first inspection with NBI followed by a second inspection with HR-WLE.

Conclusion: New generation of NBI (HQ290) may reduce polyp miss rates and be more effective in reducing polyp miss rates of flat type.

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

References

OP212 ASSOCIATION OF CHROMOSOMAL INSTABILITY AND MICROSATELLITE INSTABILITY PATHWAYS WITH POSTCOLONOCOLIC CANCER: A RETROSPECTIVE COHORT STUDY

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Introduction: Over 50% of the postcolonocolic colorectal cancers (PCCCRs) (i.e. CRC diagnosed after a colonoscopy that excluded cancer) originate from the precancerous lesion, in particular the subtle appearing non-polypoid (flat and depressed) adenomas and sessile serrated lesions. The biologic pathway of PCCCRs is unclear. We hypothesized that PCCRCs and subtle appearing precursors may share molecular features. In a retrospective, cohort study, we examined the occurrence of chromosomal instability (CIN), microsatellite instability (MSI), and CpG island methylator phenotype (CIMP) in PCCCRs and prevalent CRCs.

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 are composed of two components: precancers (insufficient bowel preparation / incomplete...
colonscopy or incomplete resection) were excluded. We reviewed clinical and pathological records. Whole-genome DNA copy number changes and mutation status of genes commonly affected in CRC (APC, KRAS, BRAF, FBXW7, PIK3CA, NRAS, SMAD4 and TP53) were examined by shallow whole-genome sequencing and targeted sequencing, respectively, using Illumina next generation sequencing platforms. MSI and CIMP status were examined using the pentaplex marker panel from Promega and the Weisenberger CIMP panel using methylation-specific PCR, respectively.

Result: In total, 120 PCCRCs and 100 prevalent CRCs were examined. Regarding clinicopathological features, PCCRCs are more often located proximally in the colon (<0.001), non-polyoid appearing (<0.001), early stage tumors (<0.008), and poorly differentiated (<0.001) compared to prevalent CRCs. Regarding DNA copy number alterations, PCCRCs contain less often 17p (p=0.002) and 18q (p=0.003) deletions than prevalent CRCs. Furthermore, PCCRCs contain less frequently APC (p=0.04), NRAS (p=0.03), and TP53 mutations (p=0.03) than prevalent CRCs. In contrast, MSI (p=0.004), CIMP (p=0.02) and BRAF mutations (p=0.04) are more frequent in PCCRCs than prevalent CRCs.

Conclusion: Both CIN and MSI pathways are associated with the occurrence of PCCRC. PCCRCs contain less often deletions of chromosomes 17p and 18q, APC, NRAS and TP53 mutations and more often MSI, CIMP and BRAF mutations than prevalent cancers. Such molecular profiles are similar to those previously described in non-polypoid (flat and depressed) adenomas and sessile serrated lesions. Taken together, our results support the hypothesis that non-polypoid lesions and sessile serrated lesions are in the origin of PCCRC.

Disclosure of Interest: S. Sanduleanu: Consultancy: Pentax Medical Systems.

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Introduction: The AER-O-Scope Colonoscopy System (GI View Ltd., Ramat Gan, Israel) is a self-propelled, joystick controlled, disposable colonoscope that provides 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 predefined 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 colonies 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 = 78 pseudo-polyps); 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 SIB) 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 institutional ethics committee.

**Result:** There were 5 (5.2%) pseudo-polyps dissolided, 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 0.96–1.00). The overall success rate was 234/240 = 97.6% (p < 0.001). The table below 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 colonoscope simulated endoscopic tool (easy to perform or only slightly complicated to perform) was very high (98%–100%) for all endoscopic tools.

<table>
<thead>
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<th>Endoscopic Tool</th>
<th>n</th>
<th>Therapeutic Successes</th>
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</thead>
<tbody>
<tr>
<td>Snare</td>
<td>140</td>
<td>138 (98.6%)</td>
<td>0.95–1.00</td>
</tr>
<tr>
<td>Biopsy Forceps</td>
<td>47</td>
<td>47 (100%)</td>
<td>0.92–1.00</td>
</tr>
<tr>
<td>Injection Needle</td>
<td>60</td>
<td>60 (100%)</td>
<td>0.94–1.00</td>
</tr>
<tr>
<td>APC</td>
<td>48</td>
<td>48 (100%)</td>
<td>0.93–1.00</td>
</tr>
</tbody>
</table>

**Conclusion:** In an ex vivo swine colon model, the Aer-O-Scope Colonoscope System demonstrated the ability to easily provide simulated endoscopic therapeutic access using standard endoscopic tools while having very high usability ratings.

**Disclosure of Interest:** S. Bezboukh: I am a consultant for GI View Ltd. I.M. Gralnek: I am a consultant for GI View Ltd.

**References**

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**OP215 OUTCOME OF ENDOCYTIC MUCOSAL RESECTION OF 424 LARGE SESSILE COLONIC POLYPS (≥20MM) OVER A 9 YEAR Aims: 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, RJR). Patient demographics, resection technique, completeness of initial resection, recurrence rate at first surveillance (SC1), polyp eradication at 2nd surveillance after at least 1 year (SC2) and complication rates were analysed.

**Results:** 364 patients were assessed for EMR, among which there were 424 completed EMRs (85% of symptomatic) by 3 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 not attempted but all were referred for surgery (cancer 18, benign polyp 14). Finally, 43 had no intervention (13 declined, 22 non-adenomatous 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%). Polyp size ≥2 cm performed by 3 operators over a 9-year period; almost 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).

**Conclusion:** This was a large single-centre series of EMR of 424 sessile colonic polyps ≥2 cm performed by 3 operators over a 9-year period; almost 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 conflicts of interest.

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**TUESDAY, OCTOBER 18, 2016**

**BARRET’S ASSOCIATED NEOPLASIA – ROOM L7**

**OP216 DEVELOPMENT AND VALIDATION OF A CLASSIFICATION SYSTEM TO IDENTIFY BARRETT’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 neo-plastic 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) formed 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 aceto-chromening - Present: Indicates presence of neoplasia - Absent: Indicates the absence of neoplasia - Surface pattern - Normal (Large uniformly distributed pits) - 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 Table 1. 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% 95.4% and 99.6% 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.

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**OP217 STEPWISE DEVELOPMENT OF A VOLUMETRIC LASER ENDOMICROSCOPY PREDICTION SCORE FOR BARRETT’S NEOPLASIA: A USING MATCHED VLE-HISTOLOGY IMAGES OF ENDOCYTIC 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
4Gastroenterology And Hepatology, Mayo Clinic, Rochester/Rochester/United States of America
5Pathology, Academic Medical Centre, Amsterdam/Netherlands

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**Introduction:** Endoscopical 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 BE patients +/- neoplasia was used. Precise
VLE-histology correlation methodology has been described previously (3). In the orientation phase, the ex-vivo VLE images correlated with formalin-fixed tissue stained for Muc5ac, a well-established marker for Barrett's esophagus: a feasibility study on histological correlation. Dis Esophagus. 2015 May;8:1-8.

**References**


**OP218 DETECTION OF DYSPLASIA IN BARRETT’S OESOPHAGUS USING LECTIN-BASED NEAR INFRA-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 localised fluorescence within dysplastic versus non-dysplastic oesophageal glandular mucosa. 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-infra-red (NIR) imaging. 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-HRP800C (1μg/mL; 10 min; room temperature); washed with PBS buffer and then imaged with a high-sensitivity NIR camera (Flaebom 2, Fluoptics). Planar fluorescence images were captured and up to two punch biopsies (2 mm diameter) were collected from each EMR specimen, undergo VLE imaging. Our data potentially predicts the use of ex-vivo and in-vivo fluorescence imaging to detect dysplasia. The EMR specimens 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. In addition, the rate of dysplasia was compared between those with and those without dysplasia. The MFI of punch biopsies taken from dysplastic and non-dysplastic areas was compared by the Wilcoxon matched-pairs signed rank test. In addition, the rate of dysplasia was compared between those with and those without dysplasia.
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 (SERR) allows for complete excision 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 SERR for BE with early neoplasia. We screened all patients treated with SERR in two centers between 2001–2014, for BE ≤5 cm with HGD/EC, without signs of invasion. >T1sm1, G3/G4 differentiation, lymph-vascular invasion or irradial deep resection margins in ER specimens. All patients who had reached endoscopic and histologically confirmed CE-neo and CE-IM after SERR were included for evaluation of long-term FU. All included patients were followed-up medically and initially acted with chemotherpy/immunotherapy and entered in a dedicated database. Duration of FU was calculated from last treatment till last FU endoscopy. Primary outcome: recurrence of HGD/EC and CE-IM (CE-neo) in 98% and all intestinal metaplasia (CE-IM) in 85% of patients.

Results: Seventy-three patients were included (64 men, mean age 66 yrs, median BE C2M3). Worst baseline pathology: HGD, n = 50; EC, n=23. Median FU was 76 months (IQR 42–102) with a median follow-up of 6 (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 in endoscopically visible BE was observed in 16 patients (of which 2 had LGD) after a median FU of 31 months. In all cases the extent of the recurrence was limited to small (<1cm) islands or tongues. Histological recurrence without visible BE was found in 25 patients: 3 patients had BB in neouosquamous biopsies (4% overall, 0.7% per patient year); 24 patients (33%) showed IM in biopsies just distal to a neouosquamous or neouosquamous area. A finding of IM in the neo-z-line (BB) in neouosquamous biopsies, and IM in biopsies obtained distal to the neo-z-line.

Conclusion: Seventy-three patients were included (64 men, mean age 66 yrs, median BE C2M3). Twelve patients (16%) had a recurrence of HGD/EC (1.4%) or IM (33%) and 24 patients (33%) showed IM in biopsies just distal to a neouosquamous area. A finding of IM in the neo-z-line (BB) in neouosquamous biopsies, and IM in biopsies obtained distal to the neo-z-line. The recurrence rate of HGD/EC was 1.4% and 33% for IM.

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

CE were equally accurate for determining extent of EGC, thus both methods are

Netherlands

VOLUMETRIC LASER ENDOMICROSCOPY
DETECTION OF EARLY BARRETT’S NEOPLASIA USING

A total of 382 patients were enrolled and were assigned to the M-NBI

was obtained from all patients.

patterns; and that of CE were 1) abrupt change of mucosal structure of the

university hospital, one cancer referral center and three general hospitals. Inclusion criteria were patients with EGC sized 1 cm or over who underwent endoscopic or surgical treatment. Exclusion criteria were history of gastric resection and high risk of bleeding for biopsy. After stratification by institution, tumor location, and histological type, patients were randomly assigned to M-NBI or CE groups. In each group, tumor extent was firstly evaluated by white light endoscopy according to difference of mucosal height and color, then oral margin of the tumor was determined by the assigned method. Diagnostic criteria of M-NBI were 1) demarcation line and 2) irregular microvessel/microsurface patterns; and that of CE were 1) abrupt change of mucosal structure of the surrounding mucosa and 2) irregular structure patterns. Biopsy specimens were taken from 5-mm-outside and -inside of the oral boundary of the tumor and sent for histological evaluation. When the outside specimen was non-cancer and the inside specimen was cancer in histology, it was defined as “successful delineation” of the primary endpoint. This was defined as proportion of successful delineation between the two groups. A study protocol was approved by institutional review board in each institution and written informed consent for study participation was obtained from all patients.

A total of 382 patients were enrolled and were assigned to the M-NBI group (n = 191) and the CE group (n = 191). Eight patients in the M-NBI group and 12 in the CE group were excluded remaining 183 in the M-NBI and 179 in the CE group for analysis. Successful delineation rates (95% CI) in the M-NBI and CE groups were 86% (91-91%) and 84% (78-89%), respectively (p = 0.498).

Conclusion: This prospective randomized controlled trial revealed M-NBI and CE were equally accurate for determining extent of EGC, thus both methods are adequate to perform in clinical practice (UMIN000014628).

Reference


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

<table>
<thead>
<tr>
<th>Type</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>90.00 (55.50-99.75)</td>
<td>79.03 (66.82-88.34)</td>
<td>40.91 (20.70-63.65)</td>
<td>90.00 (89.35-99.95)</td>
<td>80.55</td>
</tr>
<tr>
<td>Type II</td>
<td>91.43 (76.94-98.20)</td>
<td>78.38 (61.70-90.17)</td>
<td>80.00 (64.35-90.95)</td>
<td>90.62 (74.98-98.02)</td>
<td>84.72</td>
</tr>
<tr>
<td>Type III</td>
<td>96.67 (9.43-99.16)</td>
<td>80.41 (78.43-94.86)</td>
<td>20.00 (2.52-55.61)</td>
<td>98.39 (91.34-99.96)</td>
<td>87.50</td>
</tr>
</tbody>
</table>

a) Ability to predict normal mucosa. b) Ability to predict Helicobacter pylori infection. c) Ability to predict mucosa atrophy.
gastric mucosa, types 2 and 3 HP related gastritis and the type 4 gastric atrophy. (II) Induction of polyps has been schematically recorded and biopsies taken in order to correlate the images with the histology.

**Result:** A total of 72 patients were included, 35 in the dyspeptic HP (+) group and 37 in the control dyspeptic HP (-) group. The average age was 46.3 (37-58.5) years; 31 male:41 female. The images were reviewed and classified into the four patterns after the agreement of three endoscopists. There were 22 (30.6%) patients with type I, 13 (18.1%) with type II, 27 (37.5%) with type III and 10 (13.9%) with type IV pattern. Almost all patients (90%) with normal mucosa were type I. Most type II and III patterns had active chronic gastritis, which correlates with HP infection. In fact, 32/41 (95.1%) of patients with HP (+) were type II-III. The 66% of patients with atrophy had type IV pattern. The Table 1 shows the overall accuracy of the four patterns predictions. Type I predictions were 100% with HP infection, and Type IV atrophy with a sensitivity of 90%, 91% and 66.7% respectively and an accuracy of 80.5%, 84.7% and 87.5% respectively. Finally the intra and inter-observer agreement was calculated with a kappa value of 0.91 and 0.89 respectively.

**Conclusion:** Endoscopy plus optical magnification has proved to be useful in the diagnosis of normal gastric mucosa and HP associated gastritis with high accuracy, unlike gastric atrophy evaluation.

**Disclosure of Interest:** C. Robles-Medranda: Key Opinion Leader for Pentax Medical

All other authors have declared no conflicts of interest.

**Reference**


OP227 ROAD MAP FLUOROSCOPY FOR SUCCESSFUL GUIDANCE OF ENDOSCOPIC INTERVENTIONS IN THE ESOPHAGUS

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**Introduction:** Digital subtraction angiography is a method to enhance the contrast of the walls of the vessels against structures that are not of interest are deleted from the image by subtraction of image information. A variation of this technique is called Road Map Fluoroscopy (RMF) where an image at peak opacification is used as the mask for subsequent subtraction images. With this technique all catheters or cather can be viewed without additional marking or contrast injection. In summary, the opacification is only performed once but the information remains on the image throughout the investigation. In this way anatomic structures such as length or diameter of stenosis can be measured with high accuracy (1–4). Although esophageal stent placement has been reported to be safe also without fluoroscopic guidance most endoscopists prefer to use fluoroscopy during stent deployment (5–7). Mucosal marking using the injection of lipiodol for stent implantation is widely used among endoscopists but may no longer be necessary if RMF is used as guidance of the procedure. The use of RMF has so far not been evaluated for endoscopic procedures.

**Aims & Methods:** We aimed to evaluate the usefulness of Road Map Fluoroscopy to guide endoscopic interventions in the esophagus. Patients with esophageal strictures were consecutively enrolled in a monocentric observational trial. After idenitication of the stenosis, a Road Map (Philips Multidigitization Eleva, Philips Medical Systems, Munich, Germany) was performed using 20 ml of water soluble contrast media that was applied through the working channel of a gastroscopy (Fujifilm EG530NW or Olympus GIF-Q 180). RMF recording requires stable fluoroscopy of the region of interest to generate a mask for consecutive subtraction. Thereafter contrast medium is injected. After RMF application all further fluoroscopy images contain the information of the subtraction as steady overlay. Directly after the RMF was finished, the complete fluid was removed from the esophagus to avoid aspiration. Patients were all investigated in recumbent position under sedation with induction of propofol for stent implantation. All further interventions and measurements were performed by using the RM images.

**Result:** 21 investigations were performed in 18 patients (age ≥71 ± 13 years male:12 female:6). Indications for interventions were: balloon dilatation of benign strictures (n = 9 including 1 pneumatic balloon dilatation for the treatment of achalasia, bougination of benign stricture: n = 3 and diagnostic radiography without intervention: n = 1. In addition 8 stents, 5 partially covered and 3 fully covered, were placed using RMF as a guide for exact determination of stent length and diameter. The stents were also deployed under RMF guidance. Endoscopic control revealed desired stent position in all cases. The choice of stent was made by measurement of the length of the stenosis as well as diameter of healthy esophageal adjacent to the stricture. Available stents that fitted best to the measured dimensions were implanted. In all procedures RMF successfully guided the intervention. The feeling of resistance during bougination was exactly matching the location for RMF projection of the stenosis. With the help of RM imaging the advancement of guidewire through esophagus could easily monitored and on the side of the balloon. Complications did not occur.

**Conclusion:** RMF provides the possibility of permanent radiographic illustration of stenosis or anatomic changes throughout the intervention by using contrast medium only at the beginning of the intervention. RMF is reliable and secure to guide radiology based interventions in the esophagus. RMF directs the selection of stents better than endoscopy because all relevant dimensions can be measured exactly.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Aims & Methods: Aim of the study: To investigate in detail the gastrointestinal presentations and outcomes in patients living in southern England. Type 3a patients, with more severe bile acid malabsorption. This warrants separate analysis in future research.

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 enteroctye) is the main endogenous source of circulating citrulline in blood. Since celiac disease is thought to be a highly heterogeneous spectrum ranging from classic malabsorptive form to atypical potential or latent form. It is envisaged that citrulline could be an important metabolic biomarker 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 amino acid citrulline levels in both with celiac disease and their 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 typing.DQ2 & DQ8) BY SSP-PCR

Result: Mean plasma citrulline levels in 54 serology positive subjects was month follow up and the mean levels were 12.8 ± 3 umol/L, DQ2 heterodimer subjects (first degree relatives) was 24.3±umol/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 3c grade lesions, mean citrulline levels were 5.6 ± 2.5 umol/L. For Marsh 3b, mean citrulline levels were 15.0 ± 4.0 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 biomarker 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 into the remotest place in the country to suggest improvement in gut enteroctye 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 of liquid chromatography mass spectrometry may ease follow up and diagnosis of CD.

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

OP251 CELLULAR ZINC IS REQUIRED FOR INTESTINAL EPITHELIAL BARRIER FUNCTION: THE REGULATION OF CLAUDIN-3 AND OCCLUDIN EXPRESSION
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Introduction: Intracellular zinc is 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 intracellular 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’-Tetrakis(2-pyridylmethyl)ethylenediamine (TPEN). Caco-2 cells grown in 24 well transwell plate with TPEN. 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 typing.DQ2 & DQ8) BY SSP-PCR

Result: Mean plasma citrulline levels in 54 serology positive subjects was month follow up and the mean levels were 12.8 ± 3 umol/L, DQ2 heterodimer subjects (first degree relatives) was 24.3±umol/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 3c grade lesions, mean citrulline levels were 5.6 ± 2.5 umol/L. For Marsh 3b, mean citrulline levels were 15.0 ± 4.0 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 biomarker 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 into the remotest place in the country to suggest improvement in gut enteroctye 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 of liquid chromatography mass spectrometry may ease follow up and diagnosis of CD.

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 calpain inhibitor restored the basal promoter activity and the TPEN-induced decreases. Reduced egr1 expression by a specific siRNA also inhibited the claudin-3 expression and barrier function of Caco-2 human intestinal epithelial cells. Dig Dis Sci 2013; 58: 77–87.

**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. Patients replied to 49 questions regarding 10 domains of function and 9 domains of symptoms. 3 further questions asked for a global numerical rating of QOL. A final question allowed free text comments. Scores were computed if at least half of the questions in each domain were answered as per the validated process in HPN-QOL. Raw patient responses were scaled to a score of 100 for each domain. The QOL global numerical ratings had a scale of 60 to 65. Based on the rating descriptors in the HPN-QOL, we interpreted a scaled score of more than 50 as good functioning ability. A scaled score exceeding 50 in symptom domains were interpreted as frequent symptoms impairing QOL. For the QOL global numerical ratings, a scaled score of 23 or more was interpreted as good overall QOL.

Patients were grouped according to the following 4 criteria for further analysis: gender, age (> 55 and ≤ 55), presence of stoma, and aetiology of IF. Within each group, QOL scaled scores were compared in every domain using the Kruskal-Wallis test.

**Result:** 85 responses were received from 67 patients. Two responses were excluded due to insufficient information to perform any form of analysis. 22 patients (41.5%) were male and 31 female. Median age was 55 years (range 19–85). 27 patients (50.9%) were 55 years and younger and 26 patients were older than 55 years. The aetiology of intestinal failure were mesenteric ischaemia, 16 (30.2%); inflammatory bowel disease (IBD), 15 (28.3%); surgical complications, 8 (15.1%); motility disorder and radiation enteritis, 5 each (18.9% in total); and malignancy, 4 (7.5%). 37 patients (69.8%) had a stoma and 16 had no stoma. There was no difference between patient’s gender, age and waist to hip ratio. TPEN-QOL was completed in all domains except gastrointestinal (GI) symptoms (p = 0.01). This is in keeping with findings by Baxter, et al (1). In gender analysis, males reported better ability to eat and drink (p = 0.027), better perceived support from the MDT (p = 0.027), and less energy (p = 0.046). Females also reported more GI symptoms (p = 0.006). In age group analysis, patients over 55 had lower employ-ment scores (p = 0.004) and more GI symptoms (p = 0.014). The lower employ-ment scores may be confounded by advancing age alone. In analysis of aetiology, patients with motility disorders reported significantly reduced ability to eat and drink compared to those with other causes of IF except malignancy (p = 0.034). Regardless of gender, age, or presence of stoma, patients generally rated their ability to travel/holiday, physical function, employment, and general health as ≤ 60%.

**Conclusion:** As part of the holistic clinical care of patients on HPN, their QOL should be considered. Results of this study show that the majority of our HPN patients experience problems that impair their QOL. It is not possible to establish how much this relates to the underlying condition or HPN itself. This is an area that would benefit from further study.

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

**References**


**OP256 EARLY ENTERAL VERSUS TOTAL PARENTERAL NUTRITION IN PATIENTS UNDERGOING PANCREATICO DUODENECTOMY; A RANDOMIZED MULTICENTER CONTROLLED TRIAL (NUTRI DPC)**

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7 Digestive Surgery Unit, Edouard Herriot Hospital, Lyon/France
8 Department Of Hepato-biliary And Pancreatic Surgery, Edouard Herriot Hospital, Lyon/France
9 Department Of Digestive Surgery, University Hospital, Lyon/France
10 Department Of Hepato-biliary And Pancreatic Surgery, Edouard Herriot Hospital, Lyon/France

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**Introduction:** Current nutritional guidelines recommend the use of enteral over parenteral nutrition in patients undergoing gastrointestinal surgery. However, the NJJEN remains controversial in patients undergoing PD.

**Aims & Methods:** To compare nasojejunal early enteral nutrition (NJJEN) with total parenteral nutrition (TPN), after pancreaticoduodenectomy (PD), in terms of postoperative complications. Multicenter, randomized, controlled trial was conducted between 2011 and 2014. Nine centers in France analyzed 204 patients undergoing PD to NJJEN (n=113) or TPN (n=91). Primary outcome was the rate of postoperative complications according to Clavien-Dindo classification. Successful NJEEN was defined as insertion of a nasojejunal feeding tube, delivering at least 50% of nutritional needs on PoD 5, and no TPN for more than 48 hours.

**Result:** 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 pancreatico-duodenal 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 63% 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).

**Conclusion:** In patients undergoing PD, NJEEN was associated with increased overall postoperative complications rate. The frequency and the severity of POPF were also significantly increased after NJEEN. In term of safety and feasibility, NJEEN should not be recommended.

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

**References**


Disclosure of Interest:

genes. flagellin, whereas CMC increase the pro-inflammatory potential of the microbiota. The mechanisms by which P80 and CMC act are distinct, with P80 altering human gut microbiota composition, associated with an increased proportion 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 with CIPO. Patients' gut microbiota profiles of gut microbiota of mice colonized with the faecal microbiota of recipients with CIPO. Microbiota transplantation (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 CIPO 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 with CIPO. Patients’ gut microbiota profiles of gut microbiota transplantation (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 CIPO 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 with CIPO. Patients’ gut microbiota profiles of gut microbiota transplantation (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 CIPO 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 with CIPO. Patients’ gut microbiota profiles of gut microbiota transplantation (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 CIPO 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 with CIPO. Patients’ gut microbiota profiles of gut microbiota transplantation (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 CIPO 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 with CIPO. Patients’ gut microbiota profiles of gut microbiota transplantation (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 CIPO 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 with CIPO. Patients’ gut microbiota profiles of gut microbiota transplantation (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.

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Reference


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

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

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Disclosure of Interest: All authors have declared no conflicts of interest.
OP237 BILE MICROBIOTA IN PRIMARY SCLEROSING CHOLANGITIS: EFFECTS ON DISEASE STAGE 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 genetic background 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 enterohepatic circulation of PAMPs (“leaking gut”), or abnormal PAMPs (as a result of enteric microbial dysbiosis, disruption in IBD). Moreover, 16S ribosomal ribonucleic acid (rRNA) 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 FT2 (2-a-L-fucosyltransferase 2) polymorphism, a gene involved in protein glycosylation.

Aims & Methods: To study the possible role of biliary 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 PSC registry of the Clinic of Gastroenterology. The indication for ERCP examination was the documentation of diagnosis of PSC due to: 1) constantly elevated or fluctuating serum alkaline phosphatase (ALP) levels in conjunction with IBD, or 2) magnetic resonance cholangiography findings, or 3) liver biopsy suggestive of PSC, or dysplasia surveillance. During patient’s ERCP and before injecting contrast media a bile sample was aspirated from extrahepatic bile ducts using balloon catheter, whenever possible. Brush cytology was routinely performed during ERCP. ERC findings were scored according to the modified Amsterdam score (mAm score) and the number of ERC examinations were recorded in each patient group. Isolation, amplification and sequencing of the bacterial 16S rRNA gene were performed. The resulting data was analyzed with negative binomial generalized linear 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. 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 biliary microbiota. Overall, microbiotal 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 IRRITABLE BOWEL SYNDROME ARE ASSOCIATED WITH LUMINAL MICROBIOTA COMPOSITION AND SYMPTOM SEVERITY


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Introduction: Chromogranins (Cg) and secretogranins (Sg) are acidic gut hormones, which are secreted from the neuroendocrine system and may regulate immune activation. We have previously shown increased levels of faecal Cg and Sg in IBS patients (1). However, the consequences and cause of increased levels of luminal granins in IBS are still undefined.

Aims & Methods: In this study we aimed to quantify faecal granin levels in IBS patients and evaluate potential relationships between granin levels, microbiota composition and immune activation. Levels of CgA, CgB, SgII and SgIII were determined 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) and forkhead box P3 (FOXP3) was quantified by qRT-PCR.

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 (0.7 (0.4–2.4), p < 0.01) respectively (0.7 (0.4–2.4), p < 0.001, pmol/L). Faecal microbial diversity was reduced with CgA (r = −0.29, p < 0.005), CgB (r = −0.21,
Table 1 (OP239): Dysbiosis status

<table>
<thead>
<tr>
<th>Dysbiosis</th>
<th>Patients</th>
<th>Age [med.]</th>
<th>Female</th>
<th>IBD</th>
<th>CD</th>
<th>UC</th>
<th>IBDU</th>
<th>Non-IBD</th>
<th>Healthy control</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>72</td>
<td>28 (19–68)</td>
<td>43</td>
<td>22</td>
<td>18%</td>
<td>7</td>
<td>16%</td>
<td>11</td>
<td>18%</td>
<td>4</td>
</tr>
<tr>
<td>Low</td>
<td>96</td>
<td>33 (19–66)</td>
<td>49</td>
<td>33</td>
<td>28%</td>
<td>14</td>
<td>31%</td>
<td>15</td>
<td>24%</td>
<td>4</td>
</tr>
<tr>
<td>High</td>
<td>126</td>
<td>32 (18–69)</td>
<td>80</td>
<td>65</td>
<td>54%</td>
<td>24</td>
<td>53%</td>
<td>36</td>
<td>58%</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>294</td>
<td>172</td>
<td>120</td>
<td>62</td>
<td>45%</td>
<td>62</td>
<td>48%</td>
<td>48</td>
<td>22%</td>
<td>48</td>
</tr>
</tbody>
</table>

p < 0.05 and SgII (r = −0.28, p < 0.005). In addition, SgII showed a tendency to be negatively correlated with faecal microbial Shannon diversity (r = −0.19, p < 0.05). No correlations were found between any of the granins (CgA, CgB, SgII and SgIII) and mucosal-associated microbiota Shannon diversity or mucosal immune activity (i.e. calprotectin or expression of IL-8, IL-10, TNF and FOXP3). A positive correlation between total GI symptom severity (GRSS-IBS) and levels of CgA was detected (r = 0.22, p < 0.001). General psychological distress measured with total HAD score was positively correlated to CgA (r = 0.24) and CgB (r = 0.34, both p < 0.05).

**Conclusion:** This study confirms that IBS patients have increased faecal levels of CgA, SgII and SgIII as compared to healthy subjects. Negative associations were found between levels of luminal granins and luminal microbiota diversity, but not with either mucosal immune activity or mucosal-associated microbiota. GI symptom severity and psychological distress were also associated with increased levels of chromogranins in the lumen.

**Disclosure of Interest:** T. Jap: Employee at Danone
M. Derrien: Employee at Danone
B. Le Neve: Employee at Danone
H. Törnblom: Consultant/Advisory Board member for Almirall, Allergan, Danone and Shire, Speaker for Tollotts, Takeda, Shire and Almirall
L. Ohman: Unrestricted research grants from AstraZeneca; Consultant/Advisory Board member for Genetic Analysis; Speaker for Genetic Analysis, Takeda and Abbots
M. Simrén: Unrestricted research grants from Danone, and Ferring Pharmaceuticals; Consultant/Advisory Board member for AstraZeneca, Digestive, Neutal Medics, Oncorw Ltd, Allergan, Almirall, Althea, Glycom and Shire; Speaker for Tollotts, Takeda, Shire and Almirall
All other authors have declared no conflicts of interest.

**Reference**

**OP240 METABOLIC SYNDROME CORRELATES WITH MICROBIOTA ENCRUSTMENT IN HUMAN INTESTINE**

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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 microbial encrustation 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 fasted serum glucose levels. 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 to analyze bacteria localization at the surface of the intestinal mucosa.

**Result:** We found that bacterial encrustation 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.

**Conclusion:** These observations support the notion that microbiota promotion of low-grade inflammation may play a causative role in metabolic diseases in humans. These findings are important advances that will significantly impact our understanding of the epidemic of metabolic syndrome.

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

**References**
**OP241** CLINICAL FEATURES AND FECAL MICROBIOTA PROFILE IN IRITABLE 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 lactulose breath test (LB), 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 LB, while healthy controls with negative LB (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) and LBT. (2) SIBO can cause malnutrition and worsen nutritional status. (3) The intestinal permeability, systematic inflammation and visceral hypersensitivity of IBS-P are better than IBS-N. (4) Differences are observed in fecal SCFA between IBS-P and IBS-N. (5) Both IBS-P and IBS-N are different from HC in microbiota abundance and community diversity, in which IBS-P is also different from IBS-N. As a consequence, IBS-P is different from IBS-N in many physiological parameters and fecal microbiota profile, so IBS-P may be just SIBO which should be screened before diagnosis of IBS-P according to Rome II criteria.

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

**OP242** FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT C. DIFFICILE INFECTION: ANALYSIS OF FACTORS ASSOCIATED WITH THE NEED FOR MULTIPLE FECAL INFUSIONS


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Introduction: Fecal microbiota transplantation (FMT) from healthy donors is considered a highly effective treatment against recurrent Clostridium difficile infection (rCDI). A single fecal infusion is usually sufficient to resolve symptoms and eradicate rCDI, but a subgroup of these patients need multiple infusions to cure the disease. In our previously published randomized controlled trial of FMT versus vancomycin for rCDI, we observed that patients with pseudomembranous colitis (PMC) needed repeat fecal infusions to be cured, further reports confirmed our findings. To date, however, neither PMC nor other factors have been clearly proven to be associated with the need for multiple FMT.

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>IBS-P (n = 31)</th>
<th>IBS-N (n = 39)</th>
<th>HC (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinobacteria</td>
<td>Collinella</td>
<td>95(34, 146)b</td>
<td>21(2, 155)</td>
<td>47(19, 133)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Bacteroidetes</td>
<td>Prevotella_9</td>
<td>72(69, 14813)a</td>
<td>17(1, 9272)</td>
<td>41(1, 6767)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alitipes</td>
<td>434(131, 1064)b</td>
<td>155(13, 467a)</td>
<td>579(70, 849)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bacteroides bacteraeum</td>
<td>35(0, 217)b</td>
<td>3(0, 25)</td>
<td>23(0, 142)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Butyricimonas</td>
<td>22(4, 159)b</td>
<td>5(0, 15)</td>
<td>90(4, 90)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Parabacteroides</td>
<td>242(152, 683)b</td>
<td>108(45, 245a)</td>
<td>225(145, 338)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paraprevotella</td>
<td>60(3, 312)a</td>
<td>1(0, 23)</td>
<td>0(0, 28)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Odoribacter</td>
<td>35(0, 88)b</td>
<td>5(0, 47)</td>
<td>33(1, 73)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Firmicutes</td>
<td>Faecalibacterium</td>
<td>3387(1778, 6294)b</td>
<td>2174(449, 475)</td>
<td>2860(1290, 4699)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pseudobutyribrio</td>
<td>325(1248, 5860)b</td>
<td>1249(261, 3600)</td>
<td>191(1163, 3133)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subdoligranulum</td>
<td>1101(621, 2182)b</td>
<td>544(77, 166)</td>
<td>125(1316, 1962)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lachnospiraceae_NK4A136</td>
<td>234(302, 672)b</td>
<td>85(22, 468a)</td>
<td>40(16, 1446)</td>
<td>&lt;0.05</td>
<td></td>
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<tr>
<td></td>
<td>Eubacterium_caprodiotomoligenes</td>
<td>197(46, 571)b</td>
<td>90(3, 197)</td>
<td>139(10, 810)</td>
<td>NS</td>
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<tr>
<td></td>
<td>Ruminococcus_1</td>
<td>145(35, 523)b</td>
<td>7(1, 111a)</td>
<td>29(4, 346)</td>
<td>&lt;0.05</td>
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<tr>
<td></td>
<td>Eubacterium_hallii</td>
<td>313(132, 636)b</td>
<td>118(44, 367)</td>
<td>141(61, 620)</td>
<td>NS</td>
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<td></td>
<td>Christensenellaceae-R-7</td>
<td>104(4, 209)b</td>
<td>5(8, 1a)</td>
<td>616(357)</td>
<td>&lt;0.05</td>
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<td></td>
<td>Enterococcus</td>
<td>7(3, 13)</td>
<td>11(3, 30)</td>
<td>3(0, 16)</td>
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<td>Family_XIII</td>
<td>18(2, 28b)</td>
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<td>13(2, 28)</td>
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<td>Lachnospiraceae</td>
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<td>863(409, 2232)</td>
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<td>Romboutsia</td>
<td>86(15, 201)b</td>
<td>156(46, 478)</td>
<td>127(40, 284)</td>
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<td></td>
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<td>804(266, 1183)</td>
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<td>Proteobacteria</td>
<td>Escherichia_Shigella</td>
<td>49(31, 471)b</td>
<td>338(65, 1548a)</td>
<td>270(1, 216)</td>
<td>NS</td>
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<td></td>
<td>Klebsiella</td>
<td>43(6, 130b)</td>
<td>106(11, 494)</td>
<td>401(1, 172)</td>
<td>NS</td>
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<td></td>
<td>Ralstonella</td>
<td>7(3, 11a)</td>
<td>11(4, 28a)</td>
<td>20(2, 9)</td>
<td>NS</td>
<td></td>
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<tr>
<td></td>
<td>Sutterella</td>
<td>7(3, 13)</td>
<td>20(5, 7a)</td>
<td>50(6, 143)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

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.
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 if the patient recurred or failed to improve after first infusion. Gender, age, inpatient status, number or CDI recurrences (>3), poor/inadequate bowel preparation (according to Ottawa Scale), endoscopic evidence of colonic oedema, presence of PMC, use of external donors, infusion of frozen material, and infused grams of faeces were analysed as potential impact factors. Univariate associations between possible predictors and the need for repeat 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 (27.8%) received multiple infusions, for a total of 81 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 saline infusion was more common among patient who experienced a number or CDI recurrence greater 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 faecal material was significantly associated with lower need of multiple FMT (OR = 0.01; 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 repeat fecal infusions. Additionally, from our data, FMT appears to be significantly associated with a decreased need of multiple FMT. As the small sample size represents a limitation of our analysis, our findings, although promising, should be confirmed by further, larger studies.

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

References

OP243 ENDOSCOPIC BALLOON DILATION FOLLOWED BY STEROID INJECTION IN ANASTOMOTIC STRictures AFTER ESOPHAGEAL RESECTION: A MULTICENTER RANDOMIZED, DOUBLE-BLIND CONTROLLED TRIAL

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Introduction: Esophageal cancer is the fifth most common cause of cancer-related death for men and the eighth for women worldwide. Although the effectiveness of chemotherapy or chemoradiotherapy for the treatment of esophageal cancer has been shown, the standard treatment to cure esophageal cancer. Anastomotic stricture, a major complication after esophagectomy, substantially decreases patients' quality of life, and requires treatment with multiple sessions of endoscopic balloon dilation (EBD).

Aims & Methods: We conducted a multicenter randomized controlled trial to evaluate the usefulness of administration of local steroid injections to prevent the recurrence of anastomotic stricture. Patients were randomized to receive either triamcinolone or placebo immediately after EBD. The primary endpoint was the number of dilations required to resolve the stricture. Secondary end-points were restriction-free survival and adverse events. Restriction-free survival is defined as the number of days from randomization to performing EBD for any reason of dysphagia from any cause. Patients with a dysphagia symptom score of two or more after esophagectomy with anastomotic stricture confirmed by endoscopy were included. Patients and investigators were blinded to the type of agent injected. The syringe containing triamcinolone or placebo was prepared by nursing staff unconnected to the trial. Patients underwent EBD with a standard through-the-scope balloon dilator. The balloon was inflated with water, aiming for a luminal diameter of maximum 15 mm for 3 min. After EBD, a second endoscopist who was not involved in the follow-up evaluation of the patients performed the injections into the intraluminal salivary. A total of a single of triamcinolone acetonide (50 mg/5 mL; Bristol-Myers Squibb) or an identical volume of normal saline solution as a placebo was injected per single site using a 25-gauge needle. Neither the patient nor the treating physician knew which treatment was given. The response to the EGD (ESD) was performed on demand whenever patients reported dysphagia. In patients without dysphagia, EGD was performed within 3 months after EBD to evaluate the stricture. EBD was performed when the stricture was confirmed. Stricture was defined as dysphagia to solid foods (dysphagia score 2) and an inability to pass an endoscope of at least 9.2 mm diameter.

Result: Over a 4-year period, 68 patients met the inclusion criteria and were screened. Three patients declined to participate. Sixty-five consecutive patients were therefore recruited to the study and randomized: 33 to receive steroid and 32 to receive placebo. The median number of EBD sessions required to resolve stricture in the steroid group was 2 (range, 1–7), significantly smaller than the median of 4 EBD sessions (25/33) required by the control group (p < 0.001). After 6 months of follow-up, 39% of patients who received steroid injections remained recurrence-free compared with 19% of those injected with saline (p < 0.01). There were no adverse events during follow-up.

Conclusion: Steroid injection showed promising results for the prevention of stricture recurrence in patients who underwent EBD for anastomotic stricture.

Disclosure of Interest: N. Hanaka: The Japan Foundation for Research and Promotion of Endoscopy Grant

All other authors have declared no conflicts of interest.

OP244 THE "TUNNEL + CLIP" METHOD FACILITATES OESOPHAGEAL ESD PROCEDURES: A PROSPECTIVE, CONSECUTIVE BI-CENTRIC STUDY

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Introduction: ESD is the treatment of choice for superficial neoplasms of the oesophagus due to its oncological efficiency and the morbidity associated with the surgical alternative. ESD requires a high level of skill and is technically challenging and time consuming. Therefore, it is often reserved to experts. Combining the tunnel technique and the clip-line counter-traction may enable optimisation of oesophageal ESDs.

Aims & Methods: From January 2014 to April 2016 we performed a prospective bi-centre case series of consecutive "tunnel +clip" oesophageal ESDs. For young operators (fewer than 50 ESDs and fewer than 5 oesophageal ESDs) we 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 mm/min for a mean lesion size of 61.6 mm. The clip provided considerable assistance in performing the procedure. No pathological damage caused by the clipping was reported.

References

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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, allows 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

TUESDAY, OCTOBER 18, 2016
WHAT TO DO WITH SMALL COLORECTAL POLyps? – ROOM F

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. The strategy 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 and validated 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 differentiation 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

TUESDAY, OCTOBER 18, 2016
BIOMARKERS IN IBD – ROOM K

OP247 IBDOC – FIRST SMARTPHONE BASED CALPROTECTIN HOME TEST – 18 MONTHS EXPERIENCE

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Introduction: Inflammatory Bowel Disease (IBD) is a chronic inflammation of the gut presenting with phases of active inflammation, remission and relapses. IBD treatment goals are mucosal healing and persistent remission. Calprotectin measured in patients' stool 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 laboratory analysis, leading to long delays between sample collection, final test result and potential adaptations of therapies.

Aims & Methods: We have developed a smartphone-based calprotectin home test, called IBDoc®, that allows real-time information about the inflammatory activities in the gut for both, the patient and the health care provider. The IBDoc® consists of a stool collection and extraction device (CALEX Valve) and an immunochromatographic calprotectin rapid test, which is measured using a smartphone App (CalApp) controlling the phone’s camera. Once the test is...
measured the result is instantly sent to a webserver (IBDoc Portal) allowing the treating physician immediate access to the 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 iCAL® ELISA) IBDoc® correlated very well with both methods with a mean bias of 2.7% and 0.9%, 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 100 µg/m, mean bias at cut-off, -7.0 to 5.4%). Moderate/amber (100-300 µg/m) and as High/red (above 300 µg/m, 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% within-class agreement observed. We judged 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 care providers and compared well to existing calprotectin point-of-care and laboratory based methods and has proven to be a supportive tool in daily clinical routine.

Disclosures of Interest: Reinhard: Christian Reinhard is an employee of BUHLMANN Laboratories AG

A. Ritz: Alicja Ritz is an employee of BUHLMANN Laboratories AG

M. Uberschlag: Marie-Eve Uberschlag is an employee of BUHLMANN Laboratories AG

J. Weber: Jakob Weber is an employee of BUHLMANN Laboratories AG

All authors have declared no conflicts of interest.

References
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OP248 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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2Department Of Gastroenterology, Zuyderland Medical Centre, Sittarda-Henert/ Netherlands
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Introduction: Telendoscopic programmes are of interest for inflammatory bowel disease (IBD) patients, but should include adequate monitoring of mucosal inflammation to prevent long-term complications. Different clinical activity questionnaires are available, however, none are patient-reported, clear and easy to fill out and validated against endoscopy. For this reason we previously developed the MIAH (Mucosal Inflammation Activity Horizont) questionnaire and a calprotectin home test yields higher diagnostic accuracy.

Aims & Methods: Between September 2015 and April 2016 all consecutive IBD patients with a scheduled endoscopy in the Maastricht University Medical Centre+ were asked to collect a stool sample prior to bowel cleansing. Fecal calprotectin was measured and MIAH-CD questionnaire and a calprotectin home test shows a high sensitivity and thus can be used as a complement to disease activity questionnaires to identify patients who need further assessment of disease activity with biochemical markers, imaging or endoscopy.

Disclosure of Interest: M.J. de Jong: Non financial support Immunodiagnostik

All other authors have declared no conflicts of interest.

Reference

OP249 ACCURACY OF NON-INVASIVE TESTS IN THE INITIAL DIAGNOSTIC WORK-UP OF PEDIATRIC INFLAMMATORY BOWEL DISEASES

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Introduction: Upper and lower endoscopy with histology together with imaging of the small bowel is the gold standard for the diagnosis of inflammatory bowel disease (IBD) in children. Due to high costs and invasive nature of these techniques, accurate selection of patients is mandatory.

Aims & Methods: We aimed to assess the accuracy of non-invasive tests including fecal calprotectin (FC), blood inflammatory markers (BIM) and bowel ultrasound (US) alone or in combination as first level investigations in children with suspected IBD. Consecutive patients referred to our Unit for a clinical history compatible with IBD were enrolled during a 3-year period. All underwent FC (Calprotectin®, Eurospital), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and bowel US as first investigations. Endoscopy with biopsies was the gold standard for diagnosis. At US pathological findings were: BWT > 3 mm, BW vascularity, loss of stratification, enlarged mesenteric nodes. Multiple logistic analysis with stepwise method considering IBD diagnosis as dependent variable was conducted. Sensitivity (SE), specificity (SP), positive and negative predictive values (PPV and NPV) of laboratory and US parameters alone or in combination were analyzed according to the final diagnosis.

Result: 100 patients (58 males, median age 12) were enrolled. The final diagnosis was IBD in 69 (57 CD, 12 CU) other than IBD in 31. The mean values of CRP, ESR, FC and BWT were higher in IBD vs non-IBD patients (p < 0.001). Multiple logistic analysis showed that independent variables predictive of IBD were: FC (OR 44.8; p < 0.001), BWT (OR 20.4; p < 0.001) and ESR (OR 9; p < 0.001). The combination of 3 or 2 parameters was more frequent in IBD patients (p < 0.01). Table 2 shows SE, SP, PPV, NPV of these parameters alone or in combination.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SE %</th>
<th>SP %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
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<td>89</td>
<td>94</td>
<td>89</td>
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<tr>
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<td>3 (FC + BWT + ESR)</td>
<td>71</td>
<td>100</td>
<td>90</td>
<td>64</td>
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</table>

Conclusion: The combination of FC, BIM and bowel US may help to select children needing further invasive procedures and allow to avoid or delay endoscopy in patients with negative initial diagnostic work-up.

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

Reference
A. H: Home questionnaire (MIAH) (1). The score does not include laboratory tests or physical examination. The objective of this study was to investigate whether a combination of the MIAH questionnaire and a calprotectin home test yields higher diagnostic accuracy.

Aims & Methods: Between September 2015 and April 2016 all consecutive IBD patients with a scheduled endoscopy in the Maastricht University Medical Centre+ were eligible for inclusion. Patients with an ileostomy, colostomy, ileal pouch anastomosis or ileorectal anastomosis were excluded. Patients were included if they fulfilled all items of the MIAH-CD questionnaire for UC, regarding blood loss, number of stools, urgency, abdominal pain and general well-being, or the 6-item MIAH-CD questionnaire for CD, including questions on blood loss, mucus, number of stools, urgency, fatigue and general well-being. In addition, patients were included if they collected a stool sample prior to bowel cleansing. Fecal calprotectin was determined with a calprotectin home test. Mucosal inflammation was assessed with the simple endoscopic activity score (SES-CD) for Crohn’s disease (CD) and the Mayo endoscopic subscore (MES) for ulcerative colitis (UC). Sensitivity, specificity, predictive value (PPV) and negative predicted value (NPV) of the MIAH-UC and MIAH-CD in combination with the calprotectin home test were calculated.

Result: Thirty-two CD patients (50.0% male, mean age 51.4 ± 15.2 years, 43.8% active disease) were included. Thirty-two UC patients (50.0% male, mean age 57.3 ± 10.4 years, 39.3% active disease) were included. The combination of the MIAH-CD and the calprotectin home test showed a sensitivity of 100.0%, a specificity of 61.1%, a NPV of 100.0% and a PPV of 67.0%. The combination of the MIAH-UC and the calprotectin home test yielded a sensitivity of 91.7%, a specificity of 68.3%, a NPV of 91.7% and a PPV of 68.8%.

Conclusion: The MIAH is the first patient-reported questionnaire developed to predict endoscopic inflammation in IBD patients. The combination of MIAH and the calprotectin home test shows a high sensitivity and thus can be used as a complement to disease activity questionnaires to identify patients who need further assessment of disease activity with biochemical markers, imaging or endoscopy.
serological markers with the biochemical markers C-reactive protein (CRP), elevated sedimentation rate (ESR) and fecal calprotectin. 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 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 8 (26%) of the CD patients were ASCA IgA or IgG positive (p < 0.0001), 18 (49%) were positive for ASA IgA, 14 (38%) for ASA IgG, and 12 (33%) for both. There were statistically significant differences between CD and UC patients in the prevalence of antibodies against *Pseudomonas fluorescens* associated (33%, 13%), the outer membrane protein of Escherichia coli (OmpC) (8% vs. 6%) or flagellin expressed by Clostridial phylum (CIB) (22% vs. 0%, respectively). The 18 (49%) CD patients who received aggressive treatment with TNF blockers had higher presence of antibodies against ASA IgA (p = 0.085) and ASCA IgG (p = 0.048) as well as higher titers of ASA IgG (p = 0.046) compared to the 19 (51%) CD patients who received conventional treatment. IF ASCA antibodies were present at baseline the probability of receiving infliximab treatment in CD patients was 70%, with OR 8.2 (2.0-37.7), p = 0.004. The presence of pANCA antibodies was less frequent at diagnosis in TNF blocker treated CD patients compared to conventionally treated CD patients. The OR of receiving aggressive therapy being pANCA negative was 5.4, (95% CI 1.7–17). CD patients with previous infliximab treatment had significantly higher levels of fecal calprotectin, CRP and ESR at diagnosis compared to conventionally treated CD patients with median values of fecal calprotectin (mg/kg) 1586 vs. 501 (p = 0.01), CRP (mg/l) 28 vs. 7.5 (p = 0.02) and ESR (mm/h) of 32 vs. 18 (p = 0.01) respectively. Being pANCA negative and/ or ASA IgA or ASA IgG positive was associated with the need for TNF blocker therapy, even after adjustment for CRP, ESR and fecal calprotectin levels. After treatment there was no difference in antibody prevalence for ASA IgA, ASA IgG, 12, Q8, ASCA IgA and UC patients, regardless of treatment modality. Fewer UC patients, 9 (64%), tested positive for pANCA after treatment, compared to at baseline, 13 (72%), p = 0.013. Only one of the 18 UC patients received TNF blocker treatment.

Conclusion: ASCA and pANCA status was associated with the need for early aggressive therapy with TNF blockers in our CD patients. We found that being pANCA negative and/ or ASA IgA or ASA IgG positive were more predictive of receiving aggressive treatment than CRP, ESR or fecal calprotectin levels. ASCA IgG and pANCA positive regardless of treatment modality, and might be a prognostic tool at any time in the disease course.

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

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

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Introduction: Inflammatory bowel disease (IBD) is a chronic intestinal inflammatory disorder presenting with phases 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 been shown to be important for the monitoring of IBD patients. However, determination of fcalpro levels is burdening patients, since they are required to send stool samples in for laboratory analysis, resulting in a long delay between sample collection and final test results. We developed a smartphone-based calprotectin test system called QuantOnCal in cooperation with a diagnostic laboratory, allowing the patient 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 IBD: CU/CD/active/emission, 42/43:48:47; 33 IBS: UC: Div 6) were either loaded onto immunochromatographic test cassettes (TCs) or analysed with a commercial ELISA test (Immundiagnostik, Bensheim, Germany). The QuantOnCal app was installed on 4 different iPhone 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 25–20000 mg/g fcalpro of stool, covering the clinically relevant range of this biomarker. The total agreement (TA) was 96.4% with 0% false positive and 0% false negative rates. The TA for fcalpro between the 4 different iPhone models was 91.3%.

Conclusion: QuantOnCal is a new, complete and validated test system which can be used for monitoring IBD patients monitoring. IBD patients can monitor their condition 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 Immundiagnostik AG, Bensheim, Germany

J. Stein: Jürgen Stein has received payment for lectures and consultancy from Immundagnostik AG, Bensheim, Germany

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Disclosure of Interest: All authors have declared no conflicts of interest.
OP253 RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF BIOFEEDBACK FOR THE TREATMENT OF ABDOMINAL DISTENSION

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References

Disclosure of Interest: Conclusion:

T.N. Hustoft

PATIENTS WITH IBS: A RANDOMIZED CONTROLLED TRIAL

Result: IBS symptoms consistently and significantly improved after 3 weeks of LFD, with a mean overall reduction of 163.8 points (p < 0.0001). 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 = 0.001 and p < 0.001, respectively). The LFD also applied to luminal microbiota (Faecalibacterium prausnitzii and Bifidobacterium (p = 0.0084 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 levels of bacteria, but did not change the levels of cytokines nor SCFAs.

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.

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Introduction: Abdominal distension is the most bothersome complaint in patients with functional gut disorders and has no specific treatment. In a prospective study, we showed that abdominal distension is produced by diaphragmatic contraction and descent with protrusion of the anterior abdominal wall, and we developed an original biofeedback technique based on EMG-guided control of abdominal-thoracic muscular activity.

Aims & Methods: Our aim was to demonstrate the superiority of biofeedback versus placebo for the treatment of abdominal distension. We performed a randomized, placebo-controlled and in a referral center (Clinical Trials Gov Registration Number 01205100). Forty-two patients complaining of episodes of visible abdominal distension who fulfilled the Rome III criteria for functional intestinal disorders (47 women, 1 men; 21-74 year age range) were recruited and randomized to biofeedback and placebo. Abdomino-thoracic muscle activity was recorded by EMG during basal conditions (no distension) and during an episode of distension to prove the abdomino-phrenic origin of their distension. Each patient underwent three treatment sessions over a 10-day period. The biofeedback intervention is poorly defined. Abdomino-thoracic muscle activity was measured by EMG. The patients in the biofeedback group were shown the signal and instructed to control muscle activity; the patients in the control group were given and oral placebo.

The main outcome was subjective sensation of abdominal distension rated by a 0-6 graphic rating scale daily for 10 days before and after treatment

Results: Patients on biofeedback, but not on placebo, effectively learned to reduce intercostal activity (by 45.3% vs 5 ± 2% on placebo; p < 0.001) and to control intercostal muscle activity (by 101 ±10% vs. -4 ±2%). Biofeedback treatment resulted in a 56% ±1% reduction of abdominal distension (from 4.6 ±0.2 to 2.0 ±0.2 score after intervention) vs 13±8% on placebo; p< 0.001 (from 4.7 ±0.1 to 4.1 ±0.4 score after intervention).

Conclusion: Abdominal distension can be treated by biofeedback-guided control of abdominal-thoracic muscular activity.

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: FODMAP is the most common gastrointestinal (GI) disorder worldwide. In the lack of cures, different management strategies have been purposed, including a diet low in FODMAPs (fermentable oligo-, disaccharides, monosaccharides and polyols). Although being increasingly accepted and recommended as one of the most effective therapies, there is insufficient high-quality evidence of its efficacy as well as uncertainties regarding surgical and physical factors, rather than a reduction in individual symptoms, is required and may be associated with the development of diarrhoea during breath testing (multivariate analysis 1.7 (1.03-2.81), p = 0.04). No other significant associations between symptoms experienced during fructose or lactose breath testing and dietary outcome were demonstrated.

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 be a standard adequate global symptom relief question. Predictive associations were assessed by uni- and multivariate analyses.

Result: Adequate symptom relief was achieved in 81% of the 580 FGID patients, with a median response rate of patients with fructose (79%) and lactose (79%) intolerances and across all FODMAP subtypes (IBS-diarrhoea: 80%, IBS-constipation: 71%, IBS-mixed: 89%, FD: 79%). A positive history of chronic diarrhoea or puritus predicted adequate symptom relief with the FODMAP diet (univariate analyses 2.7 (1.5-4.9), p = 0.001 and 2.7 (1.5-4.9), p = 0.001 respectively, both p < 0.01), while nausea predicted inadequate relief (0.55 (0.34-0.89), p = 0.01) Multivariate analysis confirmed the associations between adequate symptom relief and a history of diarrhoea (positive predictor: 2.74 (1.52-4.94), p = 0.001) and nausea (negative predictor: 0.52 (0.35-0.81), p = 0.07). There were no significant associations between the H2 or CH4 breath concentrations and the attainment of adequate relief. A positive dietary response in patients with fructose intolerance was associated with the development of diarrhoea during breath testing (multivariate analysis 1.7 (1.03-2.81), p = 0.04). No other significant associations between symptoms experienced during fructose or lactose breath testing and dietary outcome were demonstrated.

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 be the basis for 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.

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

Introduction: FODMAPs (fermentable oligo-, disaccharides, 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. In this study we aimed to investigate the effect of a low FODMAP diet during a study period of 9 weeks. After 3 weeks intervention patients presenting with IBS-diarrhoea (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 in H2 (>20 ppm) or CH4 (>10 ppm) values during breath testing. The response to the dietary program was assessed using a standard adequate global symptom relief question. Predictive associations were assessed by uni- and multivariate analyses.

Result: Adequate symptom relief was achieved in 81% of the 580 FGID patients, with a median response rate of patients with fructose (79%) and lactose (79%) intolerance and across all FODMAP subtypes (IBS-diarrhoea: 80%, IBS-constipation: 71%, IBS-mixed: 89%, FD: 79%). A positive history of chronic diarrhoea or puritus predicted adequate symptom relief with the FODMAP diet (univariate analyses 2.7 (1.52-4.94), p = 0.001 and 2.7 (1.5-4.9), p = 0.001 respectively, both p < 0.01), while nausea predicted inadequate relief (0.55 (0.34-0.89), p = 0.01) Multivariate analysis confirmed the associations between adequate symptom relief and a history of diarrhoea (positive predictor: 2.74 (1.52-4.94), p = 0.001) and nausea (negative predictor: 0.52 (0.35-0.81), p = 0.07). There were no significant associations between the H2 or CH4 breath concentrations and the attainment of adequate relief. A positive dietary response in patients with fructose intolerance was associated with the development of diarrhoea during breath testing (multivariate analysis 1.7 (1.03-2.81), p = 0.04). No other significant associations between symptoms experienced during fructose or lactose breath testing and dietary outcome were demonstrated.

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 be the basis for modulate multiple physiological processes across the spectrum of FGIDs.
OP257 TREATMENT OF IRRETTABLE 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 achieve symptomatic relief with traditional therapeutic modalities. The healthy donors from patient’s family were screened and tested for infectious diseases before FMT. Patients were questioned with IBS severity score before and 1 month and 3 month after FMT. IBS severity score consist of 5 questions. Total score is 500. As the score is lower, their general condition is considered to be better. Study outcomes included the length of symptom-free intervals, among other pain, bloating, flatus, dyspepsia, frequency of bowel movements, and overall well-being before and after FMT.

Results: A total of 10 patients (mean age of 55 years; 60% male) were identified to be better. Study outcomes included the length of symptom-free intervals, among other pain, bloating, flatus, dyspepsia, frequency of bowel movements, and overall well-being before and after FMT. Patients were questioned with IBS severity score before and 1 month and 3 month after FMT. IBS severity score consist of 5 questions. Total score is 500. As the score is lower, their general condition is considered to be better. Study outcomes included the length of symptom-free intervals, among other pain, bloating, flatus, dyspepsia, frequency of bowel movements, and overall well-being before and after FMT.

Conclusion: This study showed that FMT may be helpful for one month. However, their effect seemed to decrease over time. FMT may be used as an adjunctive therapy with standard medication for managing IBS. Further large prospective population study is needed.

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

References

Table (OP258): Composite response rates over longer treatment intervals in ELX-treated patients who were composite or adequate relief responders over Month 1

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>ELX 75 mg BID (n = 808)</th>
<th>ELX 100 mg BID (n = 806)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>101 (12.5)</td>
<td>708 (87.5)</td>
</tr>
<tr>
<td>Non-responder</td>
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</tr>
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<td>608 (75.4)</td>
</tr>
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</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

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 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 evaluated 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; 0–10 scale) and stool consistency (Bristol Stool Scale (BSS)). The primary efficacy endpoint was composite response, based on simultaneous daily improvement of ≥30% in WAP score based on baseline and BSS score <5, with ≥50% of days demonstrating a response, evaluated over 12 and 26 weeks. Composite endpoint response rates were calculated for Weeks 1–12 and 1–26 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, 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% demonstrated sustained response over 6 months.

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L.S. Dove: Dr Dove: former employee of Furiex Pharmaceuticals, an Allergan affiliate.
C.R. Gutman: Dr Gutman: employee of Allergan plc.
P.S. Covington: Dr Covington: former employee of Furiex Pharmaceuticals, an Allergan affiliate.

Table (OP258): Composite response rates over longer treatment intervals in ELX-treated patients who were composite or adequate relief responders over Month 1

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

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OP259 HUMAN PLURIPOTENT STEM CELL-DERIVED EXOCRINE/ DUCTAL ORGANOIDS GENERATE HUMAN PANCREAS UPON ORTHOTOPIC TRANSPLANTATION AND ALLOW DISEASE MODELLING

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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 ultra-structural and functional hallmarks of human pancreas in the dish. Upon orthotopic transplantation into immunodeficient mice, these organoids form normal pancreatic ducts and acinar tissue resembling fetal human pancreas without any evidence of tumour formation or transformation. Finally, we implemented this unique phenotyping tool as a model for pancreatic facets of cystic fibrosis (CF) but also other inherited pancreatic disorders. We provided evidence that pancreatic commitment occurs generally unhindered in CF. Importantly, CFTR-activation in mutated pancreatic organoids mirrors the CF-phenotype in a series of functional assays. We also conducted a scalable proof-of-concept screen in CF-pancreatic organoids using a set of CFTR correctors and activators. Finally, we did orthotopic transplantation of CF-organoids to generate diseased human pancreata in mice and established a mRNA-mediated gene repair approach in CF-organoids. Similar assays were applied to another inherited pancreatic disorder.

Conclusion: Thus, our platform provides novel opportunities to model pancreatic disease and development but also to screen for disease rescuing agents.

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

OP260 CANCER ASSOCIATED FIBROBLASTS (CAFs) SEQUESTRER GEMCITABINE TO INCREASE INTRATUMORAL DRUG DELIVERY IN MURINE PANCREAS CANCER

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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 dissection 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-1-Cre (KPC) tumours and matched liver metastases, primary tumour cell lines, cancer associated fibroblasts (CAFs), and pancreatic stellate cells (PSCs) by liquid chromatography- mass spectrometry/mass spectrometry (LC-MS/MS). Ex vivo perfusion analysis of gemcitabine metabolism pathways was performed in vivo and in vitro. Viability of CAFs was assessed in vivo following a preclinical trial in the KPC model.

Result: Fibroblast density and collagen deposition were significantly reduced in human and murine 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 dFdCTP and greatly reduced levels of the inactive gemcitabine metabolite dFUdU were detected in PSCs and CAFs. Importantly, key metabolite enzymes for gemcitabine inactivation such as deoxycytidine kinase (Dck), cytidine deaminase (Cda) and hydrolytic cytosolic 5′-nucleotidases (Nt5c1A, Nt5c3) 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

OP261 CIRCULATING CELL-FREE DNA IS A RELIABLE TOOL TO DETECT HOT SPOT MUTATIONS IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

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2Department Of General Surgery, University Hospital Heidelberg, Heidelberg/Germany
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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is the most common cancer type of the pancreas. The three PDAC precursor lesions are: (i) pancreatic intraepithelial neoplasia (PanIN), (ii) mucinous cystic neoplasms (MCN), and (iii) IPMN. In contrast, serous cystadenomas are strictly benign cystic neoplastic lesions and rarely require surgery.

Aims & Methods: Frequently, differential diagnosis of neoplastic cysts remains cumbersome. Thus, non-invasive diagnostic stratification would be welcome. Such a test should allow both discrimination of (i) IPMN from strictly benign pancreatic cysts but also (ii) low- from high-grade IPMN.

Result: Little is known about the molecular alterations of IPMN, but GNAS mutations have been described to promote IPMN formation. A tumor-derived fraction of cell-free DNA (cfDNA) circulating in the bloodstream represents the mutational makeup of tumors and could be a tool for non-invasive monitoring. We demonstrate that cfDNA levels discriminate between a cohort of Fukuoaka-negative branch-duct IPMN but also from pancreatic cancer. Furthermore, GNAS mutations were detected in IPMN patients but were absent in serous cystadenomas (SCA) and in controls. Moreover, we observed relevant concordance between tissue and liquid biopsies-based GNAS mutations in an independent cohort of resected IPMN patients.

Conclusion: These findings establish cfDNA and targeted genotyping as a diagnostic tool for IPMN, which may aid differential diagnosis and risk stratification of cystic pancreatic lesions.

Disclosure of Interest: All authors have declared no conflicts of interest.
TUESDAY, OCTOBER 18, 2016 12:00-15:30

OP262 NOVEL GENE MUTATIONS IN NEUROGENIC CHRONIC INTESTINAL PSEUDO-OBSTICTION
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Introduction: Chronic intestinal pseudo-obstruction (CIPO) 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 RAD21 gene in a recessive form of familial CIPO1. RAD21 is a transcription factor essential for a number of functions including sister chromatid division during cell replication.

Aims & Methods: This study aimed to identify other mutated genes in a selected set of CIPO cases associated with peripheral small fiber neuropathy (SFN), a condition affecting peripheral nerves including those of the autonomic system. Whole exome sequencing (WES) was performed on genomic DNA of n = 6 patients (3 trio and 3 sporadic cases) with clinical, radiological and mano- metric symptoms of an SFN. A novel, de novo mutation identified in the SFN of all of them. Libraries were enriched with the Nimblegen SeqCap EZ v3.0 and sequenced via paired-end 30 bp reads on HiSeq2500 sequencer. Variants were annotated with the SeattleSeq137 Annotation Server. Additional patients were collected for replication study. Target resequencing on selected genes was performed using the TruSeq Amplicon panel designed with Design Studio software. Data analysis and variant calling was performed with the TruSeq Amplicon application in BaseSpace.

Results: WES analyses performed considering pathogenic variants present as autosomal recessive (compound heterozygotes), X-linked or de-novo in the affected probands, since all the parents were healthy. We identified novel/rare missense mutations in FAT1 and in CROCC genes, inherited in an autosomal recessive way (compound heterozygous) in two trios, and a de-novo variant in B3GAT2 in the affected individual of the other trio analyzed, in combination with two rare/variant in Lipoprotein Related Receptor 2 (LRP2), that binds APOB which we have previously related to CIPO1. Analysis of these genes in 77 additional CIPO patients is currently ongoing. All the identified pathogenic variants were absent in our in-house database of 1,000 Italian chromosomes.

Conclusion: We identified three novel gene defects in three different CIPO patients with SFN. FAT1 is a unconventional cadherin, B3GAT2 is a glucur- onyl transferase implicated in neuronal cellular migration and adhesion, while CROCC encodes for rootletin, a protein crucial for centrosome cohesion and separation of the mitotic cycle. Similarly, PAR4 is related to chromosome structural maintenance suggesting that recessive defects in these genes may severely impair autonomic, including enteric, neurons. WES implementation can contribute to decipher complex genetic mechanisms underlying neurogenic CIPO.

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

Reference

OP263 PROTEASE SIGNALING IN HUMAN SENSORY NEURONS
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Introduction: IBS is a functional bowel disorder characterized by abdominal pain, alteration of evacuation and/or diarrhea. Among the mediators studied in IBS, increased colonic proteolytic activity appears as a common feature in all IBS sub-groups. Through Protease-Activated Receptors (PARs) activation, proteases can activate primary afferents and act on visceral pain pathways in rodents, but the roles of PAR activation in human sensory neurons still has to be deter- mined. Thus, the objective of our study was to decipher the PAR pharmacology in human sensory neurons.

Aims & Methods: Cryo-protected or fresh human thoracic dorsal root ganglia (DRG) were obtained from the national disease resource interchange (NDRI). Expression of PAR1, PAR2, and PAR4 was studied on slices of DRG (DRG T12, n = 3) by co-staining immunohistochemistry with a pan-neuronal marker (pgrp9.5) and PAR antibodies. Calcium signaling responses to PAR agonists (PAR-AP) (TFFLR; 1, 10 and 100 µM), PARAP (SLIGRL; 100 µM) and PAR3-AP (LYPKGF; 100 µM) were recorded in DRG. PAR4-AP (100 µM) and PAR5-AP (100 µM) did not cause calcium mobilization. Thrombin (PAR1 and PAR4 agonist) did not cause calcium mobilization. Thrombin (PAR1 and PAR4 agonist) increased calcium flux in human sensory neurons. PAR5-AP-induced calcium mobilization was significantly reduced by pre-incubation with PAR2-AP, but not with PAR1-AP or any of the PAR-IP.

Conclusion: Our study demonstrates that PAR1, PAR2, and PAR4 are expressed in human sensory neurons. In contrast to PAR1 and PAR2, PAR4 activation induced calcium increase in human sensory neurons. PAR4 activation reduced calcium mobilization, thus, in Human sensory neurons PAR4 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
Table Continued

<table>
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<tr>
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<th>SBS-Vasc</th>
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<td>6 (40)</td>
<td>15 (58)</td>
<td>16 (59)</td>
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<td>Body weight, kg</td>
<td>66.6 (12.9)</td>
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</tr>
<tr>
<td>BMI, kg/m²</td>
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<td>22.6 (3.4)</td>
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<td>22.4 (3.1)</td>
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<td>SBS history</td>
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<td>-Vascular catastrophes in categories</td>
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<td>-Nonvascular causes of SBS-IF, n</td>
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<tr>
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<tr>
<td>-Colon-in-continuity, n (%)</td>
<td>13 (76)</td>
<td>12 (80)</td>
<td>10 (38)</td>
<td>13 (48)</td>
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<td>-Stoma presence, n (%)</td>
<td>2 (12)</td>
<td>4 (27)</td>
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<td>-Ileostomy</td>
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<td>9 (60)</td>
<td>5 (29)</td>
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<td>1 (7)</td>
<td>3 (15)</td>
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<tr>
<td>-Other</td>
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<td>1 (7)</td>
<td>0</td>
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<td>-Ileo-ecal valve presence, n (%)</td>
<td>9 (53)</td>
<td>4 (27)</td>
<td>5 (19)</td>
<td>8 (22)</td>
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<tr>
<td>-BMI, kg/m²</td>
<td>23.3 (3.4)</td>
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<td>22.6 (3.4)</td>
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<td>-Body weight, kg</td>
<td>66.6 (12.9)</td>
<td>63.9 (11.2)</td>
<td>58.5 (11.5)</td>
<td>62.1 (11.7)</td>
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<td>-Estimated remaining small bowel length, cm</td>
<td>40.2 (29.9)*</td>
<td>70.9 (57.8)</td>
<td>87.6 (73.6)*</td>
<td>95.8 (67.8)*</td>
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<td>PS history</td>
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<tr>
<td>-PS duration at baseline, y</td>
<td>6.1 (6.2)</td>
<td>5.4 (4.7)</td>
<td>5.8 (5.5)</td>
<td>7.2 (7.0)</td>
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<td>-PS week at baseline</td>
<td>10.2 (5.4)</td>
<td>12.4 (5.5)</td>
<td>15.5 (7.3)</td>
<td>13.3 (8.3)</td>
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<tr>
<td>-PS days per week at baseline</td>
<td>5.4 (1.8)</td>
<td>5.6 (1.6)</td>
<td>6.3 (1.2)</td>
<td>5.6 (1.8)</td>
</tr>
<tr>
<td>Data are expressed as mean (SD) unless otherwise noted.</td>
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<tr>
<td>BMI = body mass index; PBO = placebo; PS = parenteral support; SBS-IF = intestinal resection and failure associated with short bowel syndrome; TED = treadmill.</td>
<td></td>
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</table>

Disclosure of Interest: P. B. Jeppesen: Has received grant/research support and served as a consultant, advisory board member, and study investigator for NPS Pharmaceuticals, Inc.

U. Pape: Has received grant/research support and served as an advisory board member or speaker’s bureau for NPS Pharmaceuticals, Inc., Shire plc, and Reliantus GmbH, served as a study investigator for NPS Pharmaceuticals, Inc.

K. Iyer: Has received grant/research support and served as an advisory board member and consultant for NPS Pharmaceuticals, Inc. and Shire plc.

H. Lee: Employee and stockholder of Shire plc.

C. Olivier: Employee and stockholder of Shire plc.

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OP266 SUBANALYSIS OF TEDUGLUITIDE EFFICACY AND SAFETY DATA FROM PATIENTS WITH CROHN’S DISEASE AND ULCERATIVE COLITIS IN THE STEPS STUDY

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Introduction: Inflammatory bowel disease (IBD; Crohn’s disease [CD] and ulcerative colitis) is a major underlying condition for massive intestinal resection leading to intestinal failure associated with short bowel syndrome (SBS-IF).

Aims & Methods: This post hoc subgroup analysis compared response to teduglutide (TED) in patients with SBS-IF due to IBD (SBS-IF vs those with noninflammatory causes of SBS-IF [SBS-non-IF]). STEPS (NCT00798967, EnduroCT2008-066193-15) was a 24-week, phase III, placebo-controlled study of 0.05 mg/kg/day TED in patients with SBS-IF. Patients with CD were included if they had a clinical remission for ≥12 weeks at baseline. Response was ≥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 intervals (CIs); this post hoc analysis was not powered for statistical significance.

Result: The Table details patient characteristics (SBS-IF, n = 19; SBS-non-IF, n = 67). Patients with SBS-IBD had lower colon-in-continuity, higher stoma presence, and higher baseline PS volume than those with SBS-non-IF. After 24 weeks, 73% (95% CI, 39%–94%) of patients with SBS-IBD and 59% (95% CI, 41%–76%) with SBS-non-IF were responders to TED. In the patients, mean PS volume was reduced by 45% (95% CI, 31%–59%) in those 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
subgroup. No patients with SBS–IBD and 1/47 (2%) with SBS–non-IBD with a colon experience a T E A F ( T E D ) of colitis.

**Conclusion:** In this analysis, the subgroup of patients with inflammatory bowel disease (SBS–IBD) had evidence of more severe disease based on a higher frequency of stoma presence, higher PS requirements, and lower colon-in-continuity. Despite this, clinical responses to T E D were equally strong.

### Table: Demographic and Disease History Data

<table>
<thead>
<tr>
<th></th>
<th>SBS–IBD</th>
<th>Placebo</th>
<th>SBS–Non-IBD</th>
<th>Placebo</th>
<th>SBS–Non-IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD), y</td>
<td>48 (7)</td>
<td>48 (7)</td>
<td>50 (17)</td>
<td>52 (14)</td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>5 (63)</td>
<td>5 (46)</td>
<td>19 (54)</td>
<td>17 (53)</td>
<td></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>
<td></td>
</tr>
<tr>
<td>Stoma present, n (%)</td>
<td>7 (88)</td>
<td>11 (100)</td>
<td>10 (29)</td>
<td>10 (32)*</td>
<td></td>
</tr>
<tr>
<td>Colon-in-continuity, n (%)</td>
<td>1 (13)</td>
<td>1 (9)</td>
<td>22 (63)</td>
<td>24 (77)*</td>
<td></td>
</tr>
<tr>
<td>Estimated small bowel length, mean (SD), cm</td>
<td>128 (98)</td>
<td>129 (77)</td>
<td>54 (43)</td>
<td>73 (56)</td>
<td></td>
</tr>
<tr>
<td>Baseline PS, mean (SD), L/wk</td>
<td>21.6 (8.1)</td>
<td>15.9 (10.4)</td>
<td>11.5 (5.9)</td>
<td>11.2 (6.4)*</td>
<td></td>
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<tr>
<td>Baseline PS duration, mean (SD), y</td>
<td>7.2 (7.4)</td>
<td>8.1 (8.0)</td>
<td>5.6 (3.5)</td>
<td>6.1 (5.7)*</td>
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</table>

*n = 31, n = 9, n = 32, n = 30.

**Disclosure of Interest:** U. Pape: Has received grant/research support and served as an advisory board member or speaker’s bureau for NPS Pharmaceuticals, Inc. and Fresenius Kabi GmbH; served as a study investigator for NPS Pharmaceuticals, Inc. P.B. Jeppesen: Has received grant/research support and served as a consultant, advisory board member, and study investigator for NPS Pharmaceuticals, Inc. and Fresenius Kabi GmbH. H. Lee: Employee and stockholder of Shire plc. A.A. Grimm: Employee of Shire plc. S.J. O’Keefe: Has received research funding support from NPS Pharmaceuticals, Inc.

**OP268 INDICATIONS AND OUTCOMES OF INTESTINAL AND MULTIVISCERAL TRANSPLANT**

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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 5 years. Some recent transplants have been performed ‘superurgently’ for acute widespread splanchic ischaemia. Longstanding indications include complications of colorectal surgery in patients with type 3 Intestinal failure (IF)-associated liver disease (IFALD), recurrent catheter-related infections and loss of vascular access, cirsrhosis 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-con- 

**Result:** In the study period, 66 transplants were performed in 61 patients (33 Multivisceral, MVT; 7 Liver/small bowel, LSB; 9 Modified multivisceral, MMV; 17 small bowel, SB). Gafts can also contain colon and pancreas. 26 patients (39%) received a transplant for complications relating to intestinal failure (overt I ETF) 11, impending I ETF 4, recurrent sepis 1, loss of vascular access 10. 14 patients (21%) received a multivisceral graft because an isolated liver transplant was not possible due to extensive portomesenteric venous thrombosis. An increasing indication is that of ‘acute abdominal catastrophe’ – 9 patients were transplanted for this including 5 with widespread splanchic ischaemia. Less frequent indications included desmoid tumours (4), re-transplant (6), short bowel and renal failure (2). The median length of hospital stay post trans- 

**Conclusion:** In the previous study, our colleagues identified that discoidin- 

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

**Reference**

OP269 GENETIC SUSCEPTIBILITY AND FAMILY HISTORY OF COLORECTAL CANCER: HUMAN vs ANIMAL MODEL PERSPECTIVES

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Introduction: In order to identify new CRC risk factors, 2750 FDRs with colorectal cancer (CRC) have been screened. The study of CRC family history was associated with 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-penetrance genes. However, very little is known about the relevance of genetic variants in the development of colorectal preneoplastic 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 FDRs of patients with non-syndromic CRC (cases), and 750 controls (controls). SNPs downstream of PCID2 and their clinical effect were evaluated by in vitro and in vivo tumorigenicity assessment 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 downregulation was achieved using lentiviral shRNA transduction. Also, 2 SNPs (rs10795668G and rs11255841T) were significantly associated with a decreased risk of CRC development. Finally, 2 SNPs (rs10795668 and rs11255841) and patients with no family history of CRC (dominant OR: 0.22, 95% CI: 0.06–0.72 for rs10795668, and OR: 0.08, 95% CI: 0.03–0.23 respectively) were found. By contrast, 288 patients (144 cases and 144 controls) showed non-significant results. The overall effect of PCID2 was mediated through downregulating its interaction partner promyelocytic leukemia (PML) by ubiquitination. PML played a tumor suppressive role in CRC. PCID2 induced Wnt signaling pathway and inhibited p53-p21 pathway activity. PCID2 expression level was evaluated in the overall population (p = 0.01) and in stage I and II patients. Multivariate analysis revealed that patients with PCID2 overexpression were significantly correlated with CRC recurrence (p < 0.05 for cohort I, p < 0.05 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 > 0.05 for cohort II).

Conclusion: PCID2 plays a pivotal oncogenic role in colorectal carcinogenesis by upregulating Wnt signaling pathway and inhibiting p53-p21 pathway activity.

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

OP270 PREDICTION OF COMPLETE RESections AFTER CYTOREDUCTive SURgery BASED ON THE EXTENT OF COLORECTAL PERITONEAL CARCINOMATOSIS

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Introduction: The most common site of recurrence in colorectal peritoneal carcinomatosis (CRPC) is the omentum. Hypermotrophic peritoneal chemotheraphy (HIPEC) is the treatment of choice for colorectal peritoneal carcinomatosis (PC). Prior to surgery abdominal computed tomography (CT) was performed to gain insight into the extent of PC and the presence of distant metastases.

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 radiologist and peroperative evaluation was performed by the operating surgeon, based on the Dutch region count. The completeness of cytoreduction was scored after CRS. Surgical outcomes were followed for at least 2 years.

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 (p = 0.7) indicating the importance of surgical judgment. Patient characteristics were with median of 21.9 months (IQR 19.1–24.7) and 44.6 months (IQR 35.8–53.5) in patients with complete cytoreduction compared to 12.1 months (IQR 9.7–14.6) and 19.0 months (IQR 14.2–23.8) in patients with incomplete cytoreductive surgery (p = 0.001).

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

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

OP271 PREVALENCE OF LYMPH NODE METASTASIS AND LONG TERM SURVIVAL OF TI RECTAL CANCINOID TUMORS: AN ANALYSIS OF SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS (SEER) DATABASE


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Introduction: Rectal carcinoid tumors are the most common neuroendocrine tumors of the gastrointestinal tract and their incidence is increasing due to colorectal cancer screening. Several previous studies have suggested that local excision (endoscopic submucosal dissection) is effective for ≤10 mm lesions but data on long-term pathways were elucidated by promoter lucerase 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 62.0% (28/46) 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 overexpression 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), GI-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), 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. 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.
outcomes are very limited. In addition, management of 11–19 mm tumors is not well defined because of variable estimates of risk of lymph node (LN)/ distant metastasis.

Aims & Methods: The aims of this study were: 1) to determine the prevalence of metastasis of resected T1 rectal carcinoid tumors using a large national cancer database, 2) to identify risk factors for metastasis, 3) evaluate the long-term survival of patients with T1N0 rectal carcinoid tumors after local resection as compared to radical surgery. The SEER 18 database was used to identify patients aged 18–80 years with T1 histologically confirmed rectal carcinoids < 2 cm in size diagnosed between 1998 and 2012. T1 was defined as tumor invading lamina propria or submucosa. Prevalence of LN (N1) (distant metastases (M1)) at initial diagnosis and risk factors for metastases were analyzed. Cancer-specific survival (CSS) and overall survival were calculated using Kaplan-Meier's estimate and compared with log-rank test.

Result: A total of 788 patients with T1 rectal carcinoids were identified [mean age: 54.8 (SD 11.3); 49.5% men; 57% white]. Of these, 727 (92.3%) patients had tumors < 10 mm in diameter and 61 (7.7%) had tumors 11–19 mm. Submucosal invasion was 94.9%. Overall, 12% (15.1%) had LN at the time of diagnosis with prevalence of 1.1% in lesions ≤ 10 mm and 6.6% in lesions 11–19 mm in size (p = 0.01). Tumor size (OR 6.3; 95%CI 1.8 – 21.5; p = 0.003) and submucosal invasion (p = 0.03) were associated with LN distant metastasis. Median follow-up time of the entire cohort was 23 months (range 0–172). Survival of patients with T1 rectal carcinoids without N1/M1 was significantly better than those with N1/M1 with 5-yr CSS of 100% and 78%, respectively (p < 0.001). Of 550 patients with T1N0 rectal carcinoids < 10 mm in size and follow-up > 6 months, 527 (95.4%) underwent local excision and 32 (5.7%) had radical surgery. 5-yr CSS was 100% and 10-yr CSS was 98% (SE 0.01). For 46 patients with T1N0 rectal carcinoids 11–19 mm in size [39 (84.8%) who underwent local excision and 7 (15.2%) underwent radical surgery], there were no post-operative tumor-related deaths after a median follow up of 28 months (range 8–122). The overall survival of T1N0 rectal carcinoids treated by local excision versus radical surgery was comparable.

Conclusion: Rectal carcinoid tumors (11–19 mm) are at increased risk of LN metastases compared those ≤ 10 mm. Survival is worse with regional or distant metastatic disease. Hence, thorough evaluation for metastatic disease should be considered for these lesions. Local therapy is adequate for T1 rectal carcinoids < 10 mm in size with in-field and regional control. A wait-and-see approach after a clinical complete response in patients with residual fibrosis is present post-chemoradiotherapy which remains unchanged during long-term follow-up in almost all patients. A completely normalized 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 selected to undergo a wait-and-see approach.

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

Reference

TUESDAY, OCTOBER 18, 2016 14:00–15:30
GENERAL HEPATOLOGY – ROOM 1B

OP274 ACCURACY OF A POINT SHEAR WAVE ELASTOGRAPHY TECHNIQUE (ELASTIQ) IN THE NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS IN A LARGE COHORT OF LIVER PATIENTS

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Introduction: ElastIQ is a novel point shear wave elastography (PSWE) technique that assesses liver stiffness by measuring liver stiffness (kPa) with few studies published so far. The aim of this study was to determine the accuracy and feasibility for the assessment of liver stiffness in a large cohort of patients undergoing liver biopsy (LB) for various etiologies.

Aims & Methods: Consecutive patients scheduled for LB were studied by using the iU22 Philips ultrasound system with ElastIQ technique. The correlations between laboratory findings, liver stiffness and the Metavir score were analyzed using Spearman correlation and ROC curve analyses were performed to calculate AUC for F ≥ 2, ≥ 3 and F = 4.

Result: We enrolled 289 patients (176/113 males/females) who underwent LB for viral chronic (VHC) (49%); NAFLD (40%), chronic hepatopathies (HCV–90%, HBV–6%, other–4%), in which Liver stiffness measurements performed on the right lobe were reliable in all cases but eight patients (due to morbid obesity and narrow intercostal spaces). After univariate and multiple regression analysis PSWE showed a strong association with the fibrosis stage; no significant correlation was found with the degree of necroinflammation or steatosis. Mean kPa values in the whole cohort were 3.7 (range 2.3–4.9) for F0, 4.9 (range 2.6–9.6) for F1, 7.6 (2.8–20.7) for F2, 10.2 (6.1–19.9) for F3 and 20.4 (10.9–38.4) for F4 in the right lobe. AUROCs were 0.92 (95%CI 0.82–1.00), 0.92 (0.91–0.94) and 0.96 (0.95–0.98) when comparing F0 to F1, F2 to F3 and F4 respectively.

Conclusion: The present study suggests that ElastIQ is a reliable point-based shear wave elastography technique for the 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.

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

OP275 COMPARATIVE STUDY BETWEEN TWO 2D SHEAR WAVES ELASTOGRAPHY TECHNIQUES FOR THE ASSESSMENT OF LIVER STIFFNESS: 2D-SWELSI VS. 2D-SWEGE

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Introduction: Chronic liver diseases are quite frequent encountered in daily prac- tice due to chronic infections (B or C virus) and other conditions such as chronic alcohol abuse (ASH) and NAFLD. In this conditions, the evaluation of chronic liver disease's severity is mandatory, for prognosis, for management and for decision regarding therapy.

Aims & Methods: The aim of this paper was to compare the feasibility of two 2D-Shear Waves Elastography (2D-SWE) methods for the assessment of Liver Stiffness (LS) and also to compare the methods with a validated one: Transient Elastography(TE). Our study included 130 consecutive patients with chronic hepatopathies (HCV–90%, HBV-6%, other-4%), in which Liver Stiffness (LS) was evaluated in the same session by means of two 2D-SWE techniques: 2D-SW.ELLOGIQ F9, GE Healthcare) and 2D-SWELSI (SuperSonic Imagine) and also by an
elastographic reference method: Transient Elastography (TE): FibroScan, Echosense). Reliable LS values (95% CI 0.85–0.92) were achieved for 2D-SWE: the median value of 10 measurements acquired in a homogenous area and an interquartile range (IQR) <30% (1), for 2D-SWE: the median value of 3 measurements acquired in an homogenous area and an interquartile range (IQR) <30% (2). Spearman’s rank correlation coefficient (r) was used to assess the correlation of LS measurements by means of 2D-SWE, 2D-SWE.SSI and TE.

Result: Valid measurements were obtained in 96.6% (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 and TE. The values ranged from 4.17 to 20.48 kPa for 2D-SWE and 3.96 to 82.4 kPa for 2D-SWE.SSI. The mean LS values by 2D-SWE.SSI were significantly higher than for 2D-SWE: 19 ± 13.2 kPa vs. 12.1 ± 3.7 kPa (p < 0.0001). There was a significant correlation between 2D-SWE and 2D-SWE.SSI LS values (r = 0.712, p < 0.0001). The correlation between 2D-SWE and TE was 0.746, p < 0.0001 and between 2D-SWE.SSI and TE was r = 0.604, p < 0.0001 with no significant differences between them (p = 0.0565). Taking TE as the reference method, both 2D-SWE.SSI and 2D-SWE had a good value to differentiate between stages of liver fibrosis and liver cirrhosis. For 2D-SWE.SSI the best liver stiffness cut-off value to differentiate between liver cirrhosis and other stages of fibrosis was >13.7 ± 0.6 kPa with 88.57% Se, 75.68 Sp, 87.3 positive predictive value (PPV) and 78.7 negative predictive value (NPV) (AUROC = 0.831, p < 0.0001). For a liver stiffness cut-off value >10.7 ± 0.6 kPa, 2D-SWE had 91.43 Se, 78.38 Sp, 88.9 PPV, 82.9 NPV and 0.831 AUROC (p < 0.0001) for differentiating liver cirrhosis. The AUROCs of 2D-SWE.SSI and 2D-SWE 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 are significantly lower than those obtained by 2D-SWE.SSI. Both methods have good performance for predicting liver cirrhosis.

Disclosure of Interest: I. Sporea: Ioan Sporea participated in an Advisory Board for Siemens and received speaker fees from Philips, Siemens and General Electric R.L. Sirl: Roxana 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
2. Sugiyama O. Bota M. How many measurements are needed for liver stiffness assessment by 2D Shear Wave Elastography (2D-SWE) and which value should be used: the mean or median?. Med Ultrasound 2013; 15: 268-272.

OP276 UTILITY OF REAL-TIME SHEAR WAVE ELASTOGRAPHY FOR ASSESSING LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C


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Introduction: The human Toll like receptors (TLRs) family consists of ten receptors and are pivotal for recognizing and responding to diverse microbial molecules and enable the innate immune system to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses.
new-onset diabetes mellitus after kidney transplantation. From previous studies we can reasonably infer that adiponectin protein is a risk factor for the development of NODAT. However, there have been no reports to describe the association between ADIPOQ genotype polymorphism and new-onset diabetes mellitus after liver transplantation.

Methods: In the current study, we aim to investigate whether single nucleotide polymorphisms of ADIPOQ were correlated with the NODAT and also to compare the overall survival and graft survival between NODAT group and non-NODAT. The study included 256 patients who underwent liver transplanta-tion in our center from January 2009 to December 2011. They were divided into two groups: NODAT group and Non-NODAT group. We screened independent risk factors of NODAT with univariate and multivariate analyses. We further built three NODAT prediction models containing the risk factors and got optimized model with AUROC curve method. In addition, the association between metabolic syndrome and NODAT was also examined. Overall survival and graft survival were determined by the Kaplan-Meier method and tested by the log-rank statistics.

Results: Mean incidence rate of NODAT within 6 months post liver transplantation was 29% (75/181). There were 214 men and 42 women in the study and the average age was 48.0±9.9 years. Age (54.0±4.1 vs 45.4±6.9, P < 0.001), BMI (23.1±3.0 vs 22.3±3.0, P < 0.014), blood tacrolimus level at 1 month post liver transplantation (10.23±3.30 vs 8.67±1.74, P < 0.001), ADIPOQ rs1501299 (P < 0.007) and rs822396 (P = 0.013) were significantly correlated with NODAT with univariate analyses. Dominant model and recessive model confirmed these risk factors further. Three NODAT prediction models were built containing these risk factors, and we finally found the optimized model (AUROC = 0.743). Metabolic syndrome was also associated with NODAT (21% vs 8%, P = 0.003). The overall survival rate (P = 0.015) and graft survival rate (P = 0.015) between NODAT group and Non-NODAT group did not significantly differ (P = 0.847).

Conclusion: This study is the first to provide evidence of the association between recipient rs1501299 genotype polymorphism and new-onset diabetes mellitus after liver transplantation on large samples. Our findings demonstrate that re-cipient rs1501299 is associated with a higher risk of NODAT and would be a potential genetic factor to improve the predictive ability of NODAT, we also confirm age, BMI, blood tacrolimus level at 1-month after LT are independent risk factors of NODAT. These findings may be beneficial in helping to estimate the risk of NODAT development in liver transplantation and thereby in controlling modifiable risk factors.

Disclosure of Interest: All authors have declared no conflicts of interest.
regain clinical response. Detailed documentation of disease activity was retrospectively instructed. Result: In 98/376 patients ADA directed against IFX and in 61/226 patients ADA against ADL were detectable. From all 159 ADA positive patients, 17 patients had received an IM, either a thiopurine or MTX, because of secondary loss of response. Seven patients received MTX, ten a thiopurine (4 azathioprine, 4 mercaptopurine and 2 6-TG). In 7 out of 8 patients treated with IFX, addition of an IM resulted in an increase of serum drug levels accompanied with a decrease of ADA till they were undetectable. The median time for ADA to IFX to become undetectable was also 11 months (IQR 2-37). All patients receiving MTX responded clinically which resulted in continuation of the ongoing anti-TNF treatment. Conclusion: Addition of an IM to IFX or ADL monotherapy in IBD patients with secondary loss of response due to ADA formation, led to a decrease of ADA levels and an increase in serum drug concentrations in the majority of the patients. Patients who regained response due to this strategy could continue the current anti-TNF treatment and switching to another agent was not necessary.

Disclosure of Interests: G.R. van den Brink: G. van den Brink has received consulting and lecture fees from AbbVie, Coviden, Dr. Falk, Ferring Pharmaceuticals. He has received research grants from Abbott laboratoires, Merck Sharp & Dohme and Ferring Pharmaceuticals. He has received research grants from Abbott laboratories, Merck Sharp & Dohme, Receptos, Takeda, Tillots and Tramedico. He has received research grants from AbbVie, Merck Sharp & Dohme, bardcare and WIN. G. D’Haens: G. D'Haens reports having received consulting fees from AbbVie, Boehringer, Ferring, Janssen Biologics, Merck Sharp and Dohme, Takeda, Pfizer, Tillots Pharma and reports receiving research grants from Abbott Laboratories, Janssen Biologics, MSD, D’Falk Pharma. All other authors have declared no conflicts of interest.

OP281 POST-OPERATIVE COMPLICATIONS IN ELDERLY-ONSET INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY

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Aims & Methods: Among 841 elderly-onset population-based EPIMAD Cohort (1, 139 patients underwent surgery. Among those, 100 had Clohn’s Diseases (CD) and 39 Ulcerative Colitis (UC). Medical charts for early (within 30 days of surgery) and late (>30 days of surgery) PO (POC) have been reviewed according to Dindo’s classification (2). Associated factors have been tested by Cox regression models. Result: After a median follow-up of 7.3 years [Q1 = 3–Q3 = 12], 50 patients (36%) had at least one POC. No significant difference was observed for PO frequency between UC and CD. Thirty-two early POC were found in 23 patients (16.5%); 52% were severe (defined by a Dindo’s grade > 2) and 47% infectious. Among the 37 late complications observed in 33 patients (23.7%), 42 were severe (grade > 2) and 56% were mechanical (briade, evagination, anastomotic stricture). The cumulative probability of POC was 7.4% at 6 months (95% CI: 3.9–10.9%) at 1 year (6.5–18.1%), 22.8% at 5 years (16.0–32.0) and 30.5% at 10 years (21.8–41.4). In multivariate analysis, early surgery (HR = 4.46 [1.75–11.36]) and acute severe ulcerative colitis (HR = 7.84 [2.15 – 28.52]) were significantly associated with early PO. No significant differences have been observed on recent PO (exposure and co morbidities (Charlson’s index) were not independently associated with an increased risk. Female gender (HR = 2.10 [1.01 – 4.37]) and time between diagnosis and surgery (>3 months (HR = 2.09 [1.01 – 4.31]) were significantly associated with late PO.

Conclusion: In elderly onset IBD patient who underwent surgery, POC were frequent. The early POC were more severe than the late POC. Emergency surgery and acute severe ulcerative colitis were significantly associated with early complications when female gender and delay between diagnosis and surgery were associated with late POC. These results reinforce the need for specialized and dedicated management of these at-risk elderly patients.

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

References

TUESDAY, OCTOBER 18, 2016 15:45–17:15
FROM GUIDELINES TO CLINICAL PRACTICE: H. PYLORI – ROOM D

OP282 PAN-EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT AH-EUREG: INTERIM ANALYSIS OF THE SINGLE-CAPSULE BISMUTH QUADRUPLE TREATMENT (PYLERA®)


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Introduction: The most novel treatment used in H. pylori management in Europe is the single-capsule bismuth quadruple treatment (Pylera®), but there is still very little evidence of its efficacy and safety on routine clinical practice. Pylera® is still not yet commercially available in most countries in Europe and, in most of those available, it has just recently reached pharmacies.

Aims & Methods: We aimed to evaluate the use and outcomes of Pylera® in the European Registry on H. pylori Management (Hp-EuReg). Methods: A systematic prospective registry of the clinical practice of European gastroenterologists regarding H. pylori infection and treatment (31 countries and 280 recruiting investigators). A local coordinator was selected from each country. Each coordinator selected a representative group of recruiting investigators from its country. An electronic clinical registry (AH-EUREG) was created on AEG-REDCA and systematically register all adult patients infected with H. pylori. Variables included: Patient’s demographics, previous eradication attempts, prescribed eradication treatments, adverse events, and outcomes (cure rates, compliance, follow up, etc.). Patients with both eradication confirmatory test and with less than one year follow-up have been considered ongoing and were excluded from the analysis. Result: Up to now, 15,660 patients have been included, and 12,921 have finished follow up (59% females, 88% Caucasian). Mean age was 55 years. Pylera® was used in 175 patients (1.2% of all treatments registered: 44% in first-line, 27% in second, 22% in third, and 8% in following rescues). Omeprazole was used in 69% of cases and esomeprazole in 24%. Overall efficacy was 76% (95%CI = 66–86%) by ITT and 78% (69–87%) by PP. In first line, efficacy was 93% (84–100%) both by ITT and PP. Second line efficacy was 68% (51– 85%) by ITT and 74% (58–90%) by PP. Compliance with treatment was 98%. Adverse events were reported in 14% of cases and did not cause treatment discontinuation in any patient.

Conclusion: Experience with single-capsule bismuth quadruple therapy (Pylera®) is still limited. Wide confidence intervals do not allow drawing conclusions for rescue regimens; however, our preliminary data suggests that given its safety profile, compliance rates and efficacy, it may be an acceptable option as first-line treatment in Europe.

Disclosure of Interest: A.G. McNicholl: Speaker for Allergan
A. Perez Asua: Speaker for Allergan
All other authors have declared no conflicts of interest.
small bowel diseases. Secondary objectives: procedural success, - time of main and minor perforation, therapeutic success. Patients and methods: We will select gastro-intestinal bleeding (OGIB) or indeterminate iron-deficiency anaemia (IDA) or positive findings of small bowel imaging examinations were included in a two-center prospective clinical trial. In total 132 cases were enrolled to determine the overall efficacy. A rate of 25% would be considered as clinically efficacious under consideration of a two-sided non-inferiority margin of 20% in comparison to conventional enteroscopy. A novel reusable endoscope (Olympus Corp.) with an integral motor was used for rotating a disposable short spiral overtube maneuvering on the insertion of the small bowel, while the operators had to “pleat” or “unpleat” the insertion tube either on or off the insertion tube as the case rotates in a clockwise or counter-clockwise direction. All procedures were performed under general anesthesia.

Result: Thirty patients (12 f, 18 m; mean age [range]: 62 [20–92] years) with positive findings of video capsule endoscopy or other small bowel imaging modality (angiectasias n = 18, jejunal/ileal polyps n = 3, thickening of wall/stricture n = 3, other n = 1) have so far been included in the trial. 27 of 30 patients had IDA. NMSE could be performed in 29 of the 30 patients with advancement of the endoscope beyond the ligament of Treitz. In one case further insertion was not performed because of a bradycardia which caused discontinuation of the procedure. Mean insertion time to the jejunum was 6.4 [2–19] min. and to the deepest point of insertion distal from ligament of Treitz 22.6 [7–52] min. The mean insertion depth from ligament of Treitz was 393 [0–600] cm. Panenteroscopy to secum could be achieved in one patient from the oral route. The diagnostic yield of NMSE was 83.4% corresponding to no findings in 5 cases, at least one angiectasia in 18 cases, one or more benign polyps in 6 and other findings in 12 cases. Thirty-two interventions were performed in 22 patients (biopsies n = 8, APC n = 17, tattooing n = 3, clipping n = 3, EMR n = 3). Thirty withdrawal time without interventions was 14.7 [5–45] 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 safely and efficiently 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 HEALING IN PATIENTS WITH CROHN’S DISEASE ON MAINTENANCE 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 targeting the two cross-sectional pro-

cedures. 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 natalizumab). TH was evidenced in 13 patients (33%) at BS and in 12 patients (30%) at MRE (k = 0.64; P < 0.01). 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 biologics, at high agreement between BS and MRE on defining this outcome. After considering the advantages of BS (high diagnostic accuracy, low costs, high patient compliance, high availability) and the limitations or 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 pathophysiological alterations and Patient Reported Outcomes (data shown as mean ± SD)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No abnormality (n = 76)</th>
<th>1 abnormality (n = 128)</th>
<th>2 abnormalities (n = 121)</th>
<th>≥3 abnormalities (n = 82)</th>
<th>ANOVA</th>
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<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>
<td>F = 14.0, p &lt; 0.0001</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 ± 0.91</td>
<td>0.68 ± 0.98</td>
<td>F = 26.7, p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Emotional Role</td>
<td>60.6 ± 19</td>
<td>55.2 ± 24</td>
<td>44.4 ± 17</td>
<td>5.9 ± 17</td>
<td>F = 20.3, p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Mental Health</td>
<td>82.8 ± 16</td>
<td>76.6 ± 22</td>
<td>65.5 ± 20</td>
<td>51.7 ± 20</td>
<td>F = 35.4, p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Sleep</td>
<td>82.8 ± 16</td>
<td>76.6 ± 22</td>
<td>69.2 ± 24</td>
<td>58.2 ± 24</td>
<td>F = 15.3, p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Energy</td>
<td>69.2 ± 24</td>
<td>58.2 ± 24</td>
<td>48.2 ± 24</td>
<td>35.2 ± 23</td>
<td>F = 25.0, p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Physical Functioning</td>
<td>75.2 ± 20</td>
<td>74.2 ± 21</td>
<td>68.2 ± 20</td>
<td>57.2 ± 26</td>
<td>F = 11.8, p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Food</td>
<td>67.2 ± 20</td>
<td>64.2 ± 21</td>
<td>59.2 ± 18</td>
<td>55.2 ± 20</td>
<td>F = 6.3; p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Social Role</td>
<td>71.2 ± 20</td>
<td>65.2 ± 23</td>
<td>62.1 ± 20</td>
<td>51.2 ± 24</td>
<td>F = 13.5, p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Physical Role</td>
<td>64.2 ± 28</td>
<td>56.3 ± 31</td>
<td>47.4 ± 29</td>
<td>40.2 ± 28</td>
<td>F = 10.3; p &lt; 0.0001</td>
</tr>
<tr>
<td>IBSQOL Sexual</td>
<td>71.2 ± 23</td>
<td>70.2 ± 25</td>
<td>53.6 ± 25</td>
<td>50.2 ± 25</td>
<td>F = 8.2; p &lt; 0.0001</td>
</tr>
</tbody>
</table>

Disclosure of Interest: All authors have declared no conflicts of interest.
OP289 INCREASED INHIBITORY NEUROTRANSMISSION WITHIN ANTERIOR CINGULATE CORTEX IS RELATED TO COMORBID ANXIETY IN IRRITABLE BOWEL SYNDROME

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Introduction: Inspired by the concept of Irritable Bowel Syndrome (IBS) as a disorder of brain-gut-communication, alterations in central mechanisms are increasingly acknowledged in IBS pathophysiology. Given high comorbidity with affective disorders, emotional factors likely play a role in disturbed central processes in IBS. Dysfunctions particularly in brain regions involved in emotion processing, including the rostral anterior cingulate cortex (rACC) as a unique hub of both, affect regulation and anti-nociception, may constitute a central link between abdominal pain and psychiatric comorbidities. While a growing number of neuroimaging studies support a crucial role of rACC in altered pain processing and emotional disturbances in IBS, the biochemical basis of these alterations remains unknown.

Aims & Methods: We compared IBS patients and healthy controls (HC) regarding 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 comorbidities in IBS, as well as a combined MRI and MRS study; GabA and 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 3x3x3cm 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 comorbidity in altered brain processes in IBS. Altered inhibitory 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.
OP292 VISCERAL HYPERSENSIVITY IS ASSOCIATED WITH GI SYMPTOM SEVERITY IN FUNCTIONAL GI DISORDERS: CONSISTENT FINDINGS FROM FIVE DIFFERENT PATIENT COHORTS

M. Simrén, J. Tack4, W. E. Whitehead5

Our aim was to evaluate the association between visceral hypersensitivity and GI symptoms in patients with functional gastrointestinal disorders (FGIDs). A total of 5 cohorts of patients with FGIDs, who had undergone previou previously conducted baseline and follow-up measurements, were included in this study. The background characteristics including baseline LMR between the two groups showed no significant difference. Treatment after 28 days of lubiprostone demonstrated 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>0.207</td>
</tr>
<tr>
<td>day14</td>
<td>0.055 (0.023-0.047)</td>
<td>0.024 (0.019-0.029)</td>
<td>0.403</td>
</tr>
<tr>
<td>day28</td>
<td>0.028 (0.023-0.033)</td>
<td>0.017 (0.015-0.019)</td>
<td>0.0497</td>
</tr>
</tbody>
</table>

Conclusion: In our study, 28 days treatment with lubiprostone demonstrated an improvement of increased intestinal permeability after 1-week administration of diflucan 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”.

References


OP293 ORAL ADMINISTRATION OF THE CYCLASE-C AGONIST LINACLOTIDE ATTENUATES COLITIS INDUCED LONG-TERM BLADDER AFFECTER HYPERACTIVITY

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Introduction: We investigated healthy C57BL/6J mice and mice with chronic colitis (CCH) for bladder and gastrointestinal cross-talk has also been described in pre-clinical studies, whereby acute colitis in rodents is associated with altered bladder cystometry and bladder afferent sensitisation [1,2]. However, it remains to be determined if bladder overactivity persists following the resolution of colitis, in a model of chronic colonic hyper-sensitivity (CCH) [3], or if reducing colonic nociception is able to alter bladder overactivity. Linacotide, an FDA approved guanylate cyclase-C (GC-C) agonist, reduces abdominal pain in IBS patients with constipation [3], reverses colonic unrestrained Educ. Pharmacists; Consultant/ Advisory Board member for AstraZeneca, Takeda Pharmaceuticals; Consultant/ Advisory Board member for Ferring Pharmaceuticals and Ironwood Pharmaceuticals, as well as honoraria for participation in educational programs supported by these companies M. van Tijburg: Research support from Takeda for investigator initiated study. J. Tack: Almirall, AstraZeneca, Danone, Menarini, Novartis, Nycomed, Oceara, Ono Pharma, Shire, SK Life Sciences, Theravance, Xenoport, Zeria, Abbott, Almirall, AlfaWasserman, Janssen, W.E. Whitehead: Unrestricted research grants from Takeda Pharmaceuticals; unrestricted educational grants from Takeda and Ferring Pharmaceuticals; Consultant/ Advisory Board member for Ono and Ferring Pharmaceuticals and Biomerica USA.

All other authors have declared no conflicts of interest.

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Introduction: There is significant comorbidity amongst the symptoms of IBS and the urological symptoms of urgency and frequency experienced in overactive bladder and interstitial cystitis/painful bladder syndromes. Viscero-rectal cross-talk has also been described in pre-clinical studies, whereby acute colitis in rodents is associated with altered bladder cystometry and bladder afferent sensitisation [1,2]. However, it remains to be determined if bladder overactivity persists following the resolution of colitis, in a model of chronic colonic hyper-sensitivity (CCH) [3], or if reducing colonic nociception is able to alter bladder overactivity. Linacotide, an FDA approved guanylate cyclase-C (GC-C) agonist, reduces abdominal pain in IBS patients with constipation [3], reverses colonic unrestrained Educ. Pharmacists; Consultant/ Advisory Board member for AstraZeneca, Takeda Pharmaceuticals; Consultant/ Advisory Board member for Ferring Pharmaceuticals and Ironwood Pharmaceuticals, as well as honoraria for participation in educational programs supported by these companies M. van Tijburg: Research support from Takeda for investigator initiated study. J. Tack: Almirall, AstraZeneca, Danone, Menarini, Novartis, Nycomed, Oceara, Ono Pharma, Shire, SK Life Sciences, Theravance, Xenoport, Zeria, Abbott, Almirall, AlfaWasserman, Janssen, W.E. Whitehead: Unrestricted research grants from Takeda Pharmaceuticals; unrestricted educational grants from Takeda and Ferring Pharmaceuticals; Consultant/ Advisory Board member for Ono and Ferring Pharmaceuticals and Biomerica USA.

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All other authors have declared no conflicts of interest.
administration, consisting of a once daily oral gavage for 2 weeks prior to experi-
mental groups, while four cell patch clamp recordings from retro-
gradely traced thoracolumbar and lumbosacral bladder dorsal root ganglion (DRG) neurons determined neuronal excitability, whilst ex-vivo electrophysiolog-
ical recordings determined bladder afferent and contractile sensitivity to resis-
tant distension. The remaining 17 patients (17/91; 18.7%) were heterozygous carriers of
a genotype compatible with one of the tested disorders: Burton agammaglobuline-
ia, familial diarrhea, familial C20 defect, hyper-IgM syndrome or Omenn syn-
drome. The remaining 17 patients (17/91; 18.7%) were heterozygous carriers of
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 diagnosis in these patients.

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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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
containing autophagy- and inflammasome-related genes have been associated
with an increased risk of IBD. Evidential data suggest that the imbalance in
the mutual 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: Colonic biopsies of patients with CD, but not UC showed increased levels of
mRNA expression of 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 auto-
phagy-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 IκBα concomitantly with an accumulation of the autophagy proteins p62 and LC3, suggesting an autophagy blockage or-
chestrated by NLRP3. Interestingly, hypoxia significantly inhibited the
expression of TNFα, IL-6 and IL-1β, and restored autophagy in IL-10−/− mice. THP1 and HT-29 cells subjected to hypoxia showed a significant increase in
autophagy concomitantly with an increase in autophagy, evidenced by a reduction in
p62 and LC3, and the phosphorylation of mTOR, a major regulator of auto-
phagy. 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
primary and secondary 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
OP296 EPIDEMIC ALTERATIONS IN INFLAMMATORY BOWEL DISEASE - THE INFLUENCE OF GERMINE VARIATION (MEQTLS) ON GENOME-WIDE METHYLATION ALTERATIONS


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7Dept Of Gastroenterology And Hepatology, Maastricht University Medical Center
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9Servicio De Aparato Digestivo, Hospital Clinico Universitario Lozano Blesa, Zaragoza/Spain
10Cancer Centre For Genomic Regulation, Barcelona Institute Of Science and Technology, Barcelona/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 (120 controls, 150 Crohn’s disease, with one CD 167 controls, UC 261 controls (UC) using the Illumina 450k platform with covariates of age, sex, and differential cell counts, deconvoluted by the Houseman method; genotyping was performed using Illumina HumanSnow-6 (8-BeadChips. Samples were obtained from new onset IBD cases in six European centres as part of the European Commission funded IBD-Character project.

Result: 195 probes exhibited Bonferroni significant IBD-associated methylation differences, including VMP1/MIR21 (p = 3.7 × 10−9), RPS6KA2 (1.1 × 10−10), SBN02 (2.7 × 10−10), and TFN/S101 (1.1 × 10−13); data which provide important replication and confirmation of methylation differences previously reported in paediatric CD and adult IBD. Novel findings include PHOSPHO1 (1.3 × 10−7), MUC4 (5.5 × 10−13), and ITGB2 (1.3 × 10−13), and a replication of two SNPs previously described as correlated to VMP1/MIR21 methylation (rs0874242, p = 4.4 × 10−23, rs16853015, p = 7.4 × 10−21). There was an enrichment of highly significant IBD-associated methylation changes in proximity to IBD GWAS loci. Results were highly published two-probe methylation biomarker markers (8) from a new onset paediatric CD cohort accurately distinguished IBD from controls in this new onset adult cohort (AUC = 0.93).

Conclusion: These data allow methylene profiling in a large multinational cohort of IBD, including novel disease-associated methylation changes important unexplored replication of recent discoveries, together with insight into the genetic contribution to epigenetic alterations in complex disease, and the utility of peripheral blood DNA methylation as a biomarker.

Disclosure of Interest: R. Kalla: Received funding from the EU FP7 (285854) and served as a speaker for Ferring J. Jahnsen: Served as a speaker and a advisory board member for MSD, Tillot, Ferring, Abbvie, Celltrion, Orion Pharma, Takeda, Napp Pharm, Meda, AstellasPharma, Hikma and Pfizer.

References

OP297 AN AUTOPHAGY-RELATED PERIPHERAL BLOOD MICRORNA SIGNATURE DIFFERENTIATES COLONIC CROHN’S DISEASE FROM ULCERATIVE COLITIS

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Introduction: Phenotypic expression of colonic inflammation in inflammatory bowel disease (IBD) 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. PBMCs were obtained from patients with CCD and UC 10-20), RPS6KA2 (1.1 × 10−10), and TNFSF10 (1.1 × 10−10). Two out of 5 miRNAs putatively target the autophagy-related 16-like 1 (ATG16L1) gene, and 4 out of 5 miRNAs were significantly correlated with the expression of 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 ULCERATIVE COLITIS PATIENT GROUPS WITH DIFFERENT DISEASE-DRIVING PATHWAYS AND THERAPEUTIC RESPONSE TO ANTI-TNF TREATMENT
S. Pavlidis1, M. J. Loza2, P. Branigan3, C. Monast4, A. Rowe5, F. Barribaud6
1Immunology, Janssen Research & Development Ltd, High Wycombe/United Kingdom
2Immunology, Janssen Research and Development, LLC, Spring House/United States of America/P.A
3Immunology, Janssen Research and Development, LLC., High Wycombe/United Kingdom

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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 pathology 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 datasets. ESs for enrichment of 37 biological processes from GSEA (16/03/79) with a library of gene set signatures representative of various immunological and inflammatory processes as well as specific activated cell types. Patient stratification at baseline (BL) or after anti-TNF treatment (PT) in either clinical responders (R) or non-responders (NR) was queried.

Result: Gene set signatures whose ES differed significantly (ES change ≥ 0.2, p ≤ 0.05) between comparisons were identified from general linear model analyses. Comparisons were made at BL in all participants irrespective of clinical responses, and then clinical NR responders were 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 bcl2onc 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 bcl2onc 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 & Development LLC, Spring House, United States
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Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
15:45-17:15
NOVEL TECHNIQUES IN LOWER GI MALIGNANCIES – ROOM L8

OP300 THE IMPLANTABLE MEDICATED MICRORESERVOIRS IN THE TREATMENT OF COLORECTAL CANCER. THE GOOD EFFECTS OF SIMPLE PROCEDURE. EARLY RESULTS
Y. S. Bereznitsky, V. P. Sulyama, O. N. Popova
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Introduction: Colorectal cancer (CRC) is the third most frequent in the world of men, and the second - in women. In Europe remains steady increase in incidence and mortality according to Globocan 2012 and source EuropeColoPan. The main problem after surgery is local recurrences that often develop even after resection R0. Five-year survival in is developed in developed countries is not more than 66%, and in developing countries the rate is not more than 15% [1,2]. Due to this, more and more often there are ideas about intraoperative prevention of local recurrence. There are a number of studies on intraoperative radiation therapy, which achieve good results for the prevention of CRC [3]. We aimed to investigate the use of implanting microreservoirs to improve the results of surgical treatment CRC. To study the safety and efficacy of this modification surgery. Materials and methods: We have investigated the number of CRC recurrence for patients without metastases, lymph node involvement assessed by color Doppler scanner to other organs after surgery in a volume R0 for a year after surgery. The study included 87 patients (54 women and 33 men, mean age 62.4 years +/- 8.4 years) who were operated in the Dnipropetrovsk regional proctology centre from February 2014 to February 2015. The control group included 60 patients (42 patients, 17 men and 25 women) performed surgery in standard volume according to guideline. In the test group (45 patients, 16 men and 29 females) before the anosotomosis were formed medicated microreservoirs with 5-fluorouracil (5FU) supported on polyvinylpyrrolidone (PVP). In fact, it was a mixture of 30% PVP solution 5 ml and 5 ml 5FU (250 mg). This mixture was introduced into the muscle layer from the side of mucosa the 1 ml syringe with needle 0.40 x 10 mm 27G x 1 1/2 at a distance of 1-1.5 cm from the edge of the intestine. In one procedure was introduced approx. 1.5 ml of the reservoir in the area of the anastomosis. The operation was completed in a standard way. As the drug delivery system has been selected PVP in the concentration of 30% as its safety is confirmed by the FDA. [8] PVP as a delivery system allows for the gradual release of the drug, due to the differences in polymer degradation rate and drug release dependence on the drug carrier polymer. An important advantage is the fact that the PVP is practically not destroyed at a pH of less than 7 [7], which allows to delay the release of 5FU, since pH in the stage of inflammation in the tissues is reduced and consequently the release of the bulk of 5FU will begin after completion of the inflammation. The 5FU was selected as a drug for the treatment because it does not require pre-transformation to acting form and is quite effective on condition metastases in the tissues.

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

A118
United European Gastroenterology Journal 4/5(S)

A118
United European Gastroenterology Journal 4/5(S)
Aims & Methods: Between April 2012- April 2016, a total of 655 colorectal ESD procedures in LSTs.

Introduction: Endoscopic submucosal dissection (ESD) is a minimally invasive technique, providing end-bloc resection of premalignant and malignant lesions in early stage gastrointestinal (GI) cancers. Lateral Spreading Tumours (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 removal with advanced endoscopic techniques (EMR or ESD). colorectal ESD was performed to 290 lesions. Data was recorded prospectively before and after the procedure. 8 ESD cases were excluded because the lack of control endoscopy. The results of 282 ESD procedures performed in colon and rectum with diagnosed LST were analyzed retrospectively.

Result: Table: Demographic data and colorectal endoscopic submucosal dissection results [Case (n) = 273 Lesion (N) = 282]

<table>
<thead>
<tr>
<th>Lesion size, mm</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range (13; 14–176)</td>
<td>40.44 (26.2)</td>
<td>33–1476</td>
</tr>
<tr>
<td>(42; 20–198)</td>
<td>49.81 (28.9)</td>
<td>20–198</td>
</tr>
<tr>
<td>(61.5; 6–540)</td>
<td>79.5 (71.1)</td>
<td>6–540</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dissection speed, mm²/min</th>
<th>Mean (SD)</th>
<th>Range (21; 1.74–79.55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>En-Bloc resection rate, N (%)</td>
<td>257 (91.1)</td>
<td>255 (90.4)</td>
</tr>
<tr>
<td>Complete Resection, N (%)</td>
<td>255 (90.4)</td>
<td>14 (12)</td>
</tr>
<tr>
<td>Paris Classification, N (%)</td>
<td>115 (38.5)</td>
<td>102 (35.8)</td>
</tr>
<tr>
<td>2a &amp; 2c</td>
<td>11 (3.9)</td>
<td>13 (4.3)</td>
</tr>
<tr>
<td>Adverse Events, N Delayed bleeding</td>
<td>2.9</td>
<td>2.9</td>
</tr>
<tr>
<td>Localization, N Rectum Sigmoid colon</td>
<td>133</td>
<td>132</td>
</tr>
<tr>
<td>Descending colon Splenic flexura</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Transverse colon Hepatic flexura</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Ascending colon Cecal Ileocoeal valve</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Pathology, N (%) Carcinoma</td>
<td>124 (44.99)</td>
<td>124 (44.99)</td>
</tr>
<tr>
<td>Intramucosal Sm1 invasion Sm2</td>
<td>28 (9.9)</td>
<td>28 (9.9)</td>
</tr>
<tr>
<td>invasion Tubular Adenoma</td>
<td>11 (3.9)</td>
<td>11 (3.9)</td>
</tr>
<tr>
<td>Tubulovillous Adenoma Villous</td>
<td>236</td>
<td>236</td>
</tr>
<tr>
<td>Adenoma Serrated Adenoma LST LST-G LST-NG</td>
<td>46</td>
<td>46</td>
</tr>
</tbody>
</table>

Conclusion: Few studies have compared results of colorectal ESD procedures versus EMR in colon and rectum.

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

OP301 ENDOSCOPIC SUBMUCOSAL DISSECTION IN LATERALLY SPREADING TUMORS: EXPERIENCE OF 282 CASES FROM A TERTIARY REFERENCE CENTER IN TURKEY

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Introduction: Endoscopic submucosal dissection (ESD) is a minimally invasive technique, providing en-bloc resection of premalignant and malignant lesions in early stage gastrointestinal (GI) cancers. Lateral Spreading Tumours (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 removal with advanced endoscopic techniques (EMR or ESD). colorectal ESD was performed to 290 lesions. Data was recorded prospectively before and after the procedure. 8 ESD cases were excluded because the lack of control endoscopy. The results of 282 ESD procedures performed in colon and rectum with diagnosed LST were analyzed retrospectively.

Result: Table: Demographic data and colorectal endoscopic submucosal dissection results [Case (n) = 273 Lesion (N) = 282]

| Lesion size, mm, mean (SD) (median; range) (33; 14–176) | 40.44 (26.2) |
| Size, mm, mean (SD) (median; range) (42; 20–198) | 49.81 (28.9) |
| Duration of procedure, min, mean (SD) (median; range) (61.5; 6–540) | 79.5 (71.1) |
| Dissection speed, mm²/min, mean (SD) (median; range) (21; 1.74–79.55) | 24.46 (15.41) |

Conclusion: Few studies have compared results of colorectal ESD procedures versus EMR in colon and rectum.

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

OP302 EVALUATION OF RECTAL CANCER ANGIogenesis USING IMMUNOHistoCHEMICAL AND COMPUTER-ASSISTED ENDoSCOPIC MONITORING METHODS

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Introduction: The conventional way for evaluation of rectal cancer angiogenesis requires a biopsy or a tissue specimen applying specific immunohistochemical or molecular biological tests. The evaluation of microvessel density is a gold standard in the assessment of tumour angiogenesis. Doppler ultrasound is an attractive method for imaging malignancy in vivo which can be repeated without exposing the patient to any risk.

Aims & Methods: The aim of the current study is to evaluate the preoperative rectal cancer angiomatic status with Endorectal Power Doppler Ultrasound by using a new software index, and to compare results with microvessel density in surgical specimens A total of 110 patients (59 males; 51 females, mean age 61.5 years) with rectal cancer were enrolled in this study. The patients were operated and staged as follows: in stage I – 20pts (18%), stage II – 20 (18%), stage III – 47 pts (43%); stage IV 14 pts (13%). Microvessel density was evaluated by using immunohistochemical staining of surgical specimens with anti-CD-31 antibody. The PDVI of each tumor was determined using endorectal power Doppler ultrasound with computer assisted quantification of colour pixels. The PDVI was defined as the ratio of the number of the colored pixels within a tumor section to the number of total pixels in that specific tumor section, and was calculated using a software. Result: The mean microvessel density (MVD) was 163.6±6 microvessels/mm². Median MVD was used as the cutoff point divided two groups of tumours with high (≥160 vessels/mm2) and low angiogenic activity (> 160 vessels/mm2). Median PDVI was 8.9±6.0% (range: from 0 to 27.3). Median PDVI (8%) was used as the cutoff point for 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 endorectal power Vascularity Index calculated by imaging malignancy in vivo has the advantage of avoiding the need for surgery except for one patient with delayed perforation. Surgical treatment was performed in all patients with deep submucosal (sm2) invasion, however neoplasia was observed in none of these patients. Colorectal ESD is a safe and effective method to provide en-bloc and curative resection of LSTs.

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

OP303 COMPARISON OF CLINICAL OUTCOMES AMONG DIFFERENT ENDOSCOPIC MODALITIES FOR RECTAL NEOEndOCRINE TUMOR

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Introduction: Rectal neuroendocrine tumor (NET) less than 10 mm in diameter can be removed by various endoscopic techniques, such as endoscopic mucosal resection (EMR), modified EMR, and endoscopic submucosal dissection (ESD). This study aimed to compared 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-ESD group (n = 18), and ESD group (n = 21). We compared treatment outcomes and complications associated with these methods.

Result: There was no different in tumor diameter between different endoscopic procedures (ESMR-L, 4.5 ± 1.6 mm; CSI-EMR, 5.6 ± 2.0 mm; ESD, 5.0 ± 2.2 mm; p = 0.236). En bloc resection was achieved in all patients. There was no lateral margin involvement in all patients. Basal margin involvement occurred in one patients in the ESD group and two in the CSI-EMR group. The rates of pathological complete resection were 100% (17 of 17) in the ESMR-L group, 95.2% (20 of United European Gastroenterology Journal 4(5S)
21) in the ESD group, respectively (p = 0.354). Perforation or delayed bleeding did not occur. The size of ESMR-L was significantly shorter than those of the other groups and procedure time increased in order of ESMR-L, CSE-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, CSE-EMR, and ESD were effective and safe for the treatment of rectal NET, compared with CSE-EMR 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 NET that is larger than 10 mm 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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2Oporto/Portugal

Introduction: Conventional colonoscopic surveillance is the mainstay of the management of patients with a history of colorectal adenoma. Anoscopy is a useful and accessible technique to screen for anal cancer. However, the role of anal cytology in anal squamous dysplasia is still unclear.

Aims & Methods: The authors intend to estimate agreement between anal cytology and histopathology. This is a prospective study of patients receiving anal dysplasia screening between 2010 and 2015, in a proctology 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 results, 22% atypical squamous cells of undetermined significance (ASCUS), 33% low-grade squamous intraepithelial lesion (LSIL) and 4 NILM (normal). In the remaining patients, uncertain significance (ASCUS), 33% low-grade squamous intraepithelial lesion or atypical squamous cells of unknown significance (ASCUS), 25% LSIL and 4 NILM). By other hand, concerning the patients with HGD/CIS on histologic exam, 28% had dysplasia on histopathological exam (4 HGD and 5 LGD).

Conclusion: CRPs, were being considered for proctectomy and/or had failed conventional polypectomy, in another deep submucosal invasion was suspected during TASSER-ESD/P-EMR/EMA – patient had an elective laparoscopic anterior resection (T1m3,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 65–465 min. Thirty two TASSER sessions 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 (coagrasper/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 TASSER - TAE cases there was a need for a full-thickness rectal dissection due to subsequent 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 TASSER-ESD/P-EMR + EMA sub-cohorts. Treatment for those episodes comprised of hemostatic endoscopic devices (coagrasper/clips); prophylactic endoscopic clipping and in the remaining 2/6 cases only endoscopic clips were deployed. Twenty-one patients had delayed bleeding (6 after TASSER, 15 after P-EMR or ESD) in whom a defunctioning ileostomy, discharged on day 4 post operation. First follow-up was performed at 4–6 months interval in 25/31 patients showed: 21/25 with no recurrence (84%) and 4/25 (16%) with a minimal (<15 mm) polyp recurrence, amendable to endoscopic therapy. No rectal stricturing was identified and only one case was reported.

Conclusion: TASSER 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.


All 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 1.86**

**OP306 THE PROREGENERATIVE ROLE OF INTERLEUKIN-22 IN THE INTESTINAL EPITHELIUM DEPENDS ON AUTOPHAGY AND ER STRESS**

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2Division of Gastroenterology and Hepatology, Department of Medicine, Addenbrooke’s Hospital, University of Cambridge, Cambridge/United Kingdom

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 autophagosome machinery, a conserved mechanism for protein degradation. Both processes are strongly connected since impaired autophagy subsequently results in deregulation of ER function. Interleukin-22 (IL-22) is known to be a protective cytokine in mucosal regeneration by promoting epithelial proliferation via STAT3 activation. Here, we investigate the impact of the IBD risk genes ATG16L1 and XBP1 on the proregenerative role of IL-22 in intestinal epithelium in mice and humans. Human colon cancer cell HT-29 and Caco2 cells were co-treated with recombinant IL-22 and ER stress inducers like Tunicamycin or autophagy inducers like Rapamycin before they were subjected to wound healing assays, gene expression analysis and immunoblot analyses. Intestinal organoids derived from XBP1 iSIC (intestinal epithelial cell specific deletion) and ATG16L1 iSIC mice were treated with recombinant IL-22 and gene expression analysis using qRT-PCR, RNA sequencing and transcriptome analysis were performed. Secreted cytokines in supernatants from cells and organoids were detected with

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Disclosure of Interest: None of the authors have declared any potential conflicts of interest.

References:
3. Pickert G et al. STAT3 links IL-22 signaling in intestinal epithelium and spontaneous cell death in intestinal crypts which exacerbates after IL-22 treatment. Finally, IL-22 suppresses spontaneous intestinal inflammation in Atg16l1 ΔIEC/ΔIEC mice. On the flipside, same treatment of wild type control mice does not affect cell death and inflammation, underlining a genotype dependency of beneficial and adverse effects of IL-22 application.

Introduction: Contact E-mail Address: hristina.bega@umil.ch

Aims & Methods: CoIitis-associated cancer (CAC) was induced in 18-20 week old littermates C57BL/6 mice by azoxymethane (AOM) i.p. injection and 3 cycles of 2.5% oral dextran sodium sulfate (DSS) treatment. Tumor development was assessed by macroscopy, histology, and immunohistochemical analysis. Survival and proliferative index in the colon were determined by Tetra amidyl dye. Cytokine and gene expressions were measured by RT-qPCR. Smad2 phosphorylation was assayed by Western blot.

Result: Tollip KO mice had significantly lower endoscopic tumor scores than WT littermates upon AOM-DSS exposure (8.4 ± 7.8 vs 13.4 ± 6.0, p < 0.05). Likewise, tumor numbers (3.8 ± 2.5 vs 7.1 ± 3.0, p < 0.05) and size were reduced. Immunohistochemical studies demonstrated reduced apoptotic index (79.3 ± 75.0 vs 246.8 ± 152.9, p < 0.05) and lower proliferation (21.0 ± 8.5 vs 27.9 ± 7.3, ns) in Tollip KO tumors when compared to wt controls. RNA analyses showed that Tollip ablation favors an anti-tumorigenic environment with reduced Bel-7 (85.9 ± 50.9 vs 36.2 ± 39.5) and c-myc expression (6.2 ± 4.9 vs 2.1 ± 2.6). Importantly, Tollip deficiency led to reduced Foxp3 abundance (3.7 ± 2.6 vs 7.3 ± 1.7) in unchallenged colonic as well as in tumoral tissues. In addition, Tollip deficient tumors harbored reduced TGFbeta expression as well as reduced SMAD2 phosphorylation suggesting that TGFbeta signaling is dysfunctional in the absence of Tollip.

Conclusion: Our data show that Tollip partially favors colonic oncogenesis despite being protective against colitis. Putative mechanisms include reduced tumor-inflammation-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:

OP309 CONSTRUCTION OF IN VITRO 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)1.

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 by TMDU method. We analyzed cell proliferation, cell death and markers for epithelial-mesenchymal transition (EMT) marker.

Result: After 8 weeks of culture, we observed the EMT marker (E-cadherin, vimentin, N-cadherin) expression in organoids. The expression of EMT marker was significantly increased after 8 weeks of culture. Additionally, we assessed the expression of genes implicated in oncological transformation and epithelial to mesenchymal transition.

Conclusion: In conclusion, long-term inflammation leads to the development of carcinogenesis in UC. Further study is required to understand the mechanism of carcinogenesis in UC.
western blot analysis. The gene expression of transformed organoids was assessed by multiplex quantitative RT-PCR.

**Result:** The treatment with the inflammatory reagents in mouse colonic organoids showed the time-dependent induction of NF-κB target genes. Particularly, the expression of DUOX2 gene was gradually increased by the continuous stimulation with inflammatory reagents for 40 weeks. 3D immunostaining analysis showed NF-κB p65 was accumulated in nuclei 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 remained 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 organoids required neither R-spondin1 nor Wnt3a after the treatment with GS3K inhibitor for 8 weeks, indicating that the organoids 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-regulated carcinogenesis.

**Conclusion:** Long-term inflammatory and nuclear accumulation of β-catenin leads to irreversible cell transformation, which is wnt independent survival capacity of colonic organoids. 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**

OP334 CIGARETTE SMOKE EXTRACT INHIBITS FLUID AND HCO3- 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 would like to understand whether smoking has any effects on pancreatic ductal fluid and HCO3- secretion. Guinea pigs were exposed to cigarette smoke four times a day for 30 min for 6 weeks. The expression of CFTR was analysed by immunohistochemistry. Intra-interlobular pancreatic ducts were isolated from guinea pig pancreas. Cigarette smoke extract (CSE) was prepared by smoking of 15 cigarettes into 10ml distilled water by a smoking machine. Three different concentration (20, 40 and 80 mg/ml) were diluted using the stock solution. Intracellular pH was evaluated by microfluorometry. Basal and forskolin-stimulated fluid secretion was measured by video microscopy. CFTR currents were detected by whole cell configuration of patch clamp technique.

Result: Cigarette smoking significantly diminished the expression of CFTR and the forskolin-stimulated secretion in guinea pig pancreatic ducts and forskolin-stimulated CT current of CFTR CT channel (20 mg/ml by 44.5%, 40 mg/ml by 69.3% and 80 mg/ml by 91.3%).

Conclusion: Cigarette smoking and CSE inhibits pancreatic ductal fluid and HCO3- secretion and the activity of CFTR which may play a role in the smoke-induced pancreatic damage. This study was supported by OTKA, MTA and TAMOP.

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

OP335 IDENTIFICATION AND CHARACTERISATION OF A NOVEL EARLY ONSET DIABETES GENE USING HUMAN PLURIPOTENT STEM CELLS
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2Centre Of Medical Technology (mtz), Helmholtz Institute for Biomedical Engineering, Aachen/Germany
3Department Of Cell Biology, Institute for Biomedical Engineering, Aachen/Germany

Introduction: Diabetes represents one of the major burdens in the 21st century. More than 350 million people are globally affected with diabetes. Monogenic diabetes such as juvenile onset insulin-dependent diabeties (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 molecular basis of these diabeties has translated in novel avenues of treatment of common diabetes in the medicine 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 type 2 diabetes (T2D) and type 1 diabetes (T1D) may be caused by rare monogenic variants/mutations missed by the current GWAS strategies targeting common variants. The current project reports on such a novel gene relevant as regulator of human pancreatic islet formation but also as a novel early onset diabetes gene.

Result: Using stage-specific genome-wide profiling complemented with Chip-Seq data in differentiating human embryonic stem cells, we show that our gene binds and activates Nkx2.2, Nkx6.1 and Pdx1, all belonging to the core suite of islet formation transcription factors. Remarkably, this gene negatively interacts with the promoter regions of the latter genes together with Foxa2, Pdx1 and Gata4. Finally, we engineered human embryonic stem cells with previously identified mutations in JOD patients. Directed differentiation studies of these cells showed an impaired binding pattern of Nkx2.2, Nkx6.1 and Pdx1 mainly 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.

OP336 LACK OF CFTR RESULTS IN THE IMPAIRED FUNCTION OF THE PLASMA MEMBRANE CA2+- PUMP THAT CAUSES INTRACELLULAR CA2+ OVERLOAD AND MITOCHONDRIAL DAMAGE IN THE PANCREATIC DUCTAL EPITHelial CELLS OF CFTR KNOCK OUT MICE
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Introduction: The cystic fibrosis transmembrane conductance regulator (CFTR) has a significant role in pancreatic ductal epithelial secretion and it’s genetic defects damage the pancreas. The exact mechanism of this pancreatic damage is only partially known. The toxic cellular Ca2+ homeostasis of CFTR-deficient ductal acinar cells. Interestingly, the functional inhibition of CFTR with 100 µM CFT(rinh)-172 had no effect on the Ca2+ signals. Next we investigated the CFTR KO mice and found that the Ca2+ extrusion was significantly lower than in control mice. Hence we hypothesized that the Ca2+ extrusion is the primary target of the CFTR KO mice and this extrusion could be blocked by the CFTR KO mice. Therefore, we hypothesized that the Ca2+ extrusion is the primary target of the CFTR KO mice and this extrusion could be blocked by the CFTR KO mice.
in CFTR KO PDEC compared to WT due to the impaired function of the pancreatic ductal cell (PDEC). In addition, the sustained elevation of [Ca^2+] isopropylidene mitochondrial potential in CFTR KO PDEC.

**Conclusion:** Dysfunction of PMCA leads to disturbed Ca^2+ homeostasis in CFTR-deficient PDEC and the consequent cellular Ca^2+ overload impairs mitochondrial function. These changes might contribute to the pancreatic damage seen in cystic fibrosis.

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

**OP317 ENDOSCOPIC DILATION OF PANCREATIC DUCT STRUCTURES IN CHRONIC PANCREATITIS WITH MULTIPLE PLASTIC STENTS: RESULTS IN 48 PATIENTS**

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**Introduction:** Main pancreatic duct (MPD) strictures located in the head of the pancreas often occur in the course of chronic pancreatitis (CP). Common management of these strictures is endoscopic placement of a single plastic stent. Refractory strictures require repeated stent replacement or surgical pancreaticojejunostomy. Insertion of multiple plastic stents (MPS) obtained, in a series of 19 patients, symptomatic MPD stricture resolution in 84% of the cases, after 3-year follow-up (1). The aim of this study was to evaluate the results of the MPS strategy in a larger series of CP patients.

**Aims & Methods:** Forty-eight patients (34 men; mean age 44 years, range 5–86) with severe CP and a symptomatic dominant MPD stricture located in the head of the pancreas, was evaluated. All the patients experienced pain resolution following MPD drainage with a single plastic stent. The MPD stricture was refractory to single plastic stent placement in all cases and patients underwent insertion of MPS according to the following protocol: balloon dilation of the stricture of necessity, insertion of the maximum number of plastic stents allowed by the stricture tightness and pancreatic duct diameter, stents removal after 6 months.

**Result:** The median number of stents placed through the major or minor papilla was 3 (range 2–5), 8.5 to 11.5 Fr in diameter and 3 to 7 cm in length. MPS were removed after a mean time of 6.7 months (range 2–18). Eight patients (16.6%) had persistence of the MPD stricture after MPS removal and underwent replacement of an increased number of stents; 3/8 patients had a dilation of the stricture and 5/8 patients had other major placement (overall success 89.5%). Following a mean follow-up of 9.5 years (range 0.3–15.5) after MPS removal, 77.1% of patients were asymptomatic. Symptomatic MPD stricture recurrence was reported in 11 patients (22.9%), after a mean time of 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. MPS: multiple plastic stents; MPD: main pancreatic duct; EUS: endoscopic ultrasound; CT: computed tomography; ERCP: endoscopic retrograde cholangiopancreatography. No current consulting agreements in place One day animal lab in 2012 and 2013. Speaking and teaching in 2014

1 I. Boskoski: Consultant
2 G. Costamagna: Olympus Japan Grant/Research Support cook, Inc Advisory Committees or Review Panels. Grant/Research support Boston Scientific Corporation Advisory Committee or reviews panels. Taewoong Medical Inc Advisory Committees or Review Panels

All other authors have declared no conflicts of interest.

**Reference**


**OP318 CARDIOVASCULAR RISK IN PATIENTS WITH CHRONIC PANCREATITIS AND PANCREATIC EXOCRINE INSUFFICIENCY**


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**Introduction:** Mortality in patients with chronic pancreatitis (CP) is increased. Some previous studies suggest that chronic pancreatitis (CP) is an independent risk factor of cardiovascular disease (CVD). It is well known that malnutrition secondary to different diseases and conditions increases the risk of CVD too. Pancreatic exocrine insufficiency (PEI) causes major nutritional deficiencies and can lead to the development of CVD too.

**Results:** Aims of the present study was to assess the risk of CV events in patients with CP and the impact of PEI and other factors in these patients. A retrospective analysis of a prospectively collected database of patients with CP, that were subjected to ERCP with stone extraction or pancreatic duct stenting was carried out. Diagnosis of CP was based on endoscopic ultrasound (EUS), magnetic resonance cholangio-pancreatography (MRCP) and pancreatic MRI. PEI was defined as the need of pancreatic enzyme replacement therapy due to the presence of maldigestion-related symptoms and/or abnormal nutritional markers together with an abnormal 13C- MTG breath test result. Major CV events (stroke, heart attack) and peripheral arterial disease (claudication, thrombosis) during follow-up were analysed. Patients with a past history of CV events previous to the diagnosis of CP were excluded. Data about sex, age at diagnosis of CP, alcohol consumption, smoking, PEI and other comorbidities (including diabetes mellitus) were evaluated. Statistical analysis was done by logistic regression adjusted for confounding factors.

**Result:** Patients were finally included (77.8% men), with a median age of 46 years (range 15–88 years). Mean follow-up was 7.8 years. CP was secondary to alcohol and/or smoking in 301 patients (66.1%), 149 patients (32.7%) had PEI and 131 (28.8%) had diabetes mellitus. A total of 46 CV events were recorded in 39 patients (9.5%). 22 patients (4.8%) suffered from a minor CV event and the remaining 24 patients (5.3%) presented a peripheral arterial disease. CV events occurred more frequently in patients with PEI (n = 28, 18.8%) than in patients without PEI (n = 15, 4.9%) (p < 0.001). In the logistic regression analysis, PEI (OR 3.76; 95%CI 1.65–8.58), diabetes mellitus (OR 2.55; 95%CI 1.11–5.83) and smoking (OR 3.90; 95%CI 1.19–12.7) were significantly and independently associated with CV events.

**Conclusion:** Patients with CP are at high risk of CV events. PEI, diabetes mellitus and smoking are independent risk factors associated with the risk of CV events in patients with CP.

**Disclosure of Interest:** J.E. Dominguez-Munoz: has acted as speaker and advisor international of Mylan and AbbV. All other authors have declared no conflicts of interest.

**References**

OP320 WHAT KIND OF INTRAVENOUS HYDRATION SHOULD BE USED FOR THE PREVENTION OF POST-ERCP PANCREATITIS: A PROSPECTIVE RANDOMIZED MULTICENTER CLINICAL TRIAL

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Introduction: A pilot study suggests that aggressive intravenous hydration with lactated Ringer’s solution may reduce the development of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis. The present larger multicenter study aimed to determine what kind of intravenous hydration could reduce the incidence of post-ERCP pancreatitis.

Aims & Methods: In a prospective randomized multicenter clinical trial, patients who underwent first-time ERCP were randomly assigned to 3 groups (1:1:1) that received aggressive hydration with lactated Ringer’s solution (3 mL/kg/h during the procedure, a 20 mL/kg bolus after the procedure, and 3 mL/kg/h for 8 hours after the procedure), standard hydration with the same solution (1.5 mL/kg/h during the procedure, a 20 mL/kg bolus after the procedure, and 3 mL/kg/h for 8 hours after the procedure), or aggressive hydration with lactated Ringer’s solution group and 11.6% (15/129) in the standard hydration group (P = 0.001).

Results: A total of 406 patients were enrolled, and 395 of them completed the protocols. The three groups had no significant difference in demographic characteristics or other risk factors before ERCP (P > 0.05). The intention-to-treat post-ERCP pancreatitis rates were 3.0% (4/132) in the aggressive hydration with lactated Ringer’s solution group and 11.6% (15/129) in the standard hydration group (P = 0.008), whereas the per protocol (PP) post-ERCP pancreatitis rates were 1.6% (2/128) in the aggressive hydration with lactated Ringer’s solution group and 11.6% (15/129) in the standard hydration group. The primary end point, post-ERCP pancreatitis, was defined as hyperamylasemia (level of amylase > 3 times the upper limit of normal) and increased epigastric pain (>3 points on visual analogue scale) persisting for > 24 hours after the procedure.

Conclusion: A total of 406 patients were enrolled, and 395 of them completed the protocols. The three groups had no significant difference in demographic characteristics or other risk factors before ERCP (P > 0.05). The intention-to-treat post-ERCP pancreatitis rates were 3.0% (4/132) in the aggressive hydration with lactated Ringer’s solution group and 11.6% (15/129) in the standard hydration group (P = 0.008), whereas the per protocol (PP) post-ERCP pancreatitis rates were 1.6% (2/128) in the aggressive hydration with lactated Ringer’s solution group and 11.6% (15/129) in the standard hydration group. The primary end point, post-ERCP pancreatitis, was defined as hyperamylasemia (level of amylase > 3 times the upper limit of normal) and increased epigastric pain (>3 points on visual analogue scale) persisting for > 24 hours after the procedure.

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

References
for the patients that Pernecutaneous Endoscopic Gastrostomy was contraindicated. PTEG by endoscopic assistance may enhance the safety of the procedure and the new item that may enhance the reliability was developed.

Aims & Methods: The aim of this study is to evaluate the clinical usefulness of PTEG supported by endoscopy. A rupture-free balloon (RFB) catheter is inserted into the upper esophagus. Pernecutaneous balloon puncture with a specialized needle is then performed from the left side of patient’s neck under ultrasonographic control. A guide wire is inserted through the needle into the RFB, followed by a dilator and sheath. A placement tube is then inserted through the sheath, and the sheath is removed. We started to perform PTEG under endoscopy in a total of 119 patients (74 men and 45 women, mean age 71.5 years) in whom PEG was not feasible. Double Balloons equipped Overtube type RFB were used instead of primary RFB in seven cases that the puncture needle is positioned inside the overtube through the balloon. PTEG was performed for nutrition in 65 patients and for decompression in 54.

Result: Satisfactory results were achieved in all 119 patients. Median follow-up was 64.0 days in patients who received decompression because of the obstruction due to malignancies and 270.0 days in those who received nutrition. Four of 65 patients for nutrition were able to be free from tube feeding due to PTEG tube feeding support. There was one patient had tracheal penetration, which was managed conservatively. Other complications were minor oozing bleeding in seven patients that did not require blood transfusion, subcutaneous emphysema in two patients, which were managed conservatively. The complication rate was 13.4%. A stable procedure could performed in all seven cases using the new overtube and also there was no complications. No patient required surgical treatment or died after PTEG.

Conclusion: PTEG is feasible, safe, and useful. PTEG could be an optimal procedure for long-term nutrition and/or decompression even for the patients that failed percutaneous puncture. Use of endoscopic procedures enhances the safety of the procedure and allows better confirmation of each step involved. New overtube type RFB will be useful need more experience.

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

WEDNESDAY, OCTOBER 19, 2016

08:30-10:00

EOSINOLIC OESOPHAGITIS AND GORD – ROOM M

OP232 STEP-UP EMPIRIC ELIMINATION DIET FOR PEDIATRIC AND ADULT EOSINOPHILIC ESOPHAGITIS: THE 2–4–6 STUDY


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Introduction: A six-food elimination diet (SFED) for eosinophilic esophagitis (EoE) requires almost a year on a high level of dietary restriction and multiple exacerbations. A four-food elimination diet (FFED), eliminating the four most common culprit foods in EoE (animal milk, gluten-containing cereals, eggs, 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, we performed 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 milks 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 absence of food triggers 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.
OP135 A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF A NOVEL RECOMBINANT, HUMANISED, ANTI-INTERLEUKIN-13 MONOCLONAL ANTIBODY (RPC4046) IN PATIENTS WITH ACTIVE EOSINOPHILIC EOSPHAGITIS: 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 randomised 1:1:1 to receive once weekly either RPC4046 180 mg (LD) (n = 31), RPC4046 360 mg (HD) (n = 34), or PBO (n = 34). An IV dose on Day 1 was followed by weekly subcutaneous doses. Oesophageal biopsies, read by a central blinded pathologist, were obtained at baseline (BL) and Week 12 to assess mean eosinophil count, 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 count was significantly reduced from BL for both RPC4046 dose levels compared to PBO (mean change: PBO –4.4, LD –94.8, HD –122.6 (HD). At Wk16, the mean count was significantly reduced from BL for both RPC4046 dose levels compared to PBO (mean change: PBO –6.4, LD –5.3 (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 this did not achieve statistical significance (PBO –4.0, HD –9.9; both p < 0.001 vs PBO). There was a significant improvements in endoscopic features as determined by the reduction in 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 –99.9 [both p < 0.0001 vs PBO]). The rates of overall adverse events (AEs) were 64.7% (PBO), 64.5% (LD), and 53.3% (HD). The most frequent AEs were headache (PBO 14.7%, LD 20.6%, HD 16.1%, HD 14.7%), and arthralgia (PBO 0%, LD 12.9%, HD 5.9%).

Conclusion: RPC4046 demonstrated significant reductions in oesophageal eosinophilic infiltration and improvements in endoscopic features at both dose levels compared to PBO. The HD had greater symptom improvement than the 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, Regeneron, Shire pharma
M. Collins: I have received research funds (through contracts) from Receptos (now Celgene), Meritage (now Shire), Shire, and Regeneron, and I am a consultant for Banner Life Sciences and Adare.
S. Gupta: Sandeep K. Gupta received consulting fees and/or speaker fees from Abbott Laboratories, Nestle 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; AstaZeneca, AG; Apsalis Pharma; GSK; AG; Nestle S. A.; Novartis, AG; Pfizer, AG, and Regeneron.
M. Grimm: I am an employee of Celgene.
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OP136 IMPAIRMENT OF CHEMICAL CLEARANCE AND MUCOSAL INTEGRITY DISTINGUISHES REFRACTORY EOSPHAGITIS FROM FUNCTIONAL HEARTBURN

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Introduction: HPI (heartburn prevalence) may be not a reliable tool in 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 swallowed-included peristaltic wave (PSPW) index, should be used to improve the diagnosis of HE. In this analysis we compared the diagnosis of FH/HE based on symptom-reflux association analysis with the diagnosis of FH/HE independently from PPI or BET.

Methods: 75 patients with normal esophageal acid exposure time and positive symptom-reflux association examined between November 2012 and January 2014. The diagnosis of FH/HE was based on symptom-reflux association analysis. The diagnosis of FH was the absence of acid reflux episode, the diagnosis of HE was the presence of at least one acid reflux episode. 30 patients with FH were kept as controls and 45 patients with HE were evaluated. The diagnosis of FH/HE was made by 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 <72% over 24 hours), characteristic of reflux episodes (acid/weakly acidic) and symptom-reflux association using both PSPW (positive if ≥95%) and SI (positive if ≥50%). MNBI values were calculated at 3 cm above the LES, during the overnight rest, for at least 30 minutes after excluding swallows and reflux induced changes. The PSPW index was calculated by dividing the number of refluxes followed within 30 seconds by swallow-induced peristaltic waves with the number of total refluxes. The results were compared with the diagnosis of FH/HE.

Result: In PPI-dependent patients with HE, PSPW index and MNBI were the most sensitive impedance parameters; at multivariate analysis, they were independent predictors of HE. At receiver operating characteristic analysis, PSPW index with MNBI efficiently separated FH from HE: the area under the curve being 0.95 (95% CI 0.90-0.99) and 0.95 (95% CI 0.90-0.99) for MNBI and for PSPW, respectively. The area under the curve being 0.95 (95% CI 0.90-0.99) and 0.95 (95% CI 0.90-0.99) for MNBI and for PSPW, respectively.

Conclusion: In our study, we showed that the diagnosis of FH/HE based on symptom-reflux association analysis could not be considered the gold standard in our patients. The presence of acid reflux episode should be used to improve the diagnosis of FH/HE.

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

OP137 THE ADDED VALUE OF POST-REFLUX SWALLOW-INCLUDED PERISTALTIC WAVE INDEX AND NOCTURNAL BASELINE IMPEDANCE IN REFRACTORY GERD STUDIED WITH ON-THERAPY IMPEDANCE-MANOMETRY

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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 baseline impedance (MNBI), showed diagnostic yield of impedance-pH monitoring in

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investigating PPI-refractory patients studied off-therapy, further improving the meaningfulness of this new procedure.

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-thery impedance-pH tracings from consecutive patients referred for PPI-refractory heartburn with/without regurgitation (i.e. < 50% of symptom relief or magnetic healing after 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 refluxes followed by a swallow-induced peristaltic wave by the number of total refluxes. Patients were subdivided into refractory reflux esophagitis (RRE), healed reflux esophagitis (HRE), non-erosive reflux disease (NIRD; defined by abnormal acid exposure time or normal AET but positive symptom-reflux correlation) and functional heartburn (FH defined by normal AET and negative symptom-reflux correlation) according to endoscopy and conventional impedance-pH variables.

Result: Median PSPW index and MNBI were significantly lower in 39 RRE (16%; 1145 Ohms) than in 41 HRE (25%; 1741 Ohms) and in 68 NIRD (29%; 2374 Ohms) patients, and in all three GERD subgroups compared to 41 FH cases (67%; 3488 Ohms) (P < 0.0001). Comparing NERD to FH, PSPW index showed lower overall curve greater than MNBI at refluxes with positive symptom association characteristic analysis (0.886 vs. 0.677, P = 0.005). PSPW index was abnormal preoperatively in 53/53 patients with positive surgical outcome and resulted independent predictor of PPI-refractory GERD at multivariate analysis (odds ratio 0.6983, P = 0.001).

Conclusion: On-thery 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 PSPW index is superior for selecting surgical candidates.

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

OP328 PRELIMINARY RESULTS OF A PROSPECTIVE MULTI-CENTER REGISTRY OF LOWER EOSPHAGEAL SPHINCTER STIMULATION FOR GERD: THE LESS-GERD REGISTRY
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Introduction: Safety and effectiveness of electrical stimulation of the lower esophageal sphincter (LES) using the Endostim® LES Stimulation System (The Harvard University) has been demonstrated in clinical trials. Limited data available on outcomes in clinical practice.

Aims & Methods: An ongoing, prospective international multicenter web-based registry is collecting data in patients with disruptive GERD symptoms treated with LES-ES in clinical practice at baseline and at routine follow-ups for 5-years. Demographics, adverse events, GERD symptoms recorded in daily diaries, GERD health related quality of life scores (GERD-HRQL), structured GI symptom questionnaires for extra-esophageal symptoms, use of proton pump inhibitors (PPIs) and physiological data (esophageal pH & manometry) are collected when available.

Result: Data was available in 50 patients enrolled in six sites with 6 months post-op follow up from 28 patients with 12 months follow-up. Ninety-nine (43/ 46) patients experienced improvement in heartburn scores after 6 months and 93% (25/27) showed an improvement at 12 months compared to baseline. The median (IQR) composite GERD-HRQL score improved from 2.2 (1.7–2.7) at baseline to 1.5 (1.3–2.1) at 6 months (P < 0.001) and from 2.0 (1.5–2.5) to 1.3 (1.0–1.8) at 12 months (P < 0.001). At baseline, 44% of patients (22/50) complained on daily bothersome heartburn symptoms affecting sleep which decreased to 8% (4/50) at 6 months (P < 0.001) and 0% (0/28) at 12 months (P < 0.001). At baseline, 52% and 15% of subjects reported moderate or severe regurgitation, respectively which decreased to 22% and 7% at 6 months (n = 27) and 14% and 0% at 12 months (n = 14). Data on prior hospitalization due to GERD was available in 40 patients who had hospitalization data available for their 6 month visit (±1 m). Annualized hospitalization rates due to GERD before Endostim was 1.1 (±0.7) vs. 0.2 (±0.4) after Endostim. Cancer was detected during routine endoscopy. The device was removed during laparoscopic fundoplication procedure. Two events of gastroaprosis, possibly related to the device requiring hospitalization were reported in one patient.

Conclusion: The LES is safe and effective in clinical practice in treating GERD patients with disruptive GERD symptoms despite PPI. LES stimulation results in significant improvement in GERD outcomes and reduced healthcare resource utilization. LES-ES should be considered a viable treatment option for treating GERD patients with disruptive GERD symptoms despite maximal medical management.

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

WEDNESDAY, OCTOBER 19, 2016 08:30–10:00
DIAGNOSIS AND TREATMENT OF PANCREATIC CANCER AND ITS PRECURSORS – ROOM N1

OP329 SURVEILLANCE OF HIGH-RISK INDIVIDUALS DETECTS RESECTABLE PANCREATIC MALIGNANCIES AND HIGH-GRADE PRECURSORS: RESULTS OF THE CAPS SURVEILLANCE PROTOCOL FOR FAMILIAL PANCREATIC NEOPLASIA
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Introduction: Endoscopic ultrasonography (EUS) and/or magnetic resonance imaging (MRI) screening of asymptomatic individuals (HRi) at high risk for PDa to detect for early pancreatic neoplasia can lead to the detection of small pancreatic cancers in almost 40% of patients with a high risk for neoplastic progression and the natural history of low risk detected lesions after baseline screening. The long-term clinical outcomes of radiologic surveillance aiming to detect early PDA and high-grade precursor lesions (IPMNH GD and/or PDA) are also not well understood.

Aims & Methods: To determine the incidence of surveillance-detected pancreatic lesions following baseline screening and calculate the incidence rates of invasive malignancy and high-grade neoplasia in HRi undergoing long-term surveillance. We prospectively enrolled HRi from the Cancer of the Pancreas Screening (CAPS) studies from 1998 to 2014 (n = 578) at a tertiary referral academic medical center with a comprehensive multidisciplinary pancreas screening program. HRi consisted of familial PDA related or PDA-associated gene mutation carriers (BRCA 1/2, PALB2, p16, PRSS1, STK11) who had > 6-months of follow-up imaging after baseline EUS and HRi with baseline solid masses or prevalent PDA were excluded from the surveillance cohort analyses. Radiologic surveillance-detected lesion progression (noninvasive to invasive) and worrisome features were classified according to the Sendai International Consensus Guidelines (ICG) for pancreatic mucinous cysts were compared to pathologic diagnoses or repeat abdominal imaging according to clinical surveillance protocol.

Result: HRi were screened and underwent follow-up imaging with EUS and/or MRI every 6-12 months (depending on baseline findings), 293 (85%) familial PC relatives and 50 (15%) mutation carriers were studied, mean age 56.4 (range 22-81), 47% male. Mean follow-up time was 5.1 years (range 0.5-15.1). 13/341 HRi (3.8%) incident PDA and 8/343 (2.3%) incident invasive precursor (IPMNH GD) were detected during routine endoscopy. The device was removed during laparoscopic fundoplication procedure. Two events of gastroaprosis, possibly related to the device requiring hospitalization were reported in one patient.

Conclusion: There was detection of high-grade precursor lesions following baseline screening and resulted in high-grade precursor lesions detected after baseline screening. The long-term clinical outcomes of radiologic surveillance aiming to detect early PDA and high-grade precursor lesions (IPMNH GD and/or PDA) are also not well understood.

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: In our 16-year cohort with long-term surveillance, the incidence of PDAC (5.4%) was unexpectedly elevated but majority of detected cancers were asymptomatic and resectable. Surveillance also detects early stage PanNETs and HPCls. The majority of detected proven malignancies had radiologic progression but more research is needed to improve the selection of patients for surveillance and surgery.

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

Reference

OP330 CLINICAL IMPACT OF ENDOSCOPIC ULTRASONOGRAPHY IMAGING OF CHRONIC PANCREATITIS IN THE PANCREATIC 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 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 fibrosis than patients without EUS-CP findings (atrophy: 72.5% (29/40) vs. 34.5% (10/29), p = 0.003, inflammation: 45.0% (18/40) vs. 20.7% (6/29), p = 0.04).

Conclusion: In IPMN patients, detection of EUS-CP findings in the background pancreatic parenchyma was associated with a higher prevalence of invasive IPMC. Accordingly, EUS examination should not only assess the morphological features of the lesion itself, but also EUS-CP findings in the background parenchyma.

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

OP331 NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY (nCLE) FOR THE DIAGNOSIS OF SOLITARY PANCREATIC CYSTS: A PROSPECTIVE MULTICENTER STUDY

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Introduction: The diagnosis of solitary pancreatic cyst is clinically challenging due to the malignant potential of several cyst subtypes. nCLE is emerging as a powerful diagnostic tool. This large prospective study validates the 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 malignant lesions (ML, NEN), the nCLE procedure would significantly 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. Napoléon: Dr. Napoléon 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; 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; personal fees from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work.
B. Pujol: Dr. Pujol reports non financial support from Mauna Kea Technologies; personal fees from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work.
A.I. Lemaistre: Dr. Lemaistre reports personal fees from Mauna Kea Technologies, outside the submitted work.
M. Giovannini: Dr. Giovannini reports non financial support from Mauna Kea Technologies, Grants from Mauna Kea Technologies, during the conduct of the study.

References

OP332 RISK OF PROGRESSION AMONG LOW RISK IPMNs IN A LARGE MULTICENTER SURVEILLANCE COHORT STUDY

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Introduction: Intraductal papillary mucinous neoplasms (IPMNs) are pancreatic cysts that carry a risk of malignant transformation to pancreatic ductal adenocarcinoma (PDAC). Guidelines have been evolving to best identify which criteria should qualify a patient for resection and which cysts can safely remain under surveillance.
surveillance. Our aim was to understand which baseline cyst and patient features predict disease progression and malignant transformation.

**Aims & Methods:** Patients with clinically suspected IPMN who did not meet consensus criteria for resection at diagnosis and were surveyed for at least 12 months or underwent surgery after a minimum surveillance of 3 months were included. All patients evaluated by radiologic studies or endoscopic ultrasound between 1998 and 2015 were included. We defined progression as either an increase in size of the dominant cyst ≥20% or ≥2 mm or the development of worrisome features (mural nodule or mass, thick septations, main duct involvement or high grade dysplasia or cancer on cytology or surgical pathology). Statistical analysis was performed with the Chi square and Fisher exact tests for categorical variables and Mann-Whitney U test for continuous variables. All covariates of interest with p < 0.05 in the univariate analysis were included in the logistic regression model.

**Result:**

<table>
<thead>
<tr>
<th>Non-progressors (n = 248)</th>
<th>Progression by cyst size increase (n = 203)</th>
<th>Progression by development of worrisome features (n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at 1st study, mean (SD)</td>
<td>65.3 (11.3)</td>
<td>66.6 (10.7)</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>95 (38.3%)</td>
<td>80 (39%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, n (%)</td>
<td>174 (86.6%)</td>
<td>152 (74.9%)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>11 (5.5%)</td>
<td>11 (6.2%)</td>
</tr>
<tr>
<td>Asian, n (%)</td>
<td>9 (4.5%)</td>
<td>8 (4.5%)</td>
</tr>
<tr>
<td>Smoker ever, n (%)</td>
<td>100 (43.1%)</td>
<td>86 (44.1%)</td>
</tr>
<tr>
<td>Eth use ever, n (%)</td>
<td>108 (47%)</td>
<td>85 (44.7%)</td>
</tr>
<tr>
<td>CP, n (%)</td>
<td>9 (3.7%)</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>AP, n (%)</td>
<td>18 (7.5%)</td>
<td>10 (5.1%)</td>
</tr>
<tr>
<td>Cancer, n (%)</td>
<td>75 (30.5%)</td>
<td>78 (38.4%)</td>
</tr>
<tr>
<td>Colon, n (%)</td>
<td>3 (1.2%)</td>
<td>4 (2.0%)</td>
</tr>
<tr>
<td>Breast, n (%)</td>
<td>7 (2.8%)</td>
<td>12 (5.9%)</td>
</tr>
<tr>
<td>Prostate, n (%)</td>
<td>6 (2.4%)</td>
<td>12 (5.9%)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>56 (23%)</td>
<td>45 (22.4%)</td>
</tr>
<tr>
<td>Family hx of PDAC, n (%)</td>
<td>22 (9.5%)</td>
<td>21 (11%)</td>
</tr>
<tr>
<td>Baseline symptoms, n (%)</td>
<td>71 (28.6%)</td>
<td>60 (29.3%)</td>
</tr>
<tr>
<td>Abd pain, n (%)</td>
<td>65 (26.2%)</td>
<td>49 (23.9%)</td>
</tr>
<tr>
<td>Weight loss, n (%)</td>
<td>11 (4.4%)</td>
<td>18 (8.8%)</td>
</tr>
<tr>
<td>Jaundice, n (%)</td>
<td>1 (0.4%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Cyst size, mean (SD)</td>
<td>11.8 (6.0)</td>
<td>11.1 (6.4)</td>
</tr>
<tr>
<td>Cyst size 0–1 cm, n (%)</td>
<td>100 (40.3%)</td>
<td>94 (45.9%)</td>
</tr>
<tr>
<td>Cyst size 1–2 cm, n (%)</td>
<td>120 (48.4%)</td>
<td>87 (42.4%)</td>
</tr>
<tr>
<td>Cyst size 2–3 cm, n (%)</td>
<td>28 (11.3%)</td>
<td>24 (11.7%)</td>
</tr>
<tr>
<td>Multilocularity, n (%)</td>
<td>95 (38.3%)</td>
<td>72 (35.1%)</td>
</tr>
</tbody>
</table>

**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.

**OP33 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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**Introduction:** Novel treatment options in locally advanced pancreatic cancer (LAPC), including FOLFIRINOX and irreversible electroporation (IRE) have shown promising survival rates. However, outcomes are heavily influenced by selection bias as most studies were retrospective and excluded patients who did not receive FOLFIRINOX or had progressive disease.

**Aims & Methods:** We aimed to describe outcomes of multimodality treatment with chemotherapy, surgical exploration and IRE in a prospective consecutive LAPC-cohort. Patients with histologically proven LAPC (Dutch guideline: ≥90 arterial and/or >270 venous involvement) were prospectively registered (September 2013–March 2015). After 3 months of chemotherapy (FOLFIRINOX for WHO physical status 0–1 patients, otherwise gemcitabine), restaging was performed by assessing RECIST 1.1-response, resectability, and IRE-eligibility (tumor ≤5 cm, sufficient vascular patency). All patients with non-progressive disease, eligible for IRE proceeded to laparotomy, regardless of resectability. The study was registered with the Dutch trial registry NTR4230.

**Result:** Of 132 consecutive LAPC-patients, 93 (70%) received chemotherpay (59% (FOLFIRINOX). After 3 months, 59 (45%) had non-progressive disease and 36 (27%) were IRE-eligible and underwent laparotomy, resulting in 41 (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 unselcted LAPC-cohorts.

**Disclosure of Interest:** R.C. Martin: Prof. Dr. Martin 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.
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 GLYCAN CYCLASE-C AGONIST, LINACLOTIDE, REDUCES ENDOMETRIOSIS-INDUCED VAGINAL HYPERALGESIA
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Introduction: Local activation of GC-C agonist, is an FDA-approved glycan cyclase-C (GC-C) agonist, for the treatment of Irritable Bowel Syndrome with Constipation (IBS-C) and Chronic Idiopathic Constipation (CIC). Linacotide reverses colonic mechanical hypersensitivity in chronic colonic hypersensitive mice, and reduces noxious signaling in vivo to the spinal cord. Painful Bladder Syndrome/Intestinal 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 as measured by a behavior assay and ex vivo pathways involving visceros-visceral organ cross-talk. We hypothesized that linacotide may be able to similarly reduce visceral pain in other chronic pelvic pain conditions, and tested this hypothesis in a rat model of endometriosis-induced vaginal hyperalgesia.

Aims & Methods: Ovariectomy/One-horned segments of the uterine horns of female Sprague-Dawley rats were surgically removed and 4 pieces of uterine horn tissue/rat were implanted around the mesenteric arteries adjacent to the cecum (endometrium side down). Pelvic organ/tissue permeability was measured by Evans Blue dye plasma extravasation (vascular permeability). The severity of vaginal hyperalgesia was accessed by viscero-motor responses (VMR) to the cecum balloon distention. VMR was recorded by electromyography (EMG) using a wireless telemetry system (telemetric probe was surgically implanted 6 weeks prior to the surgery). Evans Blue dye plasma extravasation (vascular permeability). The severity of endometriosis was assessed by vaginal hyperalgesia and the severity of the inflammation on the cervical and vaginal tissues, and other pelvic organs.

Evans Blue dye plasma extravasation (vascular permeability). The severity of endometriosis-induced vaginal hyperalgesia, and the severity of the inflammation on the cervical and vaginal tissues, and other pelvic organs. Consistent with these findings, expression of GC-C was restricted to the small intestine, and not detected in endometrial cysts and other pelvic organs. Both, acute and chronic oral administration of linacotide (3 ug/kg/day) reduced Evans Blue plasma extravasation in the small intestine compared to vehicle (p < 0.01). In contrast, linacotide did not have an effect on the plasma extravasation of endometrial cysts and other pelvic organs. Consistent with these findings, expression of GC-C was restricted to the small intestine, and not detected in endometrial cysts and other pelvic organs. Both, acute and chronic oral administration of linacotide (3 ug/kg/day) reduced Evans Blue plasma extravasation in the small intestine compared to vehicle (p < 0.01). In contrast, linacotide did not have an effect on the plasma extravasation of endometrial cysts and other pelvic organs.

Result: Chronic oral dosing of linacotide (n = 12) significantly (p < 0.01) reduced Evans Blue plasma extravasation in the small intestine compared to vehicle (n = 12). In contrast, linacotide did not have an effect on the plasma extravasation of endometrial cysts and other pelvic organs. Consistent with these findings, expression of GC-C was restricted to the small intestine, and not detected in endometrial cysts and other pelvic organs. Both, acute and chronic oral administration of linacotide (3 ug/kg/day) reduced Evans Blue plasma extravasation in the small intestine compared to vehicle (p < 0.01). In contrast, linacotide did not have an effect on the plasma extravasation of endometrial cysts and other pelvic organs. Consistent with these findings, expression of GC-C was restricted to the small intestine, and not detected in endometrial cysts and other pelvic organs. Both, acute and chronic oral administration of linacotide (3 ug/kg/day) reduced Evans Blue plasma extravasation in the small intestine compared to vehicle (p < 0.01). In contrast, linacotide did not have an effect on the plasma extravasation of endometrial cysts and other pelvic organs. Consistent with these findings, expression of GC-C was restricted to the small intestine, and not detected in endometrial cysts and other pelvic organs. Both, acute and chronic oral administration of linacotide (3 ug/kg/day) reduced Evans Blue plasma extravasation in the small intestine compared to vehicle (p < 0.01). In contrast, linacotide did not have an effect on the plasma extravasation of endometrial cysts and other pelvic organs. Consistent with these findings, expression of GC-C was restricted to the small intestine, and not detected in endometrial cysts and other pelvic organs.

Conclusion: Oral administration of linacotide significantly reduced visceral pain in a rat model of endometriosis-induced vaginal hyperalgesia. The data 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 innervation pathways.

Disclosure of Interest: P. Ge: Employee, stock holder and stock options from Ironwood Pharmaceuticals Inc.
J. Ren: Consultant at Ironwood Pharmaceuticals, Inc.
N. Dmitrieva: Contractor at Ironwood Pharmaceuticals, Inc.
A. Silos-Santiago: Employee, stock holder and stock options from Ironwood Pharmaceuticals Inc and Decibel Therapeutics.
C. B. Kurtz: Employee, stock holder and stock options from Ironwood Pharmaceuticals Inc.
G. Hannig: Employee, stock holder and stock options from Ironwood Pharmaceuticals Inc.

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Introduction: Local activation of GC-C agonist, is an FDA-approved glycan cyclase-C (GC-C) agonist, for the treatment of 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 hypersensitivity through alterations in the GC-C/cGMP signalling pathway across different subtypes of IBS patients from the Australian population, have been shown. However, it remains to be determined if these changes extend to 1) other components of this pathway, 2) a separate U.S. cohort of IBS patients, and 3) patients with chronic idiopathic constipation (CIC).

Aims & Methods: Female Rome III IBS and CIC patients and healthy controls aged 18-75 yrs were recruited mainly by community advertising in the U.S. and Canada. Recto-sigmoid mucosal biopsies were taken at 30 cm from the anal verge during sigmoidoscopy. RNA was extracted from all biopsies and Taqman qRT-PCR was used to assess mRNA expression of 18 different known components of the GC-C/GMP signalling pathway. These targets included GC-C (GUCY2C), its endogenous ligands (GUCYA2A, GUCYA2B), PDZ proteins regulating GC-C activity (PDZD3), cGMP-dependent protein kinases (PRKG2), phosphodiesterases (PDE3A, PDE3B), components involved in ionic sequestration (PDZK1, SLC29A1, SLC26A3, SLC26A4, CFTR) and transporters of cGMP (ABCC1, ABCC4).

Result: We compared female healthy controls (N = 12, mean age 36.4 yrs) with IBS patients with constipation (N = 12, mean age 32.8 yrs), diarrhea (IBS-D; N = 11, mean age 30.7 yrs), mixed bowel habits (IBS-M; N = 10, mean age 30.7 yrs), and patients with chronic idiopathic constipation (CIC; N = 12, mean age 30.7 yrs). In IBS-C biopsies GC-C expression was significantly reduced (2-fold reduction) compared with biopsies from healthy controls (p < 0.05). However, in these IBS-C biopsies none of the other GC-C/GMP pathway components were significantly altered compared with healthy controls (P > 0.05). In contrast, biopsies from CIC patients did not display significant alterations in GC-C or the other GC-C/ cGMP pathway components compared with healthy controls (P > 0.05).

Similarly, biopsies from IBS-D and IBS-M patients did not display any significant differences in the GC-C/ cGMP pathway components compared with healthy controls (P > 0.05). Conclusion: In this cohort of female IBS-C patients, GC-C, but not other evaluated components of the GC-C/GMP pathway were significantly reduced. A lack of GC-C expression in these patients may result in a lack of cGMP production and subsequent alteration of the GC-C/cGMP signalling pathway compared with healthy controls. Given these changes were apparent in IBS-C but not in CIC, IBS-D or IBS-M patients, these changes may help to explain some aspects of the pathophysiology associated with IBS-C.

Disclosure of Interest: 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.
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 (including GI endoscopists, colorectal surgeons) and general practitioners (GPs) in the UK. Symptoms considered important in diagnosing constipation and their perceived burden, together with 10 case studies based on the Rome III criteria were investigated. Responses were compared between groups using chi-squared tests.

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</th>
<th>With GI constipation</th>
<th>Constipation specialists</th>
<th>GPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrequent bowel movements</td>
<td>28%</td>
<td>26%</td>
<td>65%</td>
<td>41%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hard stool</td>
<td>26%</td>
<td>32%</td>
<td>57%</td>
<td>66%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Straining</td>
<td>43%</td>
<td>40%</td>
<td>53%</td>
<td>61%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sense of incomplete evacuation</td>
<td>15%</td>
<td>24%</td>
<td>21%</td>
<td>13%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Manual disinhibition</td>
<td>14%</td>
<td>15%</td>
<td>32%</td>
<td>34%</td>
<td>&lt;0.001</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%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laxative use</td>
<td>37%</td>
<td>33%</td>
<td>56%</td>
<td>40%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The symptoms most frequently considered to be bothersome were different for each of the groups: manual disinhibition 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-define current diagnostic criteria for constipation in clinical practice and to ensure these are communicated widely.

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

OP338 EFFICACY AND SAFETY OF NALDEMEDINE FOR THE TREATMENT OF OPIOID-INDUCED CONSTIPATION IN SUBJECTS WITH CHRONIC NON-CANCER PAIN RECEIVING OPIOID THERAPY: RESULTS FROM TWO PHASE 3 CLINICAL TRIALS

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Introduction: Opioids effectively treat pain but their use is limited by side effects including opioid-induced constipation (OIC). Naldemedine is an oral, peripherally-acting 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 NCT01965158 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 < 0.001; Study 2: naldemedine 52.5%; placebo 33.6%, P < 0.001). The naldemedine group 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 by >5% of subjects and at a higher frequency in naldemedine relative to placebo were abdominal pain and diarrhea. In both studies, treatment with naldemedine was not associated with signs or symptoms of opioid withdrawal, and the analgesic effect of opioids was not affected.

Conclusion: Results from two identically designed Phase 3 studies demonstrated a consistent efficacy and safety profile of naldemedine as a treatment for OIC in subjects with chronic non-cancer pain. Naldemedine treatment resulted in a significantly greater proportion of responders than placebo, with improvement early on and throughout the 12-week study period. Naldemedine was generally well tolerated in these two studies.

Disclosure of Interest: M.E. Hale: I was a Principle Investigator for the Clinical Trials, and a consultant for Shionogi
J. Wild: 1) I was a Principal Investigator on Composel trial and 2) I did receive a stipend from Shionogi for clinical study review. Otherwise I have no relationship with the company.
J. Reddy: Employee of Shionogi
T. Yamada: Employee of Shionogi
J.C. Arjona Ferreira: Employee of Shionogi

OP339 PILOT STUDY COMPARING THREE METHODS OF SCREENING FOR FECAL INCONTINENCE

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Introduction: Fecal incontinence (FI) affects 8% of US adults overall including 15% over age 70. However, less than 1/3 of people with FI have discussed this problem with their physicians, and most of these 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 nurses and providers, we suggested three screening questions. We also gave
and incontinence pads (21/182, 13%). Individuals who had consulted a physician, coping strategies reported to be most effective were antidiarrheal medications status (3.32 for non-consulters vs. 4.28 for consulters, \( p < .017 \)). Only 43/182 (24%) reported that their coping burden was as effective as direct screening by the geriatrician. However, these interventions to improve screening were only partially effective: 37.5% of patients remained being asked about FI at their clinic visit.

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

**OP340 COPING WITH FAECAL INCONTINENCE: A POPULATION STUDY**

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**Introduction:** Faecal incontinence (FI) is a common and devastating condition that affects quality of life. Many individuals suffer in silence and population surveys report that fewer than 30% of those affected consult a physician. Little is known about how people prevent or cope with symptoms in the community.

**Aims & Methods:** This study aimed to describe the most common coping strategies, the impact of FI severity on ways of coping, whether those under a physician's care differ from non-consulters, and the severity of the symptoms on the quality of life.

**Result:** A total of 254 complete datasets were received, of which 182 (122 F, 56% vs. 56 M, 44%; mean age 41, range 18–86) were retained for analysis after eliminating incomplete and 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 6.8% 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. The most effective ways of coping were medication and scheduling of bowel movements (88/182, 49%), the use of anti-diarrheal medications (61/182, 33%), and instructions on how to refer to the GI Medicine Clinic.

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

**OP341 NOVEL ENDOLOOP VS. OVER-THE-SCOPE-CLIP (OTSC) IN ENDOSCOPIC CLOSURE OF GASTRIC FULL-THICKNESS DEFECT: A MULTI-CENTER STUDY**

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**Introduction:** Endoscopic full-thickness resection (EFTR) of the gastric lesion using a snaring technique has been applied for gastric subepithelial tumors. We identified criteria for the use of a novel type of nylon loop device vs. traditional 'Over the scope'-clip (OTSC) for containing artificial submucosal lesions.

**Aims & Methods:** One hundred and twenty-eight patients with submucosal tumors in gastric fundus were randomly divided into two groups, study group with 56 patients and control group with 72 patients, all patients were treated with endoscopic full-thickness resection. After the resection, novel LeCtampTM endo-device and OTSC were used respectively to close the gastric defects in the study group and control group. The closure success rate, closure time, complications and the wound-healing rate were compared.

**Result:** All lesions were removed by using EFTR technique. The closure success rates of the two groups were both 100%. Of the total of 128 patients, a comparison between the novel endoloop (n=56) and OTSC (n=72) groups demonstrated no differences in closure time (14.86±4.93 vs. 8.04±5.63 min, \( p > 0.05 \)) and reanimation rate (17.63% vs. 18.2%, \( p > 0.05 \)). The average time of removing the stomach tube in the study group was slightly longer (4.3 days vs. 1 day, \( p < 0.05 \)), and there was a significant differences in the length of hospital stay for the study group (4.32±2.45 vs. 2.1±0.63 days). 24 hours after the operation, X-ray examination showed minor subdiaphragmatic free air. Due to its low quantities and lack of symptoms, abdominal puncture was deemed unnecessary. No subcutaneous emphysema, pneumothorax, pneumomediastinum were found in 24 hours after the operations. There were no significant differences in the incidence and severity of complications rate, even though all patients experienced no postoperative complications such as bleeding, perforation and abdominal infection in control group. However one case receiving treatment of endoloop that induced localized peritonitis resulted in seosal inflammation. The patient was managed conservatively with medical therapy, such as the administration of intravenous fluids and broad-spectrum parenteral antibiotics to cover the colonic bacterial flora until the symptoms subsided. All wounds healed in two month after the operations.

**Conclusion:** Closure of gastric full-thickness defects with the novel type of endoloop device is technically feasible and effective. Both techniques should be regarded as equally acceptable reconstructive options following endoscopic full-thickness resection for gastric ulcer.

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

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References


OP343 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR DUODENAL ADENOMA: COMPLICATION RATE AND FOLLOW UP OF 38 CASES W. Margos1, H. Ivekovic2, R.C.P. Yeung3, L. Shaza4, H. Pisseaux1, P. Degraeve5
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Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are used for endoscopic treatment of superficial duodenal adenoma. Aims and Methods: In a single tertiary center, we cross-examined our database of endoscopic procedures to identify patients with duodenal adenoma treated by EMR, ESD and EMR between 2006 and 2016. We included patients with non- ampullary lesions and familial adenomatous polyposis. Procedure was classified as ESD when an endoscopic knife was used. When resection was achieved with an endoscopic knife and resection loop, the procedure was considered as HER. We divided complications in 3 groups (ASGE and ESGE recommendations): intra- procedural, early complications (occurring within 15 days) and late complications (occurring after 15 days). Results were expressed as means, 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 findings showed 45 adenocarcinomas, 34% HGD, and 60% LGD. No significant differences were observed in terms of age, sex, location of lesions or length of hospitalisation.

There were no significant differences in the procedure time (108 min ESD/HER, 79 min EMR), intra-procedural complications (46% ESD/HER, 23% EMR) and early complications (23% ESD/HER, 9% EMR). Intra-procedural complications occurred in 46% of ESD/HER vs 23% in EMR (p=0.015), including haemorrhage (25.6%, 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 treatment-related 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 highlights 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.

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Introduction: Gastric antral vascular ectasia (GAVE) represents a burden both to the healthcare system and the patients’ quality of life as the rate of transfusion dependence due to occult bleeding may be up to 60–70%. Currently,argon plasma coagulation (APC) is the gold standard treatment, however its efficacy impacts on the long term. Besides, its efficiency depends on the settings, the size of the area treated, as well as the individual variations in performance. Endoscopic band ligation (EBL) has been proven to be a good and a potentially superior alternative with less variability in the treatment of mucosal and submu- cosal lesions. Nevertheless, there is still no consensus regarding the end-point of the treatment (cessation of the endoscopic lesions or resolution of transfusion need). The optimal treatment duration and the preferable treatment settings are still unknown.

Aims and Methods: Our retrospective multicentre study aimed to evaluate and compare the efficacy of APC and EBL in patients with GAVE both in terms of required treatment sessions and hospitalization rates, and changes in haemo- globin levels and transfusion need. EBL was performed using a 4.5-mm ligation device, and the haemostasis was secured by a polypectomy snare. In case of APC, 5–6 or 7–8 band applications were performed per treatment session. The average follow-up period was 18.3 months.

Results: A total of 34 patients with GAVE were treated with either APC or EBL at one of the four centres involved throughout the study period. 26 patients presented with diffuse and 8 with linear type of GAVE. Occult gastrointestinal bleeding was present in 6 cases. 22 patients were treated with APC or EBL. Both acute and occult gastrointestinal bleeding was present in 6 cases. 22 patients were treated with APC and 12 with EBL. Both treatment methods increased haemoglobin levels and decreased transfusion need significantly (3.01 g/dl and 2.24 g/dl blood units in APC and 2.14 g/dl and 2.41 g/dl blood units in EBL). The need for blood transfusions ceased totally in 18 patients after the endoscopic resolution of the lesions. Significantly less treatment sessions were required in case of EBL compared to APC (1.50 vs. 5.23, p=0.011), with a longer interval between each session (4.50 vs. 2.69 months, p=0.480). On the other hand, APC resulted in a higher increase in haemoglobin levels (3.37 g/dl vs. 2.36 g/dl, p=0.213) and a higher decrease in the need for blood transfusion (10.41 vs. 7.78 units, p=0.566), although the differences were not significant. In case of APC, fewer treatments (4.25) and hospitalizations (2.33) were needed, and higher increase in haemoglobin level per treatment session (0.76 g/dl) could be observed with the 50 W power setting compared to the 30 W and 70 W setting (number of treat- ment sessions: 12.5 and 6.1, hospitalizations: 2.5 and 4.6, and increase in haemoglobin level/treatment session: 0.38 g/dl and 0.46 g/dl), although the small case number was a severe limiting factor. Generally, more treatment sessions were required for the endoscopic resolution of GAVE lesions compared to the one needed for the cessation of the transfusion need (4.35 vs. 3.037), but the difference was not significant in case of APC and EBL separately.

Conclusion: Both APC and EBL are effective in the treatment of GAVE. Although EBL may seem to be superior to APC in terms of the number of treatment sessions and hospitalizations, no significant difference was found in the extent to which the two methods influence the haemoglobin level and transfusion need. Optimizing APC setups may also improve the performance and efficacy. There is a pressing need for further prospective studies with homoge- neous large case number to establish recommendations about the endoscopic treatment of GAVE.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: Water pressures of 30–70 bar were tested to determine the porcine esophagus.

Results: Using 50 bar of water pressure resulted in the best balance between dissection speed and view-disturbing water buckflow. The dissection speeds for the lower, middle, and upper esophagus were 0.2, 0.9, and 0.2 cm²/min in 50 bar WJ-ESD and 1.1, 0.5, and 1.0 cm²/min in C-ESD, respectively. Minor bleeding

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

References


Phenotypically, HPCs express both markers of (immature) hepatocytes (e.g. Hepatic progenitor cells (HPCs) are small cells with a relative large poorly understood.

Mechanisms facilitating proliferation and differentiation of human HPCs are still based on human liver tissue was collected from alcoholic steatohepatitis explant livers, and methods: side population (SP), TROP-2 and EpCAM-based cell sorting. Fresh enriched cell populations from adult human liver tissue using different isolation Therefore we isolated and compared, on both protein and RNA level, HPC-control their activation and differentiation in vivo in chronic liver diseases.

Aims & Methods: Our results indicate that gene signatures of human HPCs are enriched in pathways already known to be involved in HPC activation in human and in animal models, but we also identify previously unknown pathways like TNF, IL17A and ErbB signalling pathways. 

Conclusion: Gene signatures of human HPCs are enriched in pathways already known to be involved in HPC activation in human and in animal models, but we also identify previously unknown pathways like TNF, IL17A and ErbB signalling pathways. 

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

References

OP348 SORTILIN DEFICIENCY REDUCES DUCTULAR REACTION, HEPATOCYTE APOPTOSIS AND LIVER FIBROSIS IN CHOLESTATIC-INDUCED LIVER INJURY
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Introduction: Sortilin, a member of the Vps10 domain receptor family, traffics newly synthesized proteins from the trans-Golgi network to secretory pathways, endosomes or to the cell surface. Sortilin trafficked molecules, including acid sphingomyelinase (aSMase), cathepsins and IL-6, mediate activation of hepatic stellate cells (HSC), hepatocyte apoptosis, cholangiocyte proliferation and liver inflammation and fibrosis.

Aims & Methods: We investigated sortilin role in the development of biliary damage leading to hepatocellular injury and fibrosis, based on its regulation of aSMase trafficking and on its involvement in IL-6 secretion. Cholestatic injury was induced in wild type (WT) and Sortilin-/- mice by bile duct ligation (BDL). Fibrosis was induced both by BDL and by administration of CCL4. Liver inflammation and cholangiocyte activation and proliferation were assessed by qRT-PCR for inflammatory cytokines and by immunohistochemistry with Ki67 (marker of proliferation) and with 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 amitriptyline administration. IL-6 effects was neutralized by administration of an anti-HL antibody to WT mice before BDL.

Results: Sortilin-/- mice displayed strongly attenuated liver fibrosis following BDL and CCl4 treatment, accompanied by an attenuated in vitro activation phenotype of Sortilin-/- HSCs. Reduced Sortilin-/- hepatic aSMase activity was in line with reduced hepatocyte apoptosis following BDL and CCl4 injury and reduced susceptibility of hepatocytes from Sortilin-/- mice to bile acid-induced apoptosis in vitro. The role of aSMase in hepatic apoptosis was further demonstrated using in vivo pharmacological inhibition of aSMase activity after BDL. Strikingly, Sortilin-/- mice displayed impaired inflammation and ductular reaction three days after BDL, demonstrated by reduced reactive cholangiocytes, reduced cholangiocyte proliferation and accompanied by reduced serum IL-6. 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: Sortilin mediates cholestatic liver damage and fibrosis via its effects on aSMase activity and secretion.

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

OP349 ACTIVATION OF NECROTOPSIS IN HUMAN AND EXPERIMENTAL CHOLESTITIS
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Introduction: Targeting necrosis, a programmed necrotic cell death pathway regulated by receptor-interacting protein 3 (RIP3), is being considered as a pro-fibrogenic cell death, which characterizes inflammation-driven liver diseases. Still, the role of necrosis in liver disease is not fully understood. We aimed to explore the expression of membrane markers EpCAM and TROP-2 in HPCs. Human liver was dissociated and the cell suspension was analysed and separated by FACS. The sorted cells and the whole liver extracts were evaluated on both protein level (immunohistochemical staining) and RNA level (RNA sequencing). Pathway analysis was performed using KEGG pathways, Ingenuity Pathway Analysis and Gene Set Enrichment Analysis.

Results: Immunohistochemical evaluation of the isolated fractions indicated the enrichment of HPCs in the SP, EpCAM-positive and TROP-2-positive cell fractions. Pathway analysis of the RNA sequencing data from the different isolated HPC fractions shows an enrichment and activation of known HPC pathways like Wnt/b-catenin and Notch pathways, known for their role in proliferation and differentiation of HPCs. In addition we identified several novel pathways activated in human HPC-enriched cells such as the TNF and IL17A pathways.

Conclusion: Our results indicate that gene signatures of human HPCs are enriched in pathways already known to be involved in HPC activation in human and in animal models, but we also identify previously unknown pathways like TNF, IL17A and ErbB signalling pathways. 

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

OP347 CHARACTERISATION OF DIFFERENTLY ISOLATED HEPATIC PROGENITOR CELL POPULATIONS IN HUMAN ALCOHOLIC LIVER
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Disclosure of Interest: All authors have declared no conflicts of interest.

References
of necrosis in the pathogenesis of cholestatic liver injury has been poorly understood. We previously demonstrated that transcription factor CCAAT-enhancer binding protein b (C/EBPβ) knockdown. In a complementary experiment, we found that CCRK-deletion in hepatocytes decreased MDSC expansion as shown by IL-6 rescue and antibody neutralization experiments. Given these results, we conclude that CCRK targeted negative regulators of tumor necroptosis, including RIP3 expression and activity and bile acid toxicity was established in RIP3-deficient primary hepatic cells. This RIP3 activation was also observed in the murine model of cholestasis. These findings strongly support the notion that targeting RIP3 signaling may provide a therapeutic strategy for the prevention and treatment of liver fibrosis.

Conclusion: This project was supported by the University Grants Committee through the Collaborative Research Fund (C4014/14G) and the Health and Medical Research Fund (63141376).

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

References

OP350 HEPATOMA-INTRINSIC CCRK SIGNALING PROMOTES IMMUNOSUPPRESSIVE TUMOR MICROENVIRONMENT BY REGULATING MYELOID-DERIVED SUPPRESSOR CELL ACCUMULATION

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Introduction: Myeloid-derived suppressor cells (MDSCs) comprise a heterogeneous population of immature myeloid cells that induces the exhaustion of antitumor T cells. The accumulation of CD11b+CD33+ monocytic population of immature myeloid cells that induces the exhaustion of peripheral blood mononuclear cells (PBMCs) with CCRK-over-expressing immunological role in the pathogenesis of immune-mediated inflammatory diseases. The accumulation of CD33+CD11b+HLA-DR-MDSCs in circulation. Moreover, co-culture of human peripheral blood mononuclear cells (PBMCs) with CCRK-over-expressing immortalized hepatocytes and HCC cells induced the accumulation of MDSCs. The CCRK-induced MDSCs possessed immigration properties by inhibiting T cell proliferation and interferon γ expression (IFN-γ). In contrast, knockdown of CCRK in hepatoma cells reduced the expansion and immune suppression of MDSCs. Using a Hepa-1 immortalized hcc cell model in immune-competent C57BL/6J mice, we demonstrated that CCRK deletion significantly decreased hepatic tumorigenicity and the levels of circulating and tumor-infiltrating MDSCs as well as their T cell suppressive functions. Notably, adoptive transfer of MDSCs rescued the effects of CCRK knockdown. In a complementary experiment, we found that MDSC depletion by specific IAB significantly reduced CCRK-induced liver necrosis. Cytokine profiling analysis revealed that CCRK significantly induced hepatocellular interferon-6 (IL-6) expression and production, which mediated MDSC expansion as shown by IL-6 rescue and antibody neutralization experiments. Moreover, transgenic studies demonstrated that CCRK triggered nuclear factor-kappa B (NF-κB) signaling in an enhancer of zeste homolog 2 (EZH2)-dependent manner. Simultaneously, the phosphorylation of NF-κB by CCRK facilitated the co-occupancy of IL-6 promoter by NF-κB/EZH2 complex for transcriptional activation.

Conclusion: As we also showed elevation of CD33+CD11b+HLA-DR-MDSCs and concordant over-expression of CCRK/EZH2/NF-κB/IL-6 signaling in human HCCs, our results uncover CCRK to be a critical immune regulator to promote tumor growth and angiogenesis in human HCCs, our results uncover CCRK to be a critical immune regulator to promote tumor growth and angiogenesis. This work was supported by the University Grants Committee through the Collaborative Research Fund C4017-14G and the Health and Medical Research Fund (63141376).

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

References

OP351 PROTECTIVE ROLE OF SPECIFIC PATHOGEN FREE MICROBIOTA IN BILE DUCT Ligated AND CCL4 MICE

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Introduction: In chronic liver disease the presence of gut-derived bacterial products and the resultant increase in inflammatory cytokines in the splanchic and systemic circulation may contribute to the progression of fibrosis. However, the composition of the intestinal microbiota and the host-microbe interaction in the composition of the intestinal microbiota and the host-microbe interaction in the development of liver fibrosis remains largely unknown. We hypothesized that fibrosis would be attenuated in a gnotobiotic model of limited intestinal colonization (altered Schaedler flora, ASF) compared to a more complex colonization system. Recent studies have shown that dysbiosis may contribute to the progression of liver fibrosis. However, the composition of the intestinal microbiota and the host-microbe interaction in the development of liver fibrosis remains largely unknown. We hypothesized that fibrosis would be attenuated in a gnotobiotic model of limited intestinal colonization (altered Schaedler flora, ASF) compared to a more complex colonization system. Recent studies have shown that dysbiosis may contribute to the progression of liver fibrosis.

Alternatively, ASF mice (ASF-BDL) exhibited greater bile duct hyperplasia, multifocal necrosis, fibrosis and inflammation. Concomitantly, necrosis was activated as evidenced by increased RIP3 expression and activity and sequestration of RIP3 and MLKL in the mitochondria 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 hepatocytes. The activity of bile acid hydroxylation and 7alpha activity increased 14 days after BDL in both WT and RIP3+ mice, while remaining at basal levels at day 3, indicating that apoptosis is activated at late time-points in the BDL murine model, reflecting the peak of liver fibrosis.

Conclusion: In conclusion, necrosis is triggered in BDL patients and mediates hepatic necroinflammation in BDL-induced cholestasis. Targeting necrosis 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 HSMSP/ICT/0018/2011, SFRH/BD/91192/2012, SFRH/BD/88212/2012 and SFRH/BD/104160/2014, FCT, Portugal).

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

All authors have declared no conflicts of interest.

AFS shBM AF4 shBM AFS AF4 CCL4 AFS+ CCL4 AF4+ CCL4

OPP cmH2O 8.4 11.8** 7.2 9.7* 8.5 12.2** 7.4 10.4* * p < 0.05 ** p < 0.005 *** p < 0.0005 Bacterial translocation was significantly higher in ASF mice (ASF-BDL 13.5% vs. SPF-BDL 4.8% 0.05 ** p < 0.005). In contrast, knockdown of CCRK in hepatic cells was significantly expressed by increased hepatocellular interferon-6 (IL-6) expression and production, which mediated MDSC expansion as shown by IL-6 rescue and antibody neutralization experiments. Moreover, transgenic studies demonstrated that CCRK triggered nuclear factor-kappa B (NF-κB) signaling in an enhancer of zeste homolog 2 (EZH2)-dependent manner. Simultaneously, the phosphorylation of NF-κB by CCRK facilitated the co-occupancy of IL-6 promoter by NF-κB/EZH2 complex for transcriptional activation. Cytokine profiling analysis revealed that CCRK significantly induced hepatocellular interferon-6 (IL-6) expression and production, which mediated MDSC expansion as shown by IL-6 rescue and antibody neutralization experiments. Moreover, transgenic studies demonstrated that CCRK triggered nuclear factor-kappa B (NF-κB) signaling in an enhancer of zeste homolog 2 (EZH2)-dependent manner. Simultaneously, the phosphorylation of NF-κB by CCRK facilitated the co-occupancy of IL-6 promoter by NF-κB/EZH2 complex for transcriptional activation.
OP52 IMPROVING METABOLIC PARAMETERS IN NAFLD BY TARGETING NUCLEAR RECEPTORS

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

References

OP53 AN AUTOMMUNITY-ASSOCIATED VARIANT IN PTTPN22 PROTECTS FROM DISEASE ONSET IN MOUSE MODELS OF COLITIS


Introduction: The recognition of intestinal microbiota is in part carried out by toll-like receptors (TLR), which are responsible for initiating the innate immune response. Alterations in the intestinal microbiota and its recognition may contribute to the development of intestinal inflammatory pathologies. Otherwise, hydrogen sulphide (H2S) is an endogenous gaseous signalling molecule and it potentially plays a relevant role in the intestinal motility. In mammals, two pyridoxalphosphate-dependent enzymes are responsible for H2S synthesis: cystathionine β-synthase (CBS) and cystathionine γ-lyase (CSE).

Aims & Methods: The aim of our study was to investigate the influence of TLR2 abrogation in mouse models of colitis.

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

WEDNESDAY, OCTOBER 19, 2016 08:30–10:00

MURINE MODELS OF INTESTINAL INFLAMMATION – ROOM 1.86

OP54 TOLL LIKE RECEPTOR 2 MODULATES THE INHIBITORY MOTOR RESPONSE INDUCED BY HYDROGEN SULPHIDE IN MOUSE COLON

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

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Disclosure of Interest: All authors have declared no conflicts of interest.
regulates the expression of CBS and modulates the inhibitory motor response induced by colonic distention.

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

References

HPLC system measuring the degradation rate of endorphin-2 (EM2, natural DPP IV substrate) in the presence of EMDB-1. The inhibitory activity of EMDB-1 was investigated in the model of acute and semi-chronic colitis induced by trinitrobenzenesulfonic acid (TNBS). Body weight, macroscopic score, ulcer score, colon length and thickness, as well as myeloperoxidase (MPO) activity were recorded. The selective COX-2 inhibitor was used as control.

Results: EMDB-1 is a potent and specific DPP IV inhibitor as shown by significantly decreased degradation rate of EM2 by DPP IV (t½ = 1.73 vs. 3.60 min in the absence and the presence of EMDB-1, respectively). The intracolonic (i.c.) administration of EMDB-1 (0.1, 1 and 3mg/kg, twice daily) attenuated both acute and semi-chronic TNBS-induced colitis in mice in a dose-dependent manner, as indicated by significantly reduced macroscopic parameters and MPO activity. Anti-inflammatory effect of EMDB-1 was not blocked by naloxone, thus the opioid receptors were not involved in its mechanism of action.

Conclusion: EMDB-1 is a potent inhibitor of DPP IV in vitro and exhibits substantial anti-inflammatory activity in the GI tract in vivo. Results of this study validate the EMDB-1 backbone for further development of peptide DPP IV inhibitors and suggest its use in the treatment of colitis.

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

Supported from grants from the Medical University of Lodz [502-13-156/04-03-04-03-01 to J.F.] and National Science Centre [No. UMO-2013/11/N/ZK7/02354 to M.S. No. UMO-2013/11/B/NZT/01301 and No. UMO-2014/13/B/04/N/01179 to J.F.]

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Introduction: Biologics targeting inflammatory cytokines has reveal a new era in intestinal inflammatory disease. Direct blockade of HMGB1 could be protective against intestinal inflammation.

Aims & Methods: Potential role of anti-HMGB1 neutralizing antibody (HnAb) in inhibiting intestinal inflammation and the underlying mechanism is investigated in DSS-induced mice colitis (DSS-C) models. 200μg HnAb was administrated intraperitoneally to DSS-C at d0, d3 and d6 in HnAb group, whereas 200μg anti-ILP-5 (ILP-5-CSS or DSS-C) group or normal control (ctrl) group. Colon shortening, disease activity index (DAI), histological score of colitis (HS), MPO activity and inflammatory cytokines were evaluated to determine the colonic inflammation severity. Mucosa barrier function was assessed by immuno- fluorescent staining of mucus layer (mucin2) and tight-junction (T-J) protein expression. qRT-PCR was performed to assess the extent of colitis.

Results: Treatment with HnAb significantly suppressed colonic inflammation in DSS-C mice by improving colon shortening (6.2±0.4 cm vs. 5.3±0.5 cm, p < 0.05), DAI (2.7±0.5 vs. 3.7±0.3, p < 0.05) and HS (6.0±0.2 vs. 9.0±1.0, p < 0.05) in ctrl group. Besides, MPO activity (2.6±0.8 vs. 4.8±1.0, p < 0.05) and TNF-α (1.61±0.5 vs. 3.04±1.1, p < 0.05), IFN-γ (2.14±0.6 vs. 7.87±0.21, p < 0.05) and IL-1β (1.53±0.10 vs. 2.48±0.04, p < 0.05) mRNA expression was decreased when treated with HnAb as compared to DSS-C group (p < 0.05). Relatively intact mucus layer was seen in mice colon of HnAb group as compared to DSS-C group. Significantly higher expression of tight-junction protein ZO-1 (0.38±0.01 vs. 1.15±0.05, p < 0.0001), claudin-5 (0.37±0.07 vs. 0.30±0.06, p < 0.0001) and occludin (0.85±0.09 vs. 0.39±0.31, p < 0.0001) was detected in HnAb mice as compared to mice in DSS-C group. Interestingly, colonic HMGB1 protein in both nucleus (0.58±0.02 vs. 0.79±0.03, p < 0.0001) and cytoplasm (0.23±0.01 vs. 0.06±0.01, p < 0.0001) were significantly decreased, while IFN-γ was increased. In vitro, treatment with HnAb alone as compared to DSS-C, suggesting that primary inhibition of HMGB1 by HnAb blocked sequential HMGB1 formation and release. Lastly, TLR4 (0.31±0.03 vs. 0.77±0.08, p < 0.0001) and MyD88 (0.30±0.03 vs. 0.78±0.01, p < 0.0001) protein was significantly reduced in HnAb group than mice in DSS-C group though MyD88 mRNA was relatively higher in HnAb group than DSS-C group (0.69±0.04 vs. 0.38±0.01, p < 0.05).

Conclusion: Administration of HnAb ameliorated DSS-C by suppressing inflammation and strengthening mucosa barrier function possibly through inhibition of HMGB1-TLR4-MyD88 pathway, suggesting a potential functional intention of HMGB1 in ulcerative colitis treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: The adaptive immune system plays a crucial role in the pathogenesis of inflammatory bowel diseases (IBD). The adaptive component 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 adoptive transfer colitis model. Naïve T-cells (CD4+CD25-) from WT and TDAG8-/- donor mice, were intraperitoneally injected. 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 infiltration and crypt damage in the WT group. The TDAG8-/- group displayed significantly less histopathological signs of colitis in comparison to PBS and WT groups. CD3+ and IL-17A immunoreactive cells were rarely detected in colonic tissue of TDAG8-/- in comparison to the WT group. Quantification of mRNA expression of pro-inflammatory cytokines (IFNγ, 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, RORC 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

OP359 TRANSMURAL MICROSCOPIC SURGERY VERSUS ENDOSCOPIC MUCOSAL RESSECTION FOR LARGE RECTAL ADENOMAS (MEDISUD)


Aims & Methods: The aim of this study is to clarify the short-term outcomes of NEWS for gastric tumors. Between July 2011 and March 2016, 26 patients (9 females, 17 males; mean age 65.9 years, range 49–85 years) underwent NEWS for gastric tumors. After marking around a tumor on both the mucosal and serosal surfaces and submucosal injection of sodium hyaluronate, circumferential seromuscular suturing were made laparoscopically, followed by circumferential mucosubmucosal incision endoscopically. The resected specimen was then retrieved.

Results: The mean tumor size and resected specimen were 23.3 mm (range, 7–45 mm) and 36.1 mm (range, 20–66 mm), respectively. All lesions were curatively resected in an en-bloc fashion. The operation time was 219.0 minutes (range, 198–397 minutes), and the median estimated blood loss was 0 g (range, 0–250 g). Patients started oral intake on mean postoperative day 3.1 (range, 2–4), and the mean length of postoperative hospital stay was 8.2 days (range, 6–14 days). There were no severe postoperative complications. Histopathological examination of the tumors showed 21 GISTs, 1 schwannoma and 4 early gastric cancer. No tumor residual or recurrences was confirmed by performing gastroscopy and the mean body weight loss was 2.5 kg (range, –3.2–10.9 kg) during a median follow-up of 11 months (range, 0.37–67 months).

Conclusion: NEWS is an effective full-thickness resection with minimum possible margin without contamination and tumor dissemination into the peritoneal cavity, considering the quality of life of patients. NEWS could be utilized as a novel treatment option especially for node-negative EGC difficult to resect by ESD, or EGC with possible lymph node metastasis with a combination of sentinel node navigation surgery.

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

Wednesday, October 19, 2016 10:30-12:00

UPPER GI BLEEDING – Room F1

OP361 MEDIUM- AND LONG-TERM RESULTS OF TREATMENT WITH LANREOTIDE IN CASES OF CHRONIC OR RECURRENT OBSCURE GASTROINTESTINAL BLEEDING OR DUE TO GASTROINTESTINAL ANGIODYSPASMS


Aims & Methods: Our aim is to determine the medium and long-term benefit of lanreotide in cases of chronic or recurrent obscure gastrointestinal bleeding (GB) or attributable to gastrointestinal angiodyspasms (GIADs). The long-term results with lanreotide are still very scarce.

Conclusion: Somatostatin analogues have been proposed as a rescue therapy in cases of chronic or recurrent obscure gastrointestinal bleeding (GB) or attributable to gastrointestinal angiodyspasms (GIADs). The long-term results with lanreotide are still very scarce.
Comparison in health resources consumption before and after Lanreotide.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
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<th>p value</th>
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<td>Admission days - Prior yr</td>
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<tr>
<td>1 yr - 2 yr - 3 yr</td>
<td>24.3</td>
<td>11.6</td>
<td>1.57</td>
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<td>14.3</td>
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<td>&lt;0.01</td>
<td>&lt;0.01</td>
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<tr>
<td>Iron iv doses - Prior yr</td>
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<td>6.1</td>
<td>5.9</td>
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<tr>
<td>N: Endoscopies - Prior yr</td>
<td>5.5</td>
<td>0.08</td>
<td>0.02</td>
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<td>1 yr - 2 yr - 3 yr</td>
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<td>6.5</td>
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<tr>
<td>0.08</td>
<td>&lt;0.01</td>
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</table>

SD: Standard deviation. Yr: year

iron doses, and non-diagnostic endoscopies. Differences from data before one year 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 64.1 years, range 56–90; 50% male sex) were included. Before starting treatment 19 were ASA III, 27.7% consumed antiplatelet and 31.8% anticoagulants drugs. 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 all 6 months in patients with chronic or recurrent obscure gastrointestinal bleeding or from gastrointestinal angiodyplasias, 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 ANGIODYPLASIAS 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 gastroenterological service, from January 2003 to December 2015. Controls: EBL treated patients without post-therapeutic ulcer bleeding. Matching was made for Child-Pugh-Turcotte (CPT) score and indication (bleeding vs elective) in a 1:1 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 (50.7%), HCV (29.5%) 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 impact short-term 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...
Weekend admissions have been associated with higher mortality. Contact E-mail Address: adrian.stanley@ggc.scot.nhs.uk

Aims & Methods: We studied whether out of hours (OOH) admissions had more co-morbidity, were less stable and/or had higher mortality.

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 most common location of PUD was duodenal (80.4%) and 26.8% were classified as CPT class B. The most common location of PUD was duodenal (80.4%) and 26.8% were classified as CPT class B. The severity of UGIH was not related to time period after the endoscopic treatment. The mean number of blood units transfused was 3.2 (±2.4), Rebleeding occurred in 23% and in-hospital mortality was 24%.

Conclusion: There is no difference in mortality in patients admitted with UGIH OOH compared to weekday admissions although weekday admissions had a lower haemoglobin and higher GBS. There was no evidence of delay in time to endoscopy with OOH admissions. The severity of UGIH was not related to time of admission. Similar findings were noted in all four centres.

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

References

OP366 A HISTORY OF ISCHEMIC HEART DISEASE, HIGH BLOOD UREA NITROGEN AND C-REACTIVE PROTEIN LEVELS, AND LOW HOMOGLLOBIN LEVELS: AS PREDICTIVE CLINICAL FEATURES FOR EARLY DEATH RELATED TO 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 risk factors of this procedure.

Aims & Methods: The aim of our study was to determine factors that could predict early death within 30 days following PEG. A retrospective analysis of the records of all patients who underwent PEG at Kure Medical Center and Chugoku Cancer Center from April 2008 to March 2014 period was examined clinical and preoperative 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 2.2-7.5, P < 0.0001), albumin level ≥2.7 mg/dl (OR 4.2, 95% CI 1.2-13.2, P < 0.0001), 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 impact of each factor and each of the following: history of ischemic heart disease, high blood urea nitrogen level, and low hemoglobin level.
heart disease (P < 0.01), high blood urea nitrogen (P = 0.02) and C-reactive protein levels (P < 0.01), and anemia (P < 0.0001).

Conclusion: A history of ischemic heart disease and laboratory data, such as high blood urea nitrogen and C-reactive protein levels and low hemoglobin levels may be useful predictive clinical factors for early death after PEG. If patients have a history of ischemic heart disease, high blood urea nitrogen, high C-reactive protein, or anemia, PEG should be considered carefully.

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

OP367 GLUTAMINOLYSIS INHIBITION AS A THERAPEUTIC STRATEGY IN GLUTAMINE-ADDICTED KRAS MUTANT COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) with KRAS mutations represents an unmet clinical need due to the lack of effective therapies. A defining characteristic of oncogenic KRAS-driven cancers is an altered cellular metabolism, in which glucose and glutamine metabolism are extensively rewired to satisfy their anabolic needs. In this study, we investigated the metabolic dependencies of KRAS-mutant CRC, established the role of glutaminolysis in KRAS-mutant CRC growth and evaluated the synergism between glutaminolysis inhibition and chemotherapeutic agents.

Results: Inhibition of SLC25A22-dependent glutaminolysis triggered metabolic stress, and SLC25A22 knockdown showed an attenuated entry of glutamine-derived carbon skeletons into the TCA cycle.

Conclusion: SLC25A22 represents a novel therapeutic target in KRAS mutant CRC and its combined therapeutic approaches hold promise for the treatment of KRAS mutant CRC.

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

OP369 MOLECULAR DISSECTION OF TUMOR ANGIOGENESIS IN COLORECTAL CANCER

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Introduction: Angiogenesis is a hallmark of cancer development and is considered as an attractive therapeutic target. 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 these results by qRT-PCR and immunohistochemistry in a large 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 suggest 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.

OP368 RANDOMIZED CONTROLLED TRIAL OF BACLOFEN IN THE TREATMENT OF MUSCLE CRAMPS IN PATIENTS WITH LIVER CIRRHOSIS

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2Tropical Medicine-Tanta University hospital. They were randomized to receive Baclofen was well tolerated, safe, and effective in the treatment of muscle cramps in patients with liver cirrhosis. One hundred patients with liver cirrhosis and suffering from muscle cramps signed informed consent to participate in this study. They were recruited from Department of Tropical Medicine-Tanta University hospital. They were randomized to receive either baclofen or placebo for 3 months. Patients were followed monthly and one month after withdrawal. Each visit, the clinico-epidemiological data were recorded, muscle cramp questionnaire was filled, and any drug related side effects were recorded.

Results: In the baclofen group, the frequency of muscle cramps was significantly decreased after one and three months of treatment (p < 0.005), with a significant rebound after withdrawal (P < 0.001). Patients receiving baclofen had a significant decrease in the severity and duration of muscle cramps (P < 0.001). After three months of baclofen therapy at dose of 30 mg/day, muscle cramps disappeared completely in 72%, reduced in 20%, and no change in 8% of patients. No significant changes in the frequency, severity and duration of muscle cramps were observed in the placebo group. There were few but non-significant side effects in the baclofen group when compared to placebo group.

Conclusion: Baclofen was well tolerated, safe, and effective in the treatment of muscle cramps in Egyptian patients with post-hepatitis C liver cirrhosis.
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 its associated significant short and long-term morbidity and mortality. With the amelioration of medical care, the use of antibiotics for primary and secondary prophylaxis of SBP is of interest. 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: To 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 5 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). Health-care-associated infections and Nosocomial infections were analyzed with the same variables. 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 caused by gram negative bacteria and Nosocomial-acquired SBPs were more frequently caused by gram positive bacteria (p = 0.033). SBPs secondary to MDR-bacteria were more frequent in Nosocomial-acquired group (19.64 vs 6.35%; p = 0.003). No statistically significant differences were noticed between centers when analysed microbiological isolation rate, gram staining of MDR isolations. There were no statistically significant differences between Community-acquired SBP and Nosocomial-acquired SBP for the variables age, gender, Child-Pugh, MELD, HB, leukocytes, platelets, CRP, Na, INR, bilirubin, albumin, ascites fluid characteristics, gastrointestinal bleeding, acute kidney injury and hemodynamic instability in the investigated study period. No complications were recorded.

Conclusion: Our aim was to investigate the impact of community- and nosocomial-acquired SBPs on outcomes of patients with cirrhosis and its complications. We showed that in-hospital mortality is high and the impact of MDR bacteria in mortality is significant. Nosocomial-acquired SBPs were associated with longer hospitalizations (17.8 vs 11.7 days; p = 0.007). No statistically significant difference was detected when analyzed in-hospital mortality (Nosocomial-acquired = 29.5 vs Community-acquired = 28.2%; p = 0.81); 1-year mortality (Nosocomial-acquired = 63.0 vs 51.7%; p = 0.025).

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

WEDNESDAY, OCTOBER 19, 2016
10:30-12:00
IMPROVING QUALITY OF SCREENING COLONOSCOPY – ROOM N2

OP371 SEVEN YEARS OF QUALITY ASSURANCE IN SCREENING COLONOSCOPY IN AUSTRIA
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Introduction: Screening colonoscopy only effectively prevents from colorectal cancer if performed with high quality.

Aims & Methods: Austria implemented a quality assurance program in screening colonoscopy in 2007. This study provides a report on 8 years of quality assured screening colonoscopy.

Results: In the investigated time period, 301 endoscopic units provided data of 159,246 screening colonoscopies. 49.1% were females. Significant increases over time were found for ADRs, which rose from a mean of 47.2% to 54.1% (SD 10.7%) in 2010-2013, corresponding to an average increase of 1.5% per two-year-period (95% confidence interval [95% CI] +0.9% to +2.2%, p = 0.001). Likewise, proximal lesion detection rates rose from 15.8% (SD 9.8%) to 21.7% (SD 13.3%), +2.5% per two-year-period, 95% CI +1.9% to +3.1%, p < 0.001). Adverse events occurred in 0.3%, 63% thereof were associated with polypectomy. There was a decline in complication rates of ~7.3 per 10,000 endoscopies per two-year-period (95%CI −13.1, −1.5 per 10,000 endoscopies per two-year-period, p = 0.013). Sedation induced the probability of complications in 0.2% (24% in sedated and 16% in unsedated patients, p = 0.025). Notably, all perforations occurred under sedation.

Conclusion: This study showed a strong improvement in quality of screening colonoscopy performed with high quality assurance program in Austria between 2010 and 2014. Both overall adenoma detection rate and detection rate of proximal lesions increased strongly in the investigated study period. Interestingly, the detection rate of advanced adenomas decreased.

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

OP372 ENDORINGS TM 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 away 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 endoscopists in established ADR areas. A total of 65 colonoscopies were performed, with a total of 134 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 distal tortuosity). Likewise, proximal lesion detection rate of advanced adenomas decreased.

Conclusion: Use of the Endorings™ device was associated with a significant increase in ADR. Qualitatively, the three-ring design was felt to interfere with normal intubation such that insertion technique had to be modified. An updated design iteration with two rings in slightly different positions along the central tubular core, has been produced and appears to offer a significant advantage in this regard. Furthermore, the central tube can be pushed further along the distal end of the terminal lumen to be intubated with the device in place. The Endorings™ may offer an advantage in screening colonoscopy and, in this cohort, further prospective investigation is warranted.

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

OP373 THE FIRST RANDOMISED CONTROLLED TRIAL OF ENDOCRYST VISION® ASISTED 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 Endocryst Vision® is a cap with soft flexible arms which aid the terminal end of a colonoscope to allow endoscopist to see and improve views during withdrawal. We have performed the first randomised controlled trial to identify the role of Endocryst Vision® in improving polyp detection.

Aims & Methods: Our aim was to investigate the impact of Endocryst Vision®-assisted colonoscopy on polyp detection, as compared to standard colonoscopy, in the UK Bowel Cancer Screening Programme (BCSP). This was a single-centre, four-arm randomised controlled trial. Ethics approval was obtained (ref: C13073/2013).
Table 1: E-CAP results

<table>
<thead>
<tr>
<th></th>
<th>Standard</th>
<th>EndoCap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>265</td>
<td>266</td>
</tr>
<tr>
<td>Polyps</td>
<td>470</td>
<td>436</td>
</tr>
<tr>
<td>Polyps/patient</td>
<td>1.77</td>
<td>1.64</td>
</tr>
<tr>
<td>Adenomas</td>
<td>359</td>
<td>336</td>
</tr>
<tr>
<td>Adenomas/patient</td>
<td>1.35</td>
<td>1.26</td>
</tr>
<tr>
<td>PDR</td>
<td>185/265</td>
<td>266/187</td>
</tr>
<tr>
<td>ADR</td>
<td>167/265</td>
<td>266/162</td>
</tr>
<tr>
<td>Cancer detection rate</td>
<td>15/265 = 5.7%</td>
<td>14/266 = 5.3%</td>
</tr>
</tbody>
</table>

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 EndoCap. In such settings, EndoCap Vision did not improve polyp detection rates (PDR) or ADR. However, EndoCap did not cause any adverse events, prolong procedure duration or cause additional cost. These data demonstrate the safety and feasibility of EndoCap. However, no additional gain was demonstrated in expert hands.

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

OP374 INCREASED ADENOMA DETECTION RATE BY G-EYE HIGH DEFINITION COLONOSCOPY IN COMPARISON TO STANDARD HIGH DEFINITION COLONOSCOPY: A PROSPECTIVE RANDOMIZED MULTICENTRE STUDY

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Introduction: Colorectal cancer (CRC) detection is attributed to the early detection and removal of polyps and adenomas during colonoscopy procedures. Although colonoscopy is considered to be the “gold standard” for CRC prevention, a significant number of polyps and adenomas go undetected during standard procedures. This is largely due to polyps that are hidden behind colonic folds that obscure endoscopic optics and result in interval cancers. The G-EYE colonoscopy system (Norgine, Harefield/United Kingdom) comprises a standard forward-viewing endoscope with a permanently integrated balloon at the distal end. Upon withdrawal of the endoscope, the G-EYE balloon is inflated to a partial pressure allowing for the flattening of haustral folds, centralization of the colon mucosa, reduction in bowel slippage, thus providing improved visualization of the colon anatomy and increased detection of polyps and adenomas.

Aims & Methods: This prospective, randomized, multicentre study compares the adenoma detection rate (ADR) of the G-EYE HD colonoscopy with that of standard HD colonoscopy (SC). Patients (age ≥ 50) referred to screening, surveillance, following positive FOBT, or due to change in bowel habits were randomized to either G-EYE or SC. Detected polyps were removed and sent for pathology. Polyp and adenoma detection rates were calculated.

Result: 480 patients were enrolled in the study, of which 238 subjects were randomized to SC and 242 subjects were randomized to G-EYE colonoscopy. Baseline parameters and indication for colonoscopy were similar in both groups. The ADR, adenoma per patient, number of adenomas by size and advanced adenomas for each group are presented in Table 1. G-EYE colonoscopy improved ADR by 45.6% when compared to SC. More specifically, the G-EYE endoscope increased the number of advanced adenomas and large-size adenomas by 96.9% and 96.2%, respectively. Procedural times were similar in both groups.

Conclusion: Our study shows that the G-EYE endoscope can substantially improve ADR when compared to SC. In addition to diminutive and small adenomas, the G-EYE endoscope detects a larger number of advanced and large-size adenomas. Consequently, we conclude that the G-EYE endoscope can significantly enhance the quality of CRC screening and thus reduce colonoscopic miss rates and interval cancer incidents.

Disclosure of Interest: H. Jacob: Board of directors

All other authors have declared no conflicts of interest.

OP375 EFFICACY AND SAFETY OF THE NOVEL II. PEG AND ASCORBATE BOWEL PREPARATION NER106 VERSUS TRISULFATE SOLUTION IN OVERNIGHT SPLIT-DOSING ADMINISTRATION: RESULTS FROM THE PHASE 3 STUDY NOCT.112

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2Clinical Development, Norgine/Harefield/United Kingdom
3Investigative Clinical Research, Annopolis/United States of America/MD

Introduction: Successful colon cleansing enables effective colonoscopy. PEG based splitting preparations are traditionally seen as the gold standard in cleansing, but many still require a high preparation volume intake. NER106 is the first 1L PEG3350 and ascorbate bowel preparation in phase 3 clinical development. The low volume of NER106 is achieved through the use of ascorbate in the second dose only.

Aims & Methods: This phase 3, randomised, multicentre, colonoscpist-blinded, non-inferiority study assessed the efficacy, safety and tolerability of a 2-day overnight split-dosing regimen of either NER106 (N2D) or trisulfate solution (TS) in patients undergoing colonoscopy. Two alternative primary endpoints were evaluated: overall bowel cleansing success and ‘Excellent plus Good’ cleansing in the colon ascendens using the Harefield Cleansing Scale (HCS). Secondary endpoints included hierarchical evaluation of lesion detection rates (key), and cleansing assessment using the Boston Bowel Preparation Scale (BBPS, supportive). Patient tolerability, acceptability and compliance were assessed using questionnaires. Safety was monitored through adverse events and clinical laboratory evaluation. The threshold for statistical significance in this study was P < 0.025. The confidence interval (CI) for the difference between the groups used a 10% margin to demonstrate non-inferiority vs. TS.

Result: Patients were randomised to receive either N2D (n = 310) or TS (n = 311). For N2D and TS, respectively, the mean age (SD) was 57.7 (10.36) and 57.3 (10.56) years. The distribution of males vs. females was 158 (51.6%) vs. 152 (48.4%). NER106 and TS had equivalent rates of 54.3% vs. 45.7% for TS. High overall bowel cleansing efficacy was achieved in both treatment groups (Table 1). N2D demonstrated non-inferiority (lower CI limit ≥ 10%) to TS for both alternative primary endpoints. Numerically, more patients on N2D achieved an ‘Excellent plus Good’ cleansing rate in the colon ascendas compared with TS. Non-inferiority for N2D in adenoma detection rate in the colon ascendas was not demonstrated; other key secondary endpoints were not formally tested. Tolerability and acceptability as assessed by the Bowel Cleaning Impact Review (BCIR, BCIR) Questionnaire were comparable for N2D and TS (Table 1). Compliance rates were high in both treatment groups. There were no deaths. NER106 was not associated with any serious treatment-emergent adverse events (TEAEs). The most frequently reported related TEAEs in both treatment groups were nausea and vomiting.

Conclusion: When administered as a 2-day split dosing regimen, and compared to trisulfate solution, NER106 was non-inferior in overall bowel cleansing success and in achieving an ‘Excellent plus Good’ cleansing rate in the colon ascendas. Both treatments were well tolerated; most TEAEs were mild or moderate in severity and reflected the expected safety profile of respective The
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] N2D vs. TS</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>−8.15%* [0.528]</td>
</tr>
<tr>
<td>Supporting secondary endpoint: Patients with successful overall bowel cleansing efficacy (BBPS) [n]</td>
<td>228 (82.6%)</td>
<td>227 (81.1%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>Primary endpoint: Excellent plus Good cleansing rate in colon ascendens [n]</td>
<td>99 (35.9%)</td>
<td>82 (29.3%)</td>
<td>−1.69%* [0.059]</td>
</tr>
<tr>
<td>Key secondary endpoint: Adenoma detection rate, colon ascendens</td>
<td>14.1%</td>
<td>17.1%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Adenoma detection rate, overall colon</td>
<td>33.7%</td>
<td>35.0%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Polyp detection rate, colon ascendens</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>BOCLIR 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>

* = 97.5% 1-sided CI; ** = 95% 2-sided CI; n.a. = not applicable

1L NER1006 showed high efficacy and safety in overnight split-dosing administration.

**Disclosure of Interest:** M. DeMicco: Contractor for Norgine through Anaheim Clinical Trials LLC; Principal Investigator for the NOCT study.
L.B. Clayton: Employee of Norgine
M.S. Epstein: Contractor for Norgine through Investigative Clinical Research. Investigator for the NOCT study.


**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 weather the addition of oral instructions to a self-explanatory booklet for bowel preparation increases compliance with split-dose. We prospectively enrolled consecutive 50–70yr-old outpatients undergoing screening colonoscopy from 8:00 to 10:00 am. Exclusion criteria were inability to provide consent and contraindications to the preparation adopted in the study. All patients received a low-volume preparation instructions, 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 maximizes 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**

**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 patient with overt diagnosis in the same geographic area. For the epidemiological analysis the MilCirRe 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 nM in at least two occasions) for liver disease and thrombocytopenia (<120,000/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 ICD9-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 performed.

**Conclusion:** The prevalence of overt liver cirrhosis was 1.35% in males and 0.26% in females, respectively. 0.4% of the population included individuals with liver cirrhosis, while the frequency of liver cirrhosis in healthy subjects is 0.2% (5).

**Disclosure of Interest:** All authors have declared no conflicts of interest.
was recorded. Sex distribution of these patients was similar to that of the patients with elevated transaminases (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 1.3% of the remaining patients. The epidemiological profile of these two groups was similar [M:F=1:1.59; mean age (yrs) = 65.6 vs M:F=1:1.67; mean age (yrs) = 65, p = n.s], but significantly different (p < 0.0001) compared to the normal population and to subjects with only liver enzyme alterations. Patients with overt and overt cirrhosis presented a similar prevalence of a 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

Table 1 (OP379): All-cause resource use pre- and post-RFX initiation

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>n*</th>
<th>Pre-RFX</th>
<th>Post-RFX</th>
<th>P</th>
<th>Pre-RFX</th>
<th>Post-RFX</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months (n = 114)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Mean (SD)</td>
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</tr>
<tr>
<td>2.2 (1.9)</td>
<td></td>
<td>1.0 (1.3)</td>
<td></td>
<td>&lt;0.001</td>
<td>99</td>
<td>1.7 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Hospitalisations with overnight stay per patient</td>
<td>101</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total bed days</td>
<td>101</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total bed days per inpatient</td>
<td>101</td>
<td>28.6 (31.4)</td>
<td></td>
<td>11.9 (23.2)</td>
<td></td>
<td>&lt;0.001</td>
<td>99</td>
</tr>
<tr>
<td>Critical care bed days per inpatient</td>
<td>19</td>
<td>7.9 (10.1)</td>
<td></td>
<td>2.0 (5.1)</td>
<td></td>
<td>0.018</td>
<td>61</td>
</tr>
<tr>
<td>Emergency room visits per patient</td>
<td>63</td>
<td>1.9 (2.3)</td>
<td></td>
<td>1.0 (1.0)</td>
<td></td>
<td>&lt;0.001</td>
<td>65</td>
</tr>
</tbody>
</table>

Spent by Social Security in France for HE hospitalisations with a mean cost per hospital admission estimated (4 SD: 6@ 61,411).

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. Bureau: Cristophe Bureau 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. Rivot: Emanuelle Rivot-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
**OP382 PREGNANCY OUTCOME IN MORE THAN 5000 BIRTHS TO WOMEN WITH VIRAL HEPATITIS IN A POPULATION-BASED COHORT STUDY IN SWEDEN**

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**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) and births without HCV (n = 1,429) served as population controls. Crude and adjusted relative risks (RR) were calculated using Poisson regression analysis.

**Results:** Women with HCV were more likely to smoke (47.62% vs. 8.65%) and to have alcohol dependence (18.79% vs. 1.07%) compared with population controls. Most women with HBV 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).

**Conclusion:** Both HBV and HCV are risk factors for preterm births, while HCV seems to be associated with a protective effect against preeclampsia. Future studies should corroborate these findings.

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

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**OP383 ALTERATION OF THE RENIN-ANGIOTENSIN SYSTEM IN THE CIRCULATION, TERMINAL ILEUM AND COLON IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A POTENTIAL NOVEL THERAPEUTIC TARGET**

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**Introduction:** Circulating components of the RAS were surveyed for these components by mRNA expression by qRT-PCR, associations with markers of disease activity evaluated. Terminal ileum, ascending and non-inflamed colon in patients undergoing intestinal resection and colostomy were surveyed for these components by mRNA expression by qRT-PCR, and immunohistochemical localisation and semi-quantification of particle density using in situ image processing software. ACE activity was measured in biopsy samples.

**Results:** 36 patients with CD (mean age 41 [range 21–76] y, 27 females), 45 with UC (44 [22–82] y, 19 females) and 39 non-IBD controls (46 [22–83] y, 21 females) were included. The main differences in demographic features were noted across the three groups. Circulating renin (mean 25.4 (95% CI 21.6–29.1) vs 18.6 (13.9–23.3) mU/L, p = 0.026), ACE2:ACE ratio (mean 0.61 (95% CI 0.48–0.75) vs 0.40 (0.32–0.47), p = 0.028) and Ang 1–7 (mean 22.8 (20.1–25.4) vs 17.4 (16.7–18.1) ng/ml, p = 0.003) were higher, and CD8+ and Th9 cells, both in patients with CD and non-IBD controls with 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. The disease activity in non-inflamed colon was higher, and mesenteric lymph nodes were larger in patients with IBD than in non-IBD controls. Staining intensity of Mas receptor was higher in non-inflamed colon in patients with IBD than in inflamed colon or healthy control tissue (p = 0.045, Kruskal-Wallis). All components of the classical and alternative RAS pathways are present in healthy intestinal tissue suggesting a role in normal physiology, especially in epithelial cells. Circulating and mucosal components of the alternative RAS axis are upregulated in patients with IBD, but mucosal Ang 1–7 (1–3 fold) is reduced, suggesting dysregulation and a potential role of the RAS in pathogenesis or perpetuation of inflammation in IBD. Novel therapies that increase mucosal Ang (1–7) may have a role in IBD.

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

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**OP384 BLOCKADE OF AEβ7 INTEGRIN CONTROLS TRAFFICKING OF CD8+ AND TH9 LYMPHOCYTES FROM IBD PATIENTS TO THE INFLAMED GUT IN VIVO**

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**Introduction:** The anti-α4β7 antibody vedolizumab (VDZ), which inhibits homing of lymphocytes via interaction of α4β7 with MAdCAM-1, has greatly increased therapeutic options in patients with IBD. However, lymphocyte homing may also occur via other homing molecules like the α4β1 integrin and a considerable portion of patients does not respond to VDZ therapy. The α7 integrin (ETZ) is currently tested in phase III trials and additionally blocks the binding of αEβ7 to E-Cadherin, which is believed to mediate epithelial retention of homed lymphocytes.

**Aims & Methods:** We aimed to compare lymphocyte trafficking upon blockade of αβ7 vs. α4β7 integrin. Hence, αβ7 and α4β7 expression was determined on peripheral blood and lamina propria lymphocyte subpopulations in IBD and CD patients, and healthy donors by flow cytometry or immunofluorescence staining, respectively. The regulation of αβ7 expression upon lymphocyte stimulation and incubation with cytokines was studied. In vitro adhesion assays the adherence capacity of lymphocytes to MAdCAM-1 and E-Cadherin was determined, while butyric and retinoic acid potentiating the potential of VDZ and the ETZ surrogate antibody FIB504 (ETZs) were tested. Finally, lymphocytes from UC patients were treated with either of the compounds and fluorescence labelled and injected into the ileocelecric artery of immuno-suppressed mice. Gut homing was assessed by in vivo confocal microscopy and flow cytometry of lamina propria cells.

**Results:** αβ7 expression was significantly higher on CD8+ lymphocytes than on CD4+ lymphocytes both in the peripheral blood and the gut. Among both sub-sets αβ7 expression was correlated with IL-9 secretion, while CD4+ IL9 cells expressed less αβ7 than other CD4+ subsets. At the same time, CD8+ cells exhibited a notably greater potential to increase αβ7 expression upon T cell stimulation and TGF-β treatment, while butyric and retinoic acid decreased αβ7 expression on CD8+ cells. ETZs markedly inhibited binding of CD4+ and CD8+ lymphocytes to Rh-Cadherin and blocked the adhesion of CD4+ and CD8+ lymphocytes to hMAdCAM-1 to a degree comparable with VDZ. Fewer lymphocytes bound to a mix of both ligands upon treatment with ETZs compared with VDZ. In our humanized mouse model the portion of human CD8+ cells in the murine gut was significantly reduced three hours after injection when cells were treated with ETZs vs. VDZ. Among CD4+ cells, the fraction of Tg11 cells was decreased. The expression of αβ7 on CD8+ cells from IBD patients treated with VDZ was higher in the maintenance than in the induction phase of treatment.

**Conclusion:** VDZ may not equally cover all pathogenetically relevant lymphocyte homing to inflamed intestinal tissue in IBD and CD patients. ETZs seems to offer superior reduction of intestinal lymphocyte infiltration especially concerning CD8+ and Th9 cells.

**Disclosure of Interest:** S. Zundler: The etrolizumab Surrogate antibody was produced by Genentech, San Francisco, CA, USA. The company was neither involved in conception and design of the study nor in analysis and interpretation of the results. SZ received funding from Takeda.
OP385 VITAMIN D REGULATES DENDRITIC CELL ACTIVITY AND TRAFFICKING IN CROHN’S DISEASE

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Introduction: Dendritic cells (DC) can determine whether the mucosal immune system mounts an inflammatory or regulatory response to antigen and likely contributes to the pathogenesis of Crohn’s disease. Vitamin D down-regulates DC inflammatory responses and could prove beneficial as a treatment adjunct in Crohn’s. Vitamin D also modulates DC homing marker expression. This study assessed the effect of high dose parenteral vitamin D treatment on circulating DC phenotype and function in patients with active luminal Crohn’s disease receiving anti-TNFα therapy.

Aims & Methods: Peripheral blood mononuclear cells were isolated from 14 patients with active luminal Crohn’s disease and suboptimal vitamin D levels (<75 nmol/L) prior to and 6 weeks after starting anti-TNFα (infliximab) therapy. Patients with low vitamin D (<50 nmol/L) were also given a single high dose of parenteral vitamin D (300,000 international units, 1.25(OH)₂ vitamin D3). Flow cytometry was used to identify total DC, (HLA-DR+ cells negative for markers of other cell lineages (CD3, CD14, CD16, CD19 & CD34)). DC were further subtyped as myeloid (mDC, CD14+CD123+) and plasmacytoid (pDC, CD123+CD11c–). Expression of phenotypic markers (including maturation and homing markers and pattern recognition receptors) and on-going intracellular DC cytokine production during 4 hours’ culture were assessed.

Results: Production of TNFα by myeloid DC was significantly reduced (p = 0.016) in those patients who received vitamin D alongside anti-TNFα therapy, beyond that of those who received anti-TNFα therapy alone (mean post- treatment TNFα of 24.9% vs 39.1% respectively). There was a significant correlation between increase in vitamin D level and decrease in TNFα production by myeloid DC (p = 0.025; R² = 0.76). An increase of serum 25(OH) vitamin D greater than 20 nmol/L was associated with a decrease in myeloid DC TNFα production. Anti-TNFα therapy alone induced a significant upregulation of the skin homing marker cutaneous lymphocyte antigen (CLA) on myeloid DC (p = 0.0055), an effect which was not seen in patients receiving adjunctive vitamin D.

Conclusion: High dose parenteral vitamin D, given as an adjunct to anti-TNFα therapy in Crohn’s, promotes down-regulation of circulating myeloid DC production of TNFα. This may influence the subsequent interaction of DC and T cells. TNFα promotes a TH17 response characteristic of Crohn’s inflammation; thus the ability of vitamin D to further block TNFα production may promote a more regulatory T cell response and improve outcomes when used as an adjunct to anti-TNFα therapy. The upregulation of the skin homing marker CLA following anti-TNFα therapy may explain the high rates of cutaneous side effects to this drug class. The down-regulation of CLA by vitamin D in this setting may be useful in those patients suffering cutaneous sequelae of anti-TNFα therapy.

Disclosure of Interest: P. Henty: Advisory board: DrFalk; AbbVie All other authors have declared no conflicts of interest.

OP386 CIRCULATING DENDRITIC CELL SUBSETS IN CROHN’S DISEASE SHOW ALTERATIONS IN TISSUE HOMING AND CYTOKINE PRODUCTION

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Introduction: Crohn’s disease is characterised by an exaggerated immune response to mucosal antigen. Dendritic cells (DC) play a key role in controlling dendritic cell homing markers on T cells which direct T cell migration to sites including the skin, gut and lymphoid tissue. We characterised homing marker profile and ongoing cytokine production of circulating DC subsets from patients with Crohn’s disease and from healthy controls.

Aims & Methods: DC within peripheral blood mononuclear cells from adults with active luminal Crohn’s disease or from healthy controls were characterised using flow cytometry. DC were identified as HLA-DR+ and negative for markers of other cell lineages (CD3, CD14, CD16, CD19, CD34). Myeloid DC (mDC, CD14+CD123+) and plasmacytoid DC (pDC, CD11c–CD123+) were assessed for phenotype (maturity status, homing markers and pattern recognition receptors) and on-going cytokine production by surface and intracellular staining respectively.

Results: In patients with Crohn’s disease (n = 20), a greater proportion of myeloid DC expressed a gut-homing profile (CLA+IL-7, p = 0.001) compared to healthy controls (n = 13) where most myeloid DC were not tissue-specific (CLA+IL-7, p = 0.0016). In controls, the gut-homing profile (CLA+IL-7, p = 0.001) whilst plasmacytoid DC were strongly skin (CLA+IL-7 and lymph node (CCR7+) homing (p < 0.0001). Production of pro-inflammatory cytokines was up-regulated in Crohn’s, with myeloid DC producing higher levels of TNFα and plasmacytoid DC producing higher levels of IL-12 than controls (p = 0.0042 and p = 0.013 respectively). Expression of maturation marker CD86 was increased on myeloid DC in Crohn’s but not on plasmacytoid DC (p = 0.027 and p = 0.13 respectively). Expression of IFNα, -γ, -IL-12, -CD40, -CD80, -TLR2 and -TLR4 on DC did not differ between Crohn’s and controls for either DC subset.

Conclusion: The increased myeloid DC expression of gut homing phenotype may have implications for the production of TNFα in Crohn’s disease compared with healthy controls. This study highlights the central role that this dendritic cell subset plays in the pathogenesis of Crohn’s disease. Differences between homing markers on myeloid DC (gut homing) and plasmacytoid DC (skin homing) suggest that they may have different roles in Crohn’s, with myeloid DC being central to gut inflammation whilst plasmacytoid DC might be involved in cutaneous Crohn’s disease and the skin sequelae of anti-TNFα therapy.

Disclosure of Interest: P. Henty: Advisory board: DrFalk; AbbVie

All other authors have declared no conflicts of interest.
Adenocarcinomas at the gastro-oesophageal junction (GOJ) are currently stratified according to the Siewert classification by location of the main tumour mass (GOJ1: 1–5 cm proximal to the junction, GOJ2: 1 cm proximal to 2 cm distal to the junction, GOJ3: 2–5 cm distal to the junction). However, the clinical relevance of this classification is unclear whether this also reflects the molecular phenotype and hence how this stratification might influence therapy and prognosis in an era of personalised medicine.

Aims & Methods: The aim of this study was to determine the molecular phenotypes of GOJ tumours and to relate this to the Siewert classification. The gene expression profile of 107 tumours at the gastro-oesophageal junction was assessed by the Illumina HTv4.0 beadchip array (GOJ1: 35, GOJ2: 31, GOJ3: 18, true gastric comparators: gastric fundus/proximal body: 6, distal body: 9, antrum: 8). Only tumours of intestinal Lauren type were included. Differential gene expression analysis was performed using limma in R, in unbiased sub-group assignment was performed applying a model-based algorithm using MCLUST in R. Gene-set enrichment based pathway analysis was done using GAGE in R based on KEGG and Gene Ontology terms. Whole genome sequencing data was analysed for a subset of 15 GOJ tumours (5 GOJ1, 5 GOJ2, 5 GOJ3) for matched germline to assess mutational burden, recurrently mutated genes, copy number aberrations, and mutation signatures in the identified subgroups.

Results: The Siewert classification did not reveal differential gene expression according to the genotype of the major driver which was upregulated in GOJ3 compared with GOJ1 (p = 0.003). Unbiased assignment of the gene expression profiles instead revealed three distinct groups which were not correlated with Siewert type, tumour stage or grade (p > 0.05). Group 1 showed strong expression of MUC5AC, CTSE, and CLDN18, and was enriched for pathways involved in cell metabolism and cell turnover. Group 2 was positive for CDX1, CDX2 and CDH17, and was enriched for digestive and absorptive processes. Group 3 showed high expression of genes involved in immune-cell function including CXCL10, IDO1 and HLA-genes, and was enriched for pathways involved in immune response and cell-cell communication. Immunohistochemistry for a subset of the above mentioned genes confirmed the expression of these respective groups. Whole-genome sequencing data showed comparable features across all groups with the expected recurrent mutations and trinucleotide mutational context. Survival was significantly different between groups: Group 1 had the worst overall survival (5-year survival 45.2 m, group 2: 74.5 m, group 3: 78.2 m, p = 0.019).

Conclusion: Adenocarcinomas at the GOJ comprise three distinct molecular phenotypes with distinct clinical and pathological implications. This study indicates that patients with GOJ tumours may benefit from a molecularly guided classification for treatment and prognosis.

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

Wednesday, October 19, 2016

Gastric and J pouch cancers – room 1.8

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: The 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 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 TLR4 shRNA cells (1.6 fold induction) and in KO peritoneal macrophages (1.5-fold induction) were significantly 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 shRNA cells (1.6 fold induction) and in KO peritoneal macrophages (5.0 ± 1.5) and in protein expression of pNF-κB in both gp96 shRNA (1.7) and in KO peritoneal macrophages (1.5 ± 0.6) compared with non-treated mock-transduced cells and WT peritoneal macrophages. Furthermore, LPS induced a significant increase in pIκBα and mRNA and protein expression of IL-8 (9 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.
clinical implications that targeting SRGAP1 might have therapeutic potential for GC.

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

OP392 HOXB7 PROMOTES EPITHELIAL-MESENCHYMAL TRANSITION AND METASTASIS IN GASTRIC CANCER


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Introduction: In the previous study we observed that HOXB7 is highly expressed in gastric cancer and promote migration or invasion, and inhibit apoptosis in gastric cancer cells.

Aims & Methods: We aimed in this study to demonstrate the roles of HOXB7 in development of epithelial-mesenchymal transition (EMT) and metastasis in gastric cancer using in vitro and in vivo model. We established HOXB7-expression stable cell lines (MKN45-B7) and mock cells (MKN45-mock). Western blot was performed to validate EMT markers and phospho-Akt/PTEN activity. By injection of stable cell lines, xenograft tumors were produced on the 8-week old male Balb/C nude mice (nu/nu). 4 weeks after injection, we extracted xenograft tumors, and implanted fragment of tumors on the stomach of another 8-week old nude mice. 6 weeks after implantation, mice were sacrificed and their peritoneal metastasis, perigastric lymph node and volume of gastric tumor were compared between both groups.

Results: MKN45-B7 cells frequently showed fibroblast-like mesenchymal phenotype, whereas most of MKN45-mock cells showed epithelial phenotype. Mesenchymal markers (snail, vimentin) were 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 were also significantly increased in MKN45-B7 tumor-implant 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 through 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 patients with gastric cancer. The study group included a total of 209 patients with gastric cancer in the years 2004-2014. Colonoscopy was performed on all 209 patients. The patients were divided into two groups. The first group was patients who had colorectal neoplasms and the second group was patients who did not have colorectal neoplasms. In the second group, the patients who had undergone colonoscopy were also included. 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, or more polyps or adenocarcinoma.

Results: High-risk colorectal neoplasms 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 incidence of high-risk colorectal neoplasms were associated with age, DM, colon cancer family history, and presence of gastric category 4 lesion. Patients with high-risk colorectal neoplasms and colon cancer in patient group who underwent gastric ESD was higher than that in the control group. Therefore, patients undergoing ESD with category 4 lesions may need screening colonoscopy.

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

OP394 PALLIATIVE CHEMOTHERAPY AND TARGETED THERAPIES FOR ESOPHAGEAL AND GASTRO-ESOPHAGEAL JUNCTION CANCER

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Introduction: More than 50% of patients with esophageal (EC) or gastro-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 next issue of the 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 trials on palliative chemotherapy and/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 OS in favor of the arm with addition of cytostatic or targeted therapeutic with a HR of 0.77 (95% CI 0.70 to 0.85). The median increased survival time was limited, one month for adding an additional cytostatic or targeted therapeutic to the control arm. Subanalysis with second line therapy showed a similar benefit as first line therapies. Ramirez-Ramirez 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 data was analyzed in a study that reported this outcome, often improved in the arm with an additional agent.

Conclusion: Palliative chemotherapy and/or targeted therapy significantly increases OS compared to BSC in patients with esophageal or gastro-esophageal junction carcinoma. Additionally, patients who receive multiple chemotherapies or cytostatic or targeted therapeutic agents have an increased OS, PFS and improvement of quality of life, on the expense of treatment-associated toxicity of at least grade 3. Based on this meta-analysis, palliative chemotherapy and/or targeted therapy should be considered standard care for esophageal and gastro-esophageal junction carcinoma.

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 APPENDECTOMY FOR TREATMENT OF UNCOMPLICATED ACUTE APPENDICITIS: RESULTS OF THE APPAC RANDOMIZED CLINICAL TRIAL

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OP396 SURGERY VERSUS CONSERVATIVE TREATMENT FOR RECURRENT AND ONGOING DIVERTICULITIS: RESULTS OF A MULTICENTER RANDOMIZED CONTROLLED TRIAL (DIRECT-TRIAL)


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Introduction: Appendectomy has been the standard treatment for acute appendicitis and more than 90% of 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 the treatment of acute appendicitis in patients revealed that the majority of CT-proven uncomplicated acute appendicitis patients were successfully treated with antibiotics. Most patients randomized to antibiotic treatment did not require appendectomy during the 1-year follow-up period, and those who required appendectomy did not experience significant or increased complications.

Aims & Methods: The objective of this study was to compare the treatment costs of antibiotic therapy and appendectomy for treatment of uncomplicated acute appendicitis in our Appendicitis Acuta (APPAC) randomized clinical trial. The APPAC multicenter, open-label, non-inferiority randomized clinical trial was conducted in Finland from November 2009 until June 2012. A total of 530 adult patients aged 18 to 60 years with CT-scan confirmed uncomplicated acute appendicitis were enrolled in six Finnish hospitals. Patients were randomly assigned to early appendectomy (n = 273) or antibiotic treatment (n = 257). 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 operative group, the overall societal costs were 16 times higher than in the antibiotic group. In both groups productivity losses represented a slightly higher proportion of overall societal costs than all treatment costs together, with diagnosis and medical having a minor role. Patients in the operative 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 operative treatment option generated significantly more costs in all models.

Conclusion: To our knowledge, this is the first randomized study comparing antibiotic therapy and appendectomy in uncomplicated acute appendicitis to reach a cost analysis. Avoiding surgery ranged between 1-30% savings 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 acute uncomplicated appendicitis are strongly encouraged also from an economic standpoint.

Disclosure of Interest: P. Salminen: Research grant / a government research grant (EVO) awarded to Turku University hospital. All other authors have declared no conflicts of interest.

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Introduction: Sessile Serrated Adenomas/Polyps (SSA/P) are responsible for nearly 5% of colorectal cancer (CRC). Despite the availability of novel imaging enhancement and endoscopic techniques including narrow band imaging it is difficult to differentiate hyperplastic (HP) polyps from SSA/Ps. Vast proportion of endoscopists leave the diminutive and possibly small HP polyps in situ in the recto sigmoid area (diagnose and disregard approach). Hence there is a possibility of leaving SSA/P in the recto sigmoid region which could potentially lead to CRC later in life.

Aims & Methods: We aim to estimate the prevalence of SSA/P in recto sigmoid colon at screening colonoscopy and flexible sigmoidoscopy (FS). Patients aged > 55 years underwent a screening colonoscopy (n = 500) or a flexible sigmoidoscopy (n = 500) at our institution between August 2014 and April 2015 were included. Data collected from 500 consecutive patients who underwent a colonoscopy or a FS. Demographic, procedural and polyp data were retrieved from our endoscopy database.

Results: 99.6% of (498/500) colonoscopy and 97.6% of flexible sigmoidoscopy procedures were completed. Screening colonoscopy detected 1006 polyps and FS detected 235 polyps. Polyp size ranged between 1-80 mm (colonoscopy mean size 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 operative treatment option generated significantly more costs in all models.

Conclusion: Our cohort showed a slightly higher prevalence of SSA/Ps 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.
Fourteen patients had unresectable polyps and had segmental resections. Proximal polyp burden was 31 (IQR 26.8–47.5). The median total polyp count was 43 (IQR 34–56.5) and median were higher in this group compared with those having surgery for CRC alone. Decision making should be guided by the endoscopic assessment of the SPS.

Results: A total of 164 (38%) patients underwent colorectal surgery; 114 (70%) for CRC, 31 (19%) for high polyp burden and 14 (9%) for unresetable 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 resected other malignant or premalignant tumours; of these only three have recorded formal post-operative endoscopc surveillance.

None of these patients met SPS criteria at the time of index surgery. 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 >10 mm (median 10 v 2, p = 0.0005) 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 underwent IRA. The median total polyp count was 43 (IQR 34–56.5) and median proximal polyp burden was 31 (IQR 26.3–47.5). Surgery for Unresectable Polyp Fourteen patients had unresetable 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 one-third of 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.

OP398 IMPROVED RISK CLASSIFICATION FOLLOWING COLORECTAL ADENOMA REMOVAL

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Introduction: Current colonoscopy surveillance recommendations after polyp removal are arbitrary and resource demanding. We developed a novel risk classification system for colorectal cancer following adenoma removal. Methods: We included all individuals who underwent screening colonoscopy with adequate bowel cleansing and caecal 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 hazard ratios (HR) for individuals with different adenoma characteristics compared to individuals without adenomas and derived a novel risk classification system. Results: Among 159,926 individuals (median age 56 years; 37.6% males) with a median follow-up of 7.8 years we identified 82 colorectal cancers after adenoma removal (0.31%) and 194 in individuals without adenomas (0.15%). The strongest predictors for colorectal cancer risk were adenoma size ≥20 mm in diameter (HR 8.70; 95% CI 5.43–13.95, P < 0.001), high-grade dysplasia (HR 4.15; 95% CI 2.05–8.43, P < 0.001) and ≥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%–95% CI –11.9–16.3). Conclusion: Limiting surveillance recommendations to patients with adenomas ≥20 mm in diameter or high-grade dysplasia or ≥3 adenomas significantly reduces the need of surveillance colonoscopies without increasing the risk for 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-STRAIGHTENED 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 1–4 mm and 5–9 mm, high-risk adenomatous polyps, and CRC, and finally to death from CRC.4 High-risk polyps included intramucosal cancers and adenomas with a diameter ≥10 mm, with high-grade dysplasia, or with villous histology (≥25%). The initial population comprised 100,000 average-risk individuals aged 40 years. Parameters of transition probabilities, costs, and test results were defined and based on Japanese data.5 Four surveillance
strategies were evaluated for costs, gained quality-adjusted life-years (QALYs), and the required number of CS procedures. In strategy 1, post-polypectomy surveillance CSs were performed 1 year after polypectomy regardless of the polyp results. In strategy 2, the interval between surveillance CSs and polypectomy was 3 years regardless of the polyp results. Strategy 3 was a risk-stratified one; 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 1–4 were as follows: strategy 1, 23,004 QALYs and ¥1,024.88; strategy 2, 23,000 QALYs and ¥1,009.02; strategy 3, 23,015 QALYs and ¥977.40; strategy 4, 23,046 QALYs and ¥970.31. The required numbers of CS procedures per person in strategy 1, 2, 3, and 4 were 2.143, 1.664, 1.617, and 2.548, respectively. Risk-stratified strategies (strategies 3 and 4) yielded higher QALYs with lower costs than strategies 1 and 2. Comparing strategy 1 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, risk-stratified CS surveillance programs based on the polyp results should be recommended owing to higher expected effectiveness and cost-effectiveness. Furthermore, more intense use of CS procedures in risk-stratified surveillance can heighten the effectiveness and cost-effectiveness in the Japanese setting. However, it does require a larger number of CS procedures; thus, it would be preferable to determine the most appropriate use of CS procedures in risk-stratified surveillance programs depending on the nationwide availability of CS resources.

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

References

Table (OP401)

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<th>Type 2A</th>
<th>Type 3</th>
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<td>Surface pattern</td>
<td>Regular dark or white spots</td>
<td>Regular (tubular/branched</td>
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<td>Low grade intramucosal neoplasia</td>
<td>High grade intramucosal neoplasia/Shallow submucosal invasive cancer</td>
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</tbody>
</table>

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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 polyoid and superficial lesions. To resolve these issues and unify the classifications, the Japan NBI Expert Team (JNET) was set up in 2011. The aim of this study is to scientifically evaluate the NBI scale and determine the NBI findings and diagnostic criteria used in the unified classification (The JNET classification).

Aims & Methods: The JNET classification, which is a modification of NICE classification, consists of 4 categories (Types 1, 2A, 2B, and 3) based on vessel and surface patterns without color. We made a hypothesis that each of them are correlated with the histopathological findings of hyperplastic polypl/sessile serrated polypl (SSP), low grade intramucosal neoplasia, high grade intramucosal neoplasia/shallow submucosal invasive cancer, and deep submucosal invasive cancer, respectively. A web image interpretation study using the modified Delphi (UMIN000010292: Multicenter study for developing universal NBI magnifying endoscopic classification of colorectal tumors in Japan) was conducted.

Results: Univariate and multivariate analyses and analysis on diagnosability from 5 candidate NBI magnifying findings such as 1) loose vessel areas, 2) interruption of thick vessels, 3) scattered vessels, 4) thick, linearized/meandering atypical vessels in the tumor, and 5) amorphous areas of surface patterns for Type 3, and i) variable caliber of vessels, ii) thick vessels iii) irregular distribution of vessels, iv) vessel meandering, and v) irregular or obscure surface pattern for type 2B. Among the five candidate NBI findings, three findings such as 1) loose vessel areas, 2) interruption of thick vessels, and 5) amorphous areas of surface patterns were identified as the diagnosis of type 3. In addition, three findings such as 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.


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OP402 SUBCLASSES OF TYPE-II PIT PATTERN REVEAL ALTERNATIVE TUMORGENIC PATHWAYS OF COLORECTAL SERRATED LESIONS


Aims & Methods: We aimed to identify clinicopathological and molecular features of SLs without Type II-O pits remain unclear. We analyzed the methylation of CIMP markers (MINT1, −2, −12, −31, p16 and MLH1) and BRF 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). Progression of Type II-L pit lesions to TSA was associated with KRAS mutation and CIMP-low were more frequent in lesions with Type II-L plus tumor pits. These results suggest that lesions with Type II-L pit and those with Type II-O plus tumor pits remain unclear.

Results: Endoscopic findings were classified as 41 Type II pit, 8 Type II-L pit, 92 Type II-O plus tumor pit, 21 Type II plus tumor pit, 22 Type II-L plus tumor pit, 50 Type II-O plus tumor pit and 214 tumor pit. We identified Type II-L plus tumor pit, which was specific to TSA with KRAS mutation and CIMP-low (sensitivity, 60%; specificity, 96%). As compared to lesions with only Type II-L pit, KRAS mutation and CIMP-low were more frequent in lesions with Type II-L plus tumor pits. Progression of Type II-L pit lesions to TSA was associated with KRAS mutation and accumulation of moderate DNA methylation. In contrast, BRF mutation was frequently observed in colonic tumors with Type II plus tumor pit. These results suggest that lesions with Type II-L pit and those with Type II-O plus tumor pit were the same HP.

Conclusion: Our data suggest that Type II-L plus tumor pit is a useful hallmark of the premalignant stage of CRCs with KRAS mutation and CIMP-low.

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

OP403 ARTIFICIAL INTELLIGENCE (AI) IN ENDOSCOPY–DEEP LEARNING FOR OPTICAL BIOPSY OF COLORECTAL POLYPS IN REAL-TIME ON UNALTERED ENDOSCOPIC VIDEOS


Introduction: ASGE-PIVI guidelines support a “resect and discard” strategy for diminutive colon polyps, provided that the predictive value of technology allowing for “optical biopsy” depicts at least 90% agreement in assignment of post-polypectomy surveillance intervals using pathology as standard. In addition, in order for a technology to be used to guide the decision to leave suspected diminutive rectosigmoid hyperplastic polyps in place (without resection), the technology should provide 90% negative predictive value for adenomatous histology. Such standards with optical biopsy might be achievable with experts (although even that is unclear) but do not cross over into general clinical practice. Several groups have looked at supporting the process of optical biopsy decision making on endoscopic assessment of the histology of diminutive colorectal polyps using traditional machine learning, but to date there are significant limitations in terms of (1) using still images only, and non-realtime computer support, both of which are not clinically efficient or effective, and (2) often involving magnification endoscopy that is not yet a widespread clinical practice. Deep learning is a branch of artificial intelligence which is a significant advance on traditional machine learning, and with huge computational power, machines can now recognize objects in real time. We sought to apply novel deep learning techniques to optical biopsy for colon polyps.

Aims & Methods: We aimed to evaluate deep learning applied to the classification of colorectal polyps into NICE types 1 and 2, in real-time on unaltered endoscopic videos, for the support of clinically efficient optical biopsy. We used 92 videos of small colorectal polyps (<10 mm) under white light (WL) and narrow-band imaging (NBI) (38 NICE type 1, 52 NICE type 2), using Olympus 190 series colonoscopes. “Optical biopsy” was done on all polyps by an expert with >95% accuracy (using pathology as the reference standard) prior to removal and histological confirmation. We investigated a Deep Learning Artificial Intelligence model with a proprietary deep convolutional neural network (DCNN) for the computer-assisted NICE type 1&2 differentiation. We designed a 5-class model representing Types 1, 2, and unsuitable (frames without statistically representative information–blur, bubbles, liquid). The model operated at the individual frame level, without prior segmentation. For model training purposes, each frame was manually tagged. The final dataset was split into training and validation sets, without overlap. Finally, the analysis was performed separately for NBI and WL frames, allowing for reporting of frame processing time and classification performance.

Results: A total of 33,954 training frames were used, split equally across NBI & WL, and type 1, type 2, & unsuitable classes. We performed a 5-fold cross-validation on the tagged frames for quality control. The trained DCNN model was then used to evaluate the unaltered videos in real-time, with an accuracy for polyp classification of 90% for NBI, and 83% for WL. The confusion matrix on whole-video classification of colorectal polyps gives a sensitivity of 93% and specificity of 85% for NBI. Finally, the processing time of our DCNN model ran at between 25 and 30 frames per second (fps) using a decent gamer-grade GPU (NVIDIA Titan-X) on an unaltered video feed of 60 fps, delivering near-realtime computer support.
Conclusion: To our knowledge, this is the first application of deep learning to the optical biopsy challenge for polyp differentiation into NICE types 1&2 using non-magnification colonoscopy and NBI, specifically in a clinically representative workflow where computer support is provided in realtime on unaltered endoscopic video streams. Although the present investigation was carried on a limited datasets of 92 videos, our deep learning model has shown clinically efficient and relevant performance for optical biopsy, well aligned with PIVI guidelines and the performance of experts. Ongoing work will determine if such a computer support solution could aid in the widespread adoption of a “resect and discard” strategy, and reduce the economic burden of pathological evaluation of benign diminutive colon polyps.

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<table>
<thead>
<tr>
<th>Age, mean (SD), y</th>
<th>48 (7)</th>
<th>48 (7)</th>
<th>50 (17)</th>
<th>52 (14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women, n (%)</td>
<td>5 (63)</td>
<td>5 (46)</td>
<td>19 (54)</td>
<td>17 (53)</td>
</tr>
<tr>
<td>Body mass index, mean (SD), kg/m²</td>
<td>22.6 (3.6)</td>
<td>23.3 (4.1)</td>
<td>22.2 (3.1)</td>
<td>22.2 (2.8)*</td>
</tr>
<tr>
<td>Stoma present, n (%)</td>
<td>7 (88)</td>
<td>11 (100)</td>
<td>10 (29)</td>
<td>10 (32)*</td>
</tr>
<tr>
<td>Colon-in-continuity, n (%)</td>
<td>1 (13)</td>
<td>1 (9)</td>
<td>22 (63)</td>
<td>24 (77)*</td>
</tr>
<tr>
<td>Estimated small bowel length, mean (SD), cm</td>
<td>128 (98)</td>
<td>129 (77)*</td>
<td>54 (43)*</td>
<td>73 (56)*</td>
</tr>
<tr>
<td>Baseline PS, mean (SD), L/wk</td>
<td>21.6 (8.1)</td>
<td>15.9 (10.4)</td>
<td>11.5 (5.9)</td>
<td>11.2 (6.4)*</td>
</tr>
<tr>
<td>Baseline PS duration, mean (SD), y</td>
<td>7.2 (7.4)</td>
<td>8.1 (8.0)</td>
<td>5.6 (5.3)</td>
<td>6.1 (5.7)*</td>
</tr>
</tbody>
</table>

*n = 31, 1n = 9, 2n = 32, 3n = 30.