A critical stricture were randomised to infliximab or laparoscopic ileocecal resection. Between May 2008 and October 2015, 143 patients were randomised to infliximab or laparoscopic ileocecal resection. The primary endpoint was QoL measured according to intention-to-treat until one year after start of treatment. Dutch Trial Registry NTR1150.

Between 5 months of thiopurine treatment or steroids without signs of a critical stricture were randomised to infliximab or laparoscopic ileocecal resection. Patients with a prior ileocecal resection, a disease length > 40 cm, abdominal abscesses or fluid collections or an American Society of Anaesthesiologists (ASA) score of III or IV were excluded. The primary endpoint was QoL measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) at one year follow-up. Furthermore, the mean direct costs per individual patient were prospectively documented and analysed according to intention-to-treat until one year after start of treatment. Dutch Trial Registry NTR1150.

Results: Between May 2008 and October 2015, 143 patients were randomised (32.9% male) with a median age of 27.0 years (interquartile range (IQR) 22.0–40.0). Eventually, 65 patients started with infliximab treatment and 70 patients were operated. On April 28th 2016, 96.5% of the patients have completed follow-up. On April 28th 2016, 96.5% of the patients have completed follow-up. The mean direct costs per individual patient were prospectively documented and analysed according to intention-to-treat until one year after start of treatment.

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

Conclusion: Our aim was to assess the functional integration of transplanted ENSC within recipient nNOS−/− colon. Initially, donor ENSC were obtained from Wnt1-cre;YFP transgenic mice allowing specific fluorescent labeling. FACS selection and fate mapping of cells. YFP+ ENSC were transplanted to nNOS−/−distal colon at postnatal day (P)14. Subsequently, integration and functionality were assessed using immunolabelling and organ bath physiology after 8 weeks.

Results: After 1 month, YFP+/nNOS+ neurons were identified and transcriptional analysis showed specific expression of nNOS in recipient nNOS−/− colon. In NANC (non-adrenergic non-cholinergic) conditions, organ bath physiology revealed significant increases in electrical field stimulation (EFS)-induced relaxation (Area under curve;AUC) in transplanted nNOS−/− (−1.13±0.16 g.s, n=5) compared with both C57BL/6J (8.1±0.68 g.s, n=5; P=0.0016) and sham-operated nNOS−/− (1.0±0.05 g.s, n=5). In transplanted colon segments, addition of the nitric oxide synthase blocker L-NAME resulted in significant reductions in the observed EFS-induced relaxation (−0.74±0.17 g.s vs. −0.12±0.16 g.s, n=4; P=0.0389) demonstrating restoration of nitrergic responses after transplantation. Interestingly, significant increases in basal contractile amplitude were also observed in transplanted nNOS−/−colonic segments (0.30±0.06 g.s, n=5) compared with both C57BL/6J (0.1±0.01 g.s, n=5; P=0.0093) and non-transplanted nNOS−/− mice (0.05±0.008 g.s, n=5; P=0.0025). These high-amplitude contractions were unaffected by application of tetrodotoxin, suggesting that transplantation of ENSC can also lead to changes in underlying myogenic motility patterns. To assess the mechanisms involved in these non-cell autonomous phenomena we sought to investigate potential changes in gut morphology. No significant change was observed in the diameter of the distal colon between transplanted nNOS−/− mice (1.04±0.135 mm; n=3) compared to either non-transplanted nNOS−/− mice (1.12±0.686 mm; n=3; P=0.069) or sham-operated nNOS−/− (1.05±0.022 mm; n=3; P=0.947). In addition, no change in muscle thickness was observed between transplanted nNOS−/− mice (55.33±8.67 μm; n=3) compared to either non-transplanted nNOS−/− (54.0±8.9 μm; n=3; P=0.915) or sham-operated nNOS−/− (54.33±2.96 μm; n=3; P=0.918). Ongoing work is targeting other potential processes such as modification of cell types involved in neuromuscular signalling, including interstitial cells of Cajal within the transplanted microenvironment.

Disclosure of Interest: All authors have declared no conflicts of interest.
OPP003 MULTIVARIATE MODELLING OF GUT MICROBIAL PROFILES PREDICTIVE OF SUCCESS TO A DIET LOW IN FODMAPS

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Introduction: Dietary interventions may be recommended to IBS patients yet effects on gut microbiota and factors predicting response are largely unknown.

Aims & Methods: We aimed to determine how two different diets affect gut microbiota and if bacterial profiles and modelling thereof could be used to predict patient intervention response in a secondary analysis of a previously published multicenter randomized 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 assigned a reduction of IBS-SSS >50 after the intervention. Faecal bacterial composition was evaluated by GA-map™ Dysbiosis Test which measures probe signal intensity (PSI) of 54 DNA probes targeting ≥300 bacteria on different sites and classes, respectively. The normalized scores were analyzed by multivariate discrimination analysis and graded from 1–5, relative to a healthy reference group. A dysbiosis index (DI) ≤3 signifies normal microbiota composition; ≤5 signifies altered microbiota composition (dysbiosis). For all models, both strong and moderate outliers were sequentially excluded.

Results: At baseline, 45 patients (25 randomized to traditional diet and 20 to low-FODMAP) had a DI ≥3, i.e. dysbiosis; of these, 10 patients following the traditional diet and 9 following the low-FODMAP diet experienced an improvement in DI, while 6 following the traditional diet and 11 on the low-FODMAP diet had worsening of their dysbiosis; the rest experienced no change. In the low-FODMAP group, all but one patient was on a traditional diet group, non-responders (n=19) had more severe dysbiosis than responders (n=12) (3 (3–4) DI; 2 (2–3) DI; p=0.007) at baseline. Although patients on a traditional diet consumed significantly less protein, fat and alcohol, they experienced no change in overall bacterial composition after the intervention. Patients on a low-FODMAP diet ate significantly less carbohydrates, fibre, mono- and disaccharides, fructose and total FODMAPs, and had significant reduction in potentially beneficial Bifidobacterium after the intervention. A statistical model of the traditional diet group was inadequate, showing good model fit but was not able to separate responders from non-responders (χ2 ¼ 31.6, p=0.0005) which was even more prominent in non-responders. An OPLS-DA model of the before the low-FODMAP intervention demonstrated satisfactory model discrimination, i.e. patients randomized to the low-FODMAP diet had completely different faecal bacterial profiles, whereas patients randomized to the traditional diet did not. Among these patients, clinical remission and clinical response were observed in 51 (39%), 29 (23%), and 28 (22%) patients in the PBO, q12w and q8w groups, respectively. Of 467 patients not in response at the end of induction, 21 patients (41%) as compared with 23 patients (49%) in the surgical step-up group did not need necrosectomy after drainage as first step of treatment (risk ratio 0.84: 95% CI 0.65 to 1.31, P=0.43). There was a lower incidence of pancreatic fistula (5% versus 32%; P=0.001) and length of hospital stay was shorter (median 36 days versus 69 days; P=0.03) in the endoscopic group. Furthermore, the difference in total mean costs was US$3655 (19%, BCa 95% CI -10836–35782) in favour of the endoscopic group.

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

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

MONDAY, OCTOBER 17, 2016
10:30-12:00
ESTABLISHED AND NEW DRUGS IN IBD – ROOM B

OPP005 EFFICACY AND SAFETY OF DOSE ADJUSTMENT IN IBD: A RELAYED RESPONSE TO USTEKINUMAB IN ADJUNCTIVE TREATMENT OF SEVERE CROHNS DISEASE PATIENTS: RESULTS FROM THE UST-IMUNITI MAINTENANCE STUDY

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Introduction: Ustekinumab (UST) has been shown to induce and maintain clinical response and remission in moderate to severe Crohn’s disease (CD) in 2 induction (UNITI-I and 2) and 1 maintenance (IM-UNITI) randomized, placebo controlled Phase 3 trials. We evaluated the efficacy of UST in 2 additional groups in IM-UNITI: patients who underwent dose adjustment following loss of response (LOR) and patients who did not have a clinical response to IV UST during induction and had an additional subcutaneous (SC) dose.

Aims & Methods: Patients achieving clinical response after single dose IV induction (PBO, q12w, q8w, q4w) and patients who did not have a clinical response to IV UST induction (PBO) were either dose adjusted to SC UST q12w or q8w or maintained on their induction dose. Patients who met LOR criteria, defined as a CDAI score of ≥220 and ≥100 point increase from the maintenance baseline CDAI score, were dose adjusted after week 8 of the induction phase. UST patients not in response at week 8 after the IV induction dose were given SC UST 90 mg and if in clinical response in week 8 were continued on q12w dosing. UST patients not in clinical response in week 8 after the IV induction dose were either continued on q12w or dose adjusted as follows: PBO→q8w, q12w→q8w, and q8w→q8w (no dose adjustment) and were assessed for clinical response (≥100 point decrease in CDAI) and clinical remission (CDAI <150) 16 weeks later. Separately, UST patients not in clinical response 8 weeks after the IV induction dose were given SC UST 90 mg and if in clinical response 8 weeks later were continued on q12w dosing. UST patients not in clinical response 8 weeks after the IV induction dose were either continued on q12w or dose adjusted as follows: PBO→q8w, q12w→q8w, and q8w→q8w (no dose adjustment) and were assessed for clinical response (≥100 point decrease in CDAI) and clinical remission (CDAI <150) 16 weeks later. Separately, UST patients not in clinical response 8 weeks after the IV induction dose were given SC UST 90 mg and if in clinical response 8 weeks later were continued on q12w dosing.

Results: 51 (39%), 29 (23%), and 26 (22%) patients in the PBO, q12w and q8w groups, respectively, underwent dose adjustment after meeting LOR criteria. Among these patients, clinical remission and clinical response were observed in 39% and 71% of patients adjusting 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-I/2, 59.5% and 28.9% were in clinical response and remission 8 weeks after one additional UST dose (90 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 observed in patterns of adverse events were 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 Adjustment</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>UST q12w→UST q8w</td>
<td>55%</td>
<td>41%</td>
</tr>
<tr>
<td>UST q8w→UST q8w</td>
<td>46%</td>
<td>32%</td>
</tr>
</tbody>
</table>

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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.


OP006 VEDOLOZUMAB EXPOSURE CORRELATES WITH CLINICAL, BIOLOGICAL AND ENDOSCOPIC OUTCOME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE
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Introduction: Vedolizumab (VDZ) specifically targets the α4β7 integrin on gut-homing lymphocytes and has been approved for the treatment of patients with moderate to severe Crohn’s disease (CD) and ulcerative colitis (UC). We studied the relation between serum VDZ trough concentrations (TC) and clinical, biological and endoscopic outcomes in real-life practice.

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

Primary outcome was the comparison of week 6 levels in patients with or without clinical remission at the same time-point. Association of week 2 and week 6 levels with week 14 clinical remission was also sought, as well as association of trough levels with inflammatory markers (Albumin and C-reactive protein, CRP).

Results: Seventy-two patients were included (47 CD, 25 UC), of which 14 (30%) and 15 (32%) of CD patients and 6(25%) and 8 (32%) of UC patients reached clinical remission at week 6 and 14, respectively. The median level of vedolizumab at week 6 was not different between patients who achieved remission by week 6 and those who did not (37.3 vs. 29.4 μg/ml respectively, p=0.43). Clinical remission rates at week 6 were also not associated with drug level quartiles at week 6. Similarly, neither week 2 or 6 levels were predictive of clinical remission at week 14 (35.4 vs. 44.8 μg/ml, p=0.75, 33.9 vs. 25.5 μg/ml, p=1, respectively). Vedolizumab levels were also not associated with steroid free remission (p=0.1, p=0.57) or with CRP normalization (p=0.26, p=0.73) at weeks 6 and 14, respectively. Among UC patients separately analyzed, week 2 levels were associated with clinical remission at week 14 (p=0.04). However, statistical significance for this difference was not retained after Bonferroni correction for multiple testing. Finally, multivariable analysis for clinical remission at week 6 has been performed including baseline albumin level and patient weight. When adjusting for these co-variates, week 6 vedolizumab levels were not associated with clinical remission at week 6 (p=0.56).

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. Eliakim: Prof. Eliakim has received consulting and lecture fees from Takeda, Janssen. Prof. Eliakim has received consulting and/or advisory board fees from Janssen, Takeda, Celltrion, Abbvie, & Schering-Plough and research support from Celltrion and Abbvie.

All other authors have declared no conflicts of interest.

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

<table>
<thead>
<tr>
<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>
</tr>
<tr>
<td>w6**</td>
<td>33.2 [21.8–38.5] (23)</td>
</tr>
<tr>
<td>w10***</td>
<td>37.9 [24.4–45.1] (15)</td>
</tr>
<tr>
<td>w14**</td>
<td>25.8 [16.3–39.2] (22)</td>
</tr>
<tr>
<td>w22**</td>
<td>16.1 [9.5–25.2] (23)</td>
</tr>
</tbody>
</table>

"p<0.05; **p<0.01; ***p<0.001. Endoscopic healing was achieved in 65% (15/20) of patients with UC. Patients with endoscopic healing had significantly higher VDZ TC at w6 (30.5 μg/mL [18.6–38.0]), compared to patients who did not achieve endoscopic healing (16.6 μg/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 μg/mL [22.3–37.1], n=16) and w6 (32.0 μg/mL [17.6–37.7], n=16) compared to absence of clinical response (21.6 μg/mL [16.0–25.2] and 16.6 μg/mL [11.0–20.6], resp., n=7) (p=0.03 and p=0.02).
"Kingdom (UK) aged proportions of patients do not respond to therapy or lose response over time.

Introduction: Tumour necrosis factor antagonists (anti-TNFs) are effective at severe ulcerative colitis (UC) or Crohn’s disease (CD). However, considerable

Patients with ulcerative colitis the baseline period were used.

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

Results: 195,834 individuals were diagnosed with IBD (Crohn’s disease (CD), 106 436 (31,353 incident patients); ulcerative colitis (UC), 89,398 (27,578 incident patients). Among incident patients treated with thiopurines or anti-TNFs (17 566 CD and 8035 UC patients), the first treatment was thiopurines, anti-TNFs monotherapy, and combination therapy in 69.1%, 24.8% and 6.1% of CD patients and 78.5%, 17.7% and 4.1% of UC patients, respectively. Subsequently, 36.8% and 20% of CD patients were exposed to anti-TNFs monotherapy and combination therapy, respectively, 5 years after diagnosis. More than 25% of CD and UC incident patients included between 2009 and 2012 withdrew thiopurines or anti-TNFs, during more than three months after a first treatment course. Drug withdrawal was related to hospitalization or surgical procedures in less than 30% of these patients. Nearly 50% of CD patients and 40% of UC patients went back to their initial treatment after withdrawal. Around 5% of CD patients and 4% of UC patients stopped all IBD therapy during follow-up. Five years after diagnosis, the cumulative risks of first intestinal resection in CD, and colectomy in UC were 12.8% and 3.5%, respectively.

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

Disclosure of Interest: F. Carbonnel: Franck Carbonnel had consulting fees for Genentech, Otsuka, Vifor, and lecture fees for Hospira. All other authors have declared no conflicts of interest.

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

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ulcerative colitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal Bleeding (Reference: None)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>- Passing blood alone</td>
<td>0.24 (0.06–0.97)</td>
<td>0.04</td>
</tr>
<tr>
<td>- Passing blood with stool ≥50% of time</td>
<td>0.35 (0.19–1.9)</td>
<td></td>
</tr>
<tr>
<td>- Passing blood with stool &lt;50% of time</td>
<td>0.17 (0.05–0.62)</td>
<td>0.02</td>
</tr>
<tr>
<td>Endoscopic Findings (Reference: Inactive; Mild)</td>
<td>3.19 (1.14–9.87)</td>
<td></td>
</tr>
<tr>
<td>- Moderate</td>
<td>4.86 (1.61–14.7)</td>
<td></td>
</tr>
<tr>
<td>Patients with Crohn’s Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Liquid or Soft Stools per Day</td>
<td>1.12 (1.00–1.24)</td>
<td>0.04</td>
</tr>
<tr>
<td>C-reactive Protein (CRP)</td>
<td>1.02 (1.00–1.03)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

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

Conclusion: In this cohort the majority of patients did not respond or lost response to anti-TNF therapy over time. Predictors for patients with UC included the absence of rectal bleeding and moderate/severe endoscopic scores, and for patients with UC included CRP higher and number of liquid or soft stools per day. These predictors should be considered when evaluating treatment options for patients.
Aims & Methods: Univariate analyses of the type of follow-up clinic and anti-TNF treatment to reach sustained remission compared to sustained remission. Percentages of infliximab and adalimumab use were similar in both groups, including in the group failing sustained remission. There were no differences between age, was defined as inactive disease for Of 66 anti-TNF exposed patients (median (IQR) age 13.1 (11.5–15.2) yrs, Results: Variable, number (%)

<table>
<thead>
<tr>
<th>Variable</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 infiximab</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 infiximab</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), treatment failure in 5 years (91% vs. 24%; p < .05) were associated with failure to reach sustained remission. Both colonic disease and adult follow-up (AUC = 66; both p < .04) correlated with average disease severity (no correction for multiple testing). No other correlations were found.

Conclusion: Patient phenotype at diagnosis does not predict failure to reach sustained remission despite anti-TNF exposure. Mild disease may not trigger appropriateigg, is defined as inactive disease for OP010 CHARACTERISTICS OF CHILDREN WITH CROHN'S DISEASE United European Gastroenterology Journal 4(5S)

Disclosure of Interest: E. Funds: None communicated F. Fontaine: None communicated M. De H. Peeters: None communicated P. Baert: None communicated S. Vermeiren: Grant from MSD to Bespghan. Advisory board Abbvie, MSD, Takeda, Pfizer, Galapagos, Genentech/Roche, Mundipharma, Celgene, Hospira, Second Genome. G. Veereman: Grant from MSD to Bespghan. Advisory board Janssen and Boehringer Ingelheim. Consulting Mead Johnson. All other authors have declared no conflicts of interest.

Aims & Methods: Their first Health check-up persons, who underwent compre-
sensive screening including endoscopy and H. pylori test from 2003 to 2013, were
evered. 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
peptic ulcers were detected. In adjusted analysis, age (OR 1.06, 95% CI
1.04–1.08) and current infection of H. pylori (OR 2.39, 95% CI 1.53–3.74)
first degree relatives with gastric cancer (OR 2.08, 95% CI 1.30–3.32), and
high glucose (OR 1.66, 95% CI 1.04–2.65) increased the risk of gastric cancer, whereas
high HDL (≥60 mg/dL) reduced the risk of gastric cancer (OR 0.49, 95% CI
0.22–0.94). In case of H. pylori infection, age was a common risk factor of gastric.
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 gastric cancer 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.

MAYDAY, Thursday 17, 2016
8:00–12:00
AN UPDATE ON THE MANAGEMENT OF HEPATOCELLULAR CARCINOMA
– ROOM G –

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 compre-
sensive 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
peptic ulcers were detected. In adjusted analysis, age (OR 1.06, 95% CI
1.04–1.08) and current infection of H. pylori (OR 2.39, 95% CI 1.53–3.74)
first degree relatives with gastric cancer (OR 2.08, 95% CI 1.30–3.32), and
high glucose (OR 1.66, 95% CI 1.04–2.65) increased the risk of gastric cancer, whereas
high HDL (≥60 mg/dL) reduced the risk of gastric cancer (OR 0.49, 95% CI
0.22–0.94). In case of H. pylori infection, age was a common risk factor of gastric.
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 gastric cancer 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.

References
1. Kang T. W., Yevsa T., Wolfer N., Hoenicke L., Wuestefeld T., Dauch D.,
2. Yildir G., Arslan-Ergul A., Bagislar S., Konu O., Yuzugullu H., Gursoy-
Yuzugullu O., Orturk N., Oren C., Orduz H., Erdal E., et al. Genome-wide transcriptional reorganization associated with senescence-to-immortality
switch during human hepatocellular carcinogenesis. PLoS One 2013; 8:
e64016.
Aims & Methods: The study aimed to evaluate the characteristics of NL-LSL and the safety and efficacy of endoscopic treatment by Cold Forcesps 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 (ERIE effect 4, 80W). Scheduled surveillance colonoscopy was performed at 5 months (SC1) and 18 months (SC2) post the index procedure. The primary outcome was endoscopic and histological evidence of adenoma clearance. The secondary outcome was safety. 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 colol) were referred for WF-EMR. 33 lesions were excluded due to suspicion for submucosal invasive cancer and the patients referred for surgery. EMR was performed on 83 NL-LSL and 664 standard LSL. 14 lesions were excluded at initial EMR as a two-stage procedure was required for their resection. Key comparisons between NL-LSL and standard LSL are presented in table 1. PANL-LSL (n = 33) were smaller and more likely to be non-granular (62.5 versus 33.9%, p = .003) than standard LSL. NNL (n = 50) were also more likely to be non-granular (46 versus 33.9%, p = .12) and were associated with previous biopsy (32 vs 13.8%, p = .001) and carbon particle suspension injection within 10 mm of the lesion (26 vs 3.8%, p < .001). Neither intra-procedural bleeding nor deep injury were more common in NL-LSL treated with CFA and STSC. The technique was technically successful in all cases. One perforation was recognised secondary to CFA in a previously attempted lesion and was successfully closed with endoscopic clips with no sequelae. Endoscopic recurrence at SC1 was not significantly different for PANL-LSL treated with CFA and STSC than LSLs treated with complete snare excision, whereas NNL-LSL recurred more frequently (16.0 vs 12.2%, p = .578 and 28.2 vs 12.2%, p = .005 respectively).

Conclusion: CFA and adjunctive 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.

Abstract No: OP015

Table I: lesions where cold forcesps 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, ICC – ileocolic 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>
<th>p</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>
<td>.578</td>
</tr>
<tr>
<td>Male, (%)</td>
<td>18 (54.5)</td>
<td>.598</td>
<td>29 (58.0)</td>
<td>.266</td>
<td>324 (49.8)</td>
<td>.966</td>
</tr>
<tr>
<td>Lesion</td>
<td></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>
<td>.578</td>
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<tr>
<td>Morphology (%)</td>
<td></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>
<td>.001</td>
</tr>
<tr>
<td>Non granular</td>
<td>20 (62.5)</td>
<td>.910</td>
<td>23 (46.0)</td>
<td>209 (33.9)</td>
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<td></td>
</tr>
<tr>
<td>Unclassified</td>
<td>4 (12.5)</td>
<td>.509</td>
<td>5 (10.0)</td>
<td>85 (13.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location (%)</td>
<td></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>
<td>.001</td>
</tr>
<tr>
<td>Splenic to sigmoid</td>
<td>6 (18.8)</td>
<td>.125</td>
<td>11 (23.9)</td>
<td>.300</td>
<td>98 (15.2)</td>
<td></td>
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<tr>
<td>Transverse</td>
<td>5 (15.6)</td>
<td>.307</td>
<td>14 (28.0)</td>
<td>132 (20.5)</td>
<td></td>
<td></td>
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<tr>
<td>Ascending and caecum (+ICV)</td>
<td>10 (31.3)</td>
<td>.578</td>
<td>15 (32.6)</td>
<td>294 (45.6)</td>
<td></td>
<td></td>
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<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>
<td></td>
</tr>
<tr>
<td>Previous attempt at resection (%)</td>
<td>33 (100)</td>
<td>&lt;.001</td>
<td>0 (0)</td>
<td>.030</td>
<td>56 (8.7)</td>
<td></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>
<td></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>
<td></td>
</tr>
<tr>
<td>Histopathology (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Conventional adenoma</td>
<td>25 (75.8)</td>
<td>.324</td>
<td>44 (90.0)</td>
<td>.147</td>
<td>482 (77.5)</td>
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<tr>
<td>Serrated adenoma</td>
<td>2 (6.4)</td>
<td>.815</td>
<td>4 (10.0)</td>
<td>135 (21.7)</td>
<td></td>
<td></td>
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<tr>
<td>Cancer</td>
<td>0 (0)</td>
<td></td>
<td>0 (0)</td>
<td>4 (0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0 (0)</td>
<td></td>
<td>0 (0)</td>
<td>1 (0.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration, minutes, median (IQR)</td>
<td>35 (18-45)</td>
<td>.004</td>
<td>25 (15–40)</td>
<td>.003</td>
<td>20 (10–30)</td>
<td></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>
<td></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>
<td></td>
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<tr>
<td>Outcomes</td>
<td></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>
<td></td>
</tr>
</tbody>
</table>
**OP018 THERMAL ABATION OF THE MARGIN OF THE POST ENDOSCOPIC MUCOSAL RESECTION (EMR) MUCOSAL DEFECT:**

**SCAR Study**

A. Klein1, V. Jayasekaran1, L. Hourigan2, D. J. Tate3, R. Singh4, G. Brown5, F. Bahin6, N. Burgess7, S. J. Williams8, E. Lee9, M. J. Bourke9

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

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

**Aims & Methods:** A prospective multi-center randomized control study was performed (NCT01789749). The primary end-point was endoscopic and histological recurrence at SC1. Standard inspect and resect EMR technique was used for all lesions. Exclusion criteria included previously attempted lesions, incomplete snare excision or involvement of the ileocecal valve. After successful complete LSLS excision by EMR and careful inspection of the defect to ensure no residual adenoma, mucosal defects were randomized 1:1 to either thermal ablation of the defect edges (using STSC) or sham (SC1). Endoscopic and histologic recurrence rates at SC1 were significantly lower in the active arm (8/124 (6.5%) versus 26/129 (20.2%), p = 0.002, relative risk (RR) = 0.29 (95% CI: 0.14–0.61) and 6/104 (5.8%) versus 20/97 (20.6%), p = 0.002, RR = 0.28 (95% CI: 0.12–0.67) respectively) (Table 1). Endoscopic assessment of the post EMR scar had a sensitivity of 100%, a specificity of 98% and a negative predictive value of 100% for correctly identifying recurrence when compared to histology results. There was no difference in the rate of delayed bleeding between the active and null groups (8/124 (6.5%) versus 9/136 (6.6%), p = 0.957) and no difference in delayed perforation (0/124 (0%) versus 1/136 (0.7%), p = 0.341).

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

<table>
<thead>
<tr>
<th>Endoscopic recurrence (95% CI)</th>
<th>Null arm</th>
<th>Active arm</th>
<th>RR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopic recurrence (95% CI)</td>
<td>26/129 20.2%</td>
<td>8/138 5.8%</td>
<td>0.29</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>(14.1–27.9%)</td>
<td>(2.9–11.0%)</td>
<td>(1.04–0.61)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histological recurrence (95% CI)</td>
<td>20/97 20.6%</td>
<td>6/104 5.8</td>
<td>0.28</td>
<td>0.002</td>
</tr>
<tr>
<td>(13.8–29.7%)</td>
<td>(2.7–12.0%)</td>
<td>(0.12–0.67)</td>
<td></td>
<td></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.
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 years, range: 19–100 years) in March 2016. We compared 57 lesions performed using hemoclips with 170 lesions treated with the twin-grasper. The hemoclip 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 superficial type, 22 (9.7%) LSTs of the submucosal type, 48 (21.1%) polypoid lesions. Histological examination findings showed that 102 lesions (44.9%) were intramucosal carcinomas, 22 (9.7%) were shallow submucosal invasive carcinomas (<1,000 µm), 25 (11.0%) were deep submucosal invasive carcinomas (>1,000 µm), and 78 (34.4%) were tubular adenomas. The mean size of the resected tumors was 32.0 ± 14.9 mm, and the median procedure time was 76.5 minutes (range: 10–420 minutes). The rates of en bloc resection, histological complete resection, and R0 resection were 98.2% (223/227 lesions), 93.8% (222/237 lesions), and 98.2% (227/232 lesions), respectively, and 98.2% (222/237 lesions), 93.8% (213/227), and 85.0% (193/227), respectively. All lesions were treated easily and safely without an unexpected incision, and no perforations occurred during the procedure. Delayed perforations and rectal stricture occurrence rate were 3.8% (6/227), 0.4% (1/227), and 0.4% (1/227) of the lesions, respectively, and all of these complications were cured conservatively. The median follow-up time was 35 months (range, 18–976 days). Local recurrence was observed in only 0.8% of the lesions (2/227). One patient (0.5%) died of colorectal cancer, and 5 patients (2.3%) died of other diseases. The 5-year overall survival rate and disease-specific survival rate were 94.8% and 98.7%, respectively.

Conclusion: ESD performed with an SB knife Jr is a technically efficient and safe method that is associated with favorable long-term outcomes in cases of early colorectal neoplasms.

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

References

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

References

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

References
It is important to highlight that only one session of Spyglass + EHL was performed in each patient of our protocol. Better success rates can be achieved with two or more sessions and increase up to 90%. Cross-over of the failure cases in both groups is bringing us a very interesting result and suggests that in some cases the methods can be complementary. There was no statistical difference between the groups, although the Spyglass group had numerically a little higher success rate. The study provides us an evidence-based algorithm of difficult stenosis 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

MONDAY, OCTOBER 17, 2016 10:30–12:00
PREVENTION OF GI CANCERS: NUTRITION AND CHEMOPREVENTION – ROOM 1.61/1.51
OP023 CD24 INDUCES THE ACTIVATION OF B-CAracTENIN 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 WT 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. Apo Min and Cd24 knockout (KO) mice, both on a C57BL/6J genetic background, were crossed to generate double KO transgenic mice. Genotypes were routinely verified by analysis of DNA extracted from tail biopsies. Small and large bowel polyps were counted macroscopically following methylene blue staining and histology was verified microscopically. Colonic polyps were measured and counted
BUT PROTECTS FROM COLORECTAL TUMOUR FORMATION

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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 gastrointestinal (GI) tract. This 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 transduodenal 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 accessed 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 nitinol with increased flexibility (1). Aims & Methods: 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 selected. EUS-FNA was performed with the 19-gauge flexible needle (Expect™ 19 Flex and Slimline Expect™ 19 F) 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, with an overall good performance of 76.8%. 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 acute pancreatic edema, one perforation that required surgery, and one duodenal hematoma that resolved spontaneously. Considering malignant vs. non-malignant disease, the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic accuracy were 70.7% (95% CI, 63.4–76.6), 100% (95% CI, 79.6–100), 35.3 (95% CI, 2.3–54.9), 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 where 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 needle for transduodenal EUS-FNB. Thus, the current recommendation is 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 improving as expected with the use of an experienced endoscopist. In conclusion, our results suggest...
Comparison of procedure outcomes according to needle size and use of suction

<table>
<thead>
<tr>
<th>ROSE-Diagnostic adequacy: n (%)</th>
<th>22G No Suction (n = 88)</th>
<th>22G Suction (n = 88)</th>
<th>25G No Suction (n = 85)</th>
<th>25G Suction (n = 91)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of passes for onsite diagnostic adequacy</td>
<td>Mean (SD)</td>
<td>1.8 (1.5)</td>
<td>2.8 (2.7)</td>
<td>1.7 (1.5)</td>
<td>2.0 (2.2)</td>
</tr>
<tr>
<td>Specimen bloodiness: n (%)</td>
<td>Mild</td>
<td>52 (59.1)</td>
<td>32 (36.4)</td>
<td>55 (64.7)</td>
<td>43 (47.3)</td>
</tr>
<tr>
<td>Moderate</td>
<td>20 (22.7)</td>
<td>34 (38.6)</td>
<td>20 (23.5)</td>
<td>30 (33.0)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>16 (18.2)</td>
<td>22 (25.0)</td>
<td>10 (11.8)</td>
<td>18 (19.8)</td>
<td></td>
</tr>
<tr>
<td>ROSI-Diagnostic performance: % (95% CI)</td>
<td>Accuracy</td>
<td>98.9 (93.8–100)</td>
<td>92.6 (83.7–97.6)</td>
<td>97.1 (89.9–99.7)</td>
<td>98.8 (95.3–99.7)</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>100 (75.1–99.9)</td>
<td>95.0 (71.5–99.9)</td>
<td>100 (79.4–100)</td>
<td>100 (58.7–99.8)</td>
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<tr>
<td></td>
<td>PPV</td>
<td>98.6 (92.7–100)</td>
<td>98.4 (91.6–100)</td>
<td>99.0 (94.6–100)</td>
<td>98.8 (93.2–100)</td>
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<tr>
<td></td>
<td>NPV</td>
<td>90.0 (76.8–100)</td>
<td>79.2 (57.8–92.9)</td>
<td>88.9 (65.3–98.6)</td>
<td>90.9 (58.7–99.8)</td>
</tr>
<tr>
<td>Diagnostic cell block: n (%)</td>
<td>71 (80.7)</td>
<td>63 (71.6)</td>
<td>56 (65.9)</td>
<td>67 (73.6)</td>
<td>0.177</td>
</tr>
<tr>
<td>EUS-FNA-Diagnostic Performance: % (95% CI)</td>
<td>Accuracy</td>
<td>98.9 (93.8–100)</td>
<td>92.6 (83.7–97.6)</td>
<td>98.8 (93.6–100)</td>
<td>98.9 (94.0–100)</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>100 (75.1–99.9)</td>
<td>95.0 (71.5–99.9)</td>
<td>100 (79.4–100)</td>
<td>100 (71.5–99.8)</td>
</tr>
<tr>
<td></td>
<td>PPV</td>
<td>98.6 (92.7–100)</td>
<td>98.4 (91.6–100)</td>
<td>100 (94.7–100)</td>
<td>100 (95.4–100)</td>
</tr>
<tr>
<td></td>
<td>NPV</td>
<td>93.8 (69.9–99.8)</td>
<td>78.2 (57.8–92.9)</td>
<td>94.1 (71.3–99.9)</td>
<td>91.7 (61.5–99.8)</td>
</tr>
<tr>
<td>Technical failure: n (%)</td>
<td>5 (5.7)</td>
<td>5 (5.7)</td>
<td>1 (1.2)</td>
<td>7 (7.7)</td>
<td>0.179</td>
</tr>
<tr>
<td>Adverse events: n (%)</td>
<td>4 (4.5)</td>
<td>3 (3.4)</td>
<td>7 (8.2)</td>
<td>10 (11.0)</td>
<td></td>
</tr>
</tbody>
</table>

that the use of the 19-gauge flexible needle for transduodenal FNB cannot be<br>warranted due to a high level of tissue oversampling, particularly with 22G needles.

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

All other authors have declared no conflicts of interest.

References

OP026 RANDOMIZED TRIAL COMPARING THE 22 AND 25 GAUGE NEEDLES USING THE SUCTION-IN AND NO-SUCTION (SENS) TECHNIQUES FOR EUS-GUIDED FNA OF PANCREATIC MASSES

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Introduction: Prior studies comparing the 22 and 25G needles and utility of suction during EUS-FNA have yielded conflicting results. The primary aim of this study was to evaluate the impact on patient heterogeneity and small sample size. Also, the optimal tissue acquisition technique for onsite and offsite specimen assessment is unclear.

Aims & Methods: We aimed to compare the 22 and 25G needles and evaluate the role of suction in EUS-FNA of pancreatic masses. Methods: Consecutive patients with solid pancreatic masses were randomized to 1 of 4 cohorts: 22G needle with suction, 22G needle without suction, 25G needle with suction and 25G needle without suction. After two dedicated passes were performed for cell block (offsite) evaluation, an experienced pathologist rendered rapid onsite evaluation (ROSE) for specimen adequacy. Cross-over to alternate arms was permitted if ROSE was indeterminate at 8 passes. Diagnostic accuracy of ROSE was confirmed by final pathology interpreted by a second independent pathologist.

Final diagnosis was established by surgical pathology or patient follow-up at 12 months. Main outcome measures were to compare diagnostic adequacy and accuracy of ROSE, number of passes to establish onsite diagnostic adequacy, specimen bloodiness, diagnostic accuracy of cell block and operating characteristics between cohorts. To detect a 15% difference in diagnostic accuracy and cell block yield between the type of needles and use of suction at 80% power and type I error of 0.05, the total sample size was estimated at 352 patients.

Results: The median age of 352 patients was 69 years, 54.3% male, median size of mass was 3cm with vascular invasion in 55.4% and FNA passes were transduodenal in 68.5%. The final diagnosis was adenocarcinoma or other malignancy in 290 (82.4%) and benign or chronic pancreatitis in 62 (17.6%) patients. Interim analysis pending completion of 12-month follow-up is shown in the Table.

Conclusion: While there was no overall difference in operating characteristics between the 22 and 25G needles, the use of suction must be avoided in centers utilizing 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.

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

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2Endoscopy, Paul Calmettes Institute, Marseille/France
3Biostatistique, Institut Paul Calmette, Marseille/France
4paoli calmettes institute, marseille/France
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Introduction: For 10 years, EUS-guided biliary drainage has been an option as EUS guided cholecodo-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 to duodenal involvement or previous Surgery as gastrectomy or Whipple resection.

Aims & Methods: Inclusion criteria were: benign or malignant obstructive jaundice with failure of ERCP. Exclusion criteria were: ascites, blood coagulation disorders, stenosis of the right bile duct. Randomization ratio was 1: 1, with a minimization of the patient heterogeneity and small sample size. Also, the optimal tissue acquisition technique for onsite and offsite specimen assessment is unclear.

Aims & Methods: Inclusion criteria were: benign or malignant obstructive jaundice with failure of ERCP. Exclusion criteria were: ascites, blood coagulation disorders, stenosis of the right bile duct. Randomization ratio was 1: 1, with a minimization of the patient heterogeneity and small sample size. Also, the optimal tissue acquisition technique for onsite and offsite specimen assessment is unclear.

Aims & Methods: Inclusion criteria were: benign or malignant obstructive jaundice with failure of ERCP. Exclusion criteria were: ascites, blood coagulation disorders, stenosis of the right bile duct. Randomization ratio was 1: 1, with a minimization of the patient heterogeneity and small sample size. Also, the optimal tissue acquisition technique for onsite and offsite specimen assessment is unclear.

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Aims & Methods: Inclusion criteria were: benign or malignant obstructive jaundice with failure of ERCP. Exclusion criteria were: ascites, blood coagulation disorders, stenosis of the right bile duct. Randomization ratio was 1: 1, with a minimization of the patient heterogeneity and small sample size. Also, the optimal tissue acquisition technique for onsite and offsite specimen assessment is unclear.
Endoscopic enteral stenting (ES) in malignant gastric outlet obstruction (GEO)

Introduction:

United States of America

Tokyo/Japan

United States of America

Aims & Methods:

This is a multicenter retrospective study of all consecutive patients who underwent either EUS-GE at 4 centers between 2013 and 2015 or ES at one center between 2008 and 2010.

Results:

A total of 205 patients (mean age 34.8±12.5 years, 181 males) underwent either EUS-GE drainage or with BFMS. Technical success was achieved in 203 patients (99%). Per-procedure adverse events occurred in 8 (3.9%) patients (bleeding in 6 and perforation in 2). WON resolved with BFMS in 158 (77.2%) patients. Endoscopic re-intervention was required in 49 (23.9%) patients, for persistent or new onset symptoms, was approached in step-up manner. At first, de-bugging of BFMS alone succeeded in 10 out of 21. Second step of nacy-oscopic placement through BFMS followed by irrigation with saline and hydrogen per-oxide improved 16 out of 21. 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-aneous 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 for DEN. Success rate incrementally improves with endoscopic step-up approach.

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

References


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

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2Dept. Of Endoscopy, Paoli-Calmettes Institute, Marseille Cedex; France
3Dept. Of Digestive Oncology, Timone Hospital, Assistance Publique Hôpitaux de Marseille, Marseille Cedex; France
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Introduction: Biliary obstruction secondary to colorectal cancer liver metastases is associated with a poor prognosis with drainage especially when chemotherapy 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 (ERC/P) 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 ERC/P, 2 underwent PTC, drainage, and 7 underwent both techniques. Overall median survival was 115 days (5–1876). In univariate analysis, a previous liver surgery, a technical and a functional success of drainage and restated chemotherapy were significantly associated with an improved survival. Chemotherapy was restarted after a median of 27 days. When drainage was efficient survival improved from 33 days to 262 days (p = 0.001). In multivariate analysis, protective factors for survival included a previous hepatectomy (hazard ratio (HR) 0.81, 95% CI [0.22–0.73], 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 < 0.001), and fever before drainage (HR 2.97, 95% CI [1.39–6.36], p = 0.005).

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

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: Primary sclerosing cholangitis (PSC) is a chronic inflammatory disease of biliary epithelium leading to strictures intra- and extrabiliary 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 biliary dysplasia and cholangiocarcinoma (2). SIR ranging from 55 to 973 (3–4). The lifetime risk of CCA is around 10% (5). CCA is the most common reason for death among PSC patients (6–7). CCA is thought to develop through metaplasia, low-grade dysplasia, and high-grade-dysplasia (8). Chronic inflammation has been regarded as risk factor for dysplasia and malignancy. Because CCA is generally a contraindication for liver transplantation (LT) and the prognosis of CCA is dismal, it would be feasible to screen the dysplastic changes of the biliary epithelium to treat patients with LT before development of advanced malignancy, detected based on imaging methods or symptoms.

Aims & Methods: We aimed to evaluate the grade of bile duct inflammation as a risk factor for dysplasia and cholangiocarcinoma in PSC patients. In total, 210 patients with confirmed PSC referred for ERC for disease surveillance were included (121 females, 179 males). After cannulation of the common bile duct patients with confirmed PSC referred for ERC for disease surveillance were included. ERC score was performed by the attending gastroenterologist. The ERC score was calculated by the attending gastroenterologist. The ERC score was calculated using a previously reported inflammation score (9). Brush cytology (BC) was collected both from extra- and intrahepatic bile ducts for Papanicolau staining for grading dysplasia and inflammation. Neutrophilic inflammation in BC was evaluated semiquantitatively (0 = neutrophils+epithelial cells <0.05, 1 = neutrophils+epithelial cells 0.05–0.4, 2 = neutrophils+epithelial cells >0.4). Bile concentrations of calprotectin were analyzed using ELISA method. Liver function tests were taken at the time of ERC. ERC findings were scored according to modified Amsterdam score, [Helsinki score (9)].

Result: Bile duct inflammation assessed by biliary calprotectin correlated significantly with neutrophils in BC, with S-CA19-9, S-ALP and S-AST levels and interestingly with S-IgG. Patients with dysplasia or CCA had markedly elevated B-calprotectin, as compared to those without dysplasia (347 vs 40 mg/l, respectively), see table. The risk of dysplasia was associated with advanced bile duct disease, (mERC score > 8 vs < 4, OR 15.2 [95% 1.8–127.9], p = 0.012), increased bile duct inflammation based on BC-neutrophils (BC-Neutrophil 1 vs 0, OR 8.2 [95% 1.1–84.0], p = 0.044). B-calprotectin higher than 45 mg/l (OR 3.3 [95% 1.1–9.9], p = 0.0032) and S-CA19-9 > 26 kU/l vs ≤26 kU/l (OR 7.4 [95% 2.0–27.6], P = 0.003). 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>
</tr>
</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>&lt;0.0001</td>
</tr>
<tr>
<td>Bil-Neutrophils</td>
<td>- 0</td>
<td>74</td>
<td>0.2 [0.1–1.1]</td>
</tr>
<tr>
<td>- 1</td>
<td>100</td>
<td>5.3 [0.9–22.9]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>- 2</td>
<td>36</td>
<td>172.8 [39.1–286.8]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dysplasia</td>
<td>- No</td>
<td>203</td>
<td>4.0 [0.2–41.0]</td>
</tr>
<tr>
<td>- Yes</td>
<td>14</td>
<td>34.7 [4.8–99.5]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-CA19-9 kU/l</td>
<td>≤ 26 (UNL)</td>
<td>198</td>
<td>2.7 [0.2–28.5]</td>
</tr>
<tr>
<td>≥ 26 (UNL)</td>
<td>12</td>
<td>57.4 [19.4–179.3]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-ALP, U/l</td>
<td>≤ 105 (UNL)</td>
<td>101</td>
<td>1.2 [0.2–9.6]</td>
</tr>
<tr>
<td>&gt; 105 (UNL)</td>
<td>109</td>
<td>6.1 [0.5–81.9]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-AST, U/l</td>
<td>≤ 40 (UNL)</td>
<td>141</td>
<td>1.4 [0.1–21.0]</td>
</tr>
<tr>
<td>&gt; 40 (UNL)</td>
<td>69</td>
<td>8.3 [1.0–80.9]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-IgG, g/l</td>
<td>≤ 15 (UNL)</td>
<td>177</td>
<td>2.8 [0.2–27.0]</td>
</tr>
<tr>
<td>&gt; 15 (UNL)</td>
<td>33</td>
<td>19.5 [1.3–112.1]</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

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

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

References

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

References
OP053 GUT BARRIER FAILURE BIOMARKERS ARE ASSOCIATED WITH PRIMARY OUTCOME IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS


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

Aim & Methods: 48 PSC patients (median age [range]: 32–79 years, concomitant IBD: 67% and cirrhosis: 20%) were assessed for a short-term follow-up (median: 94 months). 159 healthy subjects (HCONT) and 179 ulcerative colitis (UC) patients were the controls.

Results: In PSC, median I-FABP level was similar to that in HCONT (216 vs. 244 pmol/L, p > 0.05) but higher than in UC (176 pmol/L, p < 0.05). sIgA level (95.7 mg/ml) was two-fold higher compared to either the HCONT or the UC (p < 0.001, for both). 28.4%, 9% and 20.9% of PSC patients were positive for AAA IgA, AGA IgA and AGA IgG, respectively. Frequencies of AAA IgA (p < 0.001, for both) and AGA IgG (p = 0.01, for both) but not AGA IgA were significantly higher compared to HCONT and UC. Regarding disease specific characteristics, sIgA level was significantly lower in PSC patients with concomitant IBD (80.7 vs. 160.4 mg/ml) in Kaplan-Meier analysis only target specific IgAs and AGA (>157 mg/ml) were associated with a shorter time to OLTs and/or liver-related death, whereas total IgA or IgG2/IgA ratio and I-FABP were not. All markers remained significant after adjusting for the presence of cirrhosis in Cox-regression analysis (HR [95%CI]: 3.67 [1.05–12.82] for sIgA, 5.15 [2.7–20.86] for AAA IgA and 5.07 [2.5–20.54] for AGA IgA. Combination of these markers further enhanced their predicative potential (HR [95%CI]: 11.30 [2.84–44.93] for ≥ 2 marker positivity).

Conclusion: This study, sIgA antibody type identified PSC patients with progressive disease, further highlighting the importance of the gut-liver interaction in PSC.

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

References

OP055 SELECTIVE TARGETING OF FXRA ISOFORMS BY NOVELBILE ACID DERIVATIVES IS ASSOCIATED WITH INHIBITION OF LIPOTOXICITY IN LIVER CELLS

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Introduction: Nuclear receptors, such as the farnesoid X receptor (FXR), a bile acid (BA)-activated nuclear receptor, plays a critical role in maintaining lipid, glucose and BA homeostasis. FXR expression is significantly decreased in livers of non-alcoholic fatty liver disease (NAFLD) patients and genetic ablation leads to hepatosteatosis and hyperlipidemia. The FXR gene expression is regulated by multiple factors, including BA derivatives, which modulate FXR activity.

Aims & Methods: To assess the potential for BA-derived FXR agonists for their ability to selectively activate different FXR isofoms and protect liver cells against free fatty acid (FFA)-induced steatosis and cytotoxicity. Nine novel BA derivatives, synthesized based on the cholic (CA), deoxycholic (DCA), chenodeoxycholic (CDCA) and ursodeoxycolic (UDCA) acid scaffolds were incubated with primary mouse hepatocytes. The expression of FXR isofoms, when compared to pretreatment specific activities, were then measured. Results: Day 8 showed differential activation of the FXR 1–4 isoforms, when compared to pretreatment specific activities, were then measured. Note, FXR1 was preferentially expressed in primary mouse hepatocytes.

Conclusion: These new molecules preferentially activate FXR1 and therefore revert most of the FFA-induced cell death and lipid accumulation. Of note, BA derivatives, synthesized based on the cholic (CA), deoxycholic (DCA), chenodeoxycholic (CDCA) and ursodeoxycolic (UDCA) acid scaffolds were incubated with primary mouse hepatocytes. The expression of FXR1–4 isoforms, when compared to pretreatment specific activities, were then measured. Note, FXR1 was preferentially expressed in primary mouse hepatocytes.

Disclosure of Interest: All authors have declared no conflicts of interest.
of isoleucine to methionine at position 148 (I148M) causes a loss of function.

Results:

Concomitant IBD was diagnosed in 80% of the males and 60% the females.

Aims & Methods:

The PNPLA3 I148M variant did not have any significant impact on progression of ERC score/month (p = 0.44).

PNPLA3 rs738409 in PSC

Variable, mean(SD)                  CC, n = 334  CG, n = 197  GG, n = 32  p for linearity

Males, n (%):                         193(58) 124(63) 17(53) 0.75

Age at diagnosis of PSC, y:          38(14) 36(13) 35(13) 0.62

Weight, kg, males:                   82(14) 80(15) 81(14) 0.37

Weight, kg, females:                 69(7)  70(7)  71(13) 0.62

IBD, n (%):                          26(71) 15(77) 21(65) 0.49

Age at diagnosis of IBD:             26(11) 26(11) 29(12) 0.74

ERC-score (0–16):                    5.8(3.5) 5.4(3.3) 5.7(3.7) 0.88

Dominant traits, n (%):              128(38) 63(31) 9(28) 0.061

Progression of ERC score/month*:     0.014 0.002 0.004 0.44

Advanced fibrosis F3/4, (%)*:        8.8 1.5 2.5

S-ALP, U/l ≤105:                     183(148) 194(170) 182(135) 0.60

S-GT, U/l ≤60:                       191(249) 236(289) 189(154) 0.94

S-ALT, U/l ≤50:                      74(125) 78(96) 61(50) 0.35

S-AST, U/l ≤45:                      55(7) 54(6) 59(41) 0.68

*Adjusted for sex, age and IBD Cholangiocarcinoma was diagnosed in 12 (3.6%) patients with CC, in 6 (3.1%) of CG an in none of GG, (p for linearity=0.42; adjusted for sex, age and IBD). 49 patients underwent liver transplantation during 5 years mean follow up: 2.5% (95% CI: 1.2 to 5.1) in CC, 3.1% (95% CI: 1.3 to 7.3) in CG and 7.1% (95% CI: 1.8 to 24.4) in GG, (p for linearity =0.12; adjusted for sex, age and IBD).

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

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

References:


Disclosure of Interest:

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Introduction: PNPLA3 (pataxin-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 p.I148M 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 increased risk of bile duct stenosis in male PSC patients (6). Survival free of liver transplantation is reduced in male PSC patients with development of 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 (35.7%) 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. Summary of the results are presented in the table.

PNPLA3 rs738409 in PSC

Progression of ERC score/month*: 0.014 0.002 0.004 0.44

Advanced fibrosis F3/4, (%)*: 8.8 1.5 2.5

S-ALP, U/l ≤105: 183(148) 194(170) 182(135) 0.60

S-GT, U/l ≤60: 191(249) 236(289) 189(154) 0.94

S-ALT, U/l ≤50: 74(125) 78(96) 61(50) 0.35

S-AST, U/l ≤45: 55(7) 54(6) 59(41) 0.68

*Adjusted for sex, age and IBD Cholangiocarcinoma was diagnosed in 12 (3.6%) patients with CC, in 6 (3.1%) of CG an in none of GG, (p for linearity=0.42; adjusted for sex, age and IBD). 49 patients underwent liver transplantation during 5 years mean follow up: 2.5% (95% CI: 1.2 to 5.1) in CC, 3.1% (95% CI: 1.3 to 7.3) in CG and 7.1% (95% CI: 1.8 to 24.4) in GG, (p for linearity =0.12; adjusted for sex, age and IBD).

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

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

References:

1. Lin S, Wang D, Iyer S, Ghaleb AM, Shim H, Yang VW, et al. The absence of LPA2 attenuates tumor progression in rodent models of colorectal cancer, but whether overexpression of LPA2 alone can lead to malignant transformation in the intestinal tract has not been studied.

Aims & Methods: The aim of this study is to determine whether increased LPA2 expression in intestinal epithelial cells (IECs) alone is sufficient to induce spontaneous transformation in the intestinal tract. In this study, we expressed human LPA2 in IECs under control of the villin promoter. The transgenic DNA was injected into the promulc of fertilized eggs of C57BL/6j mice. The transgenic mice were identified by PCR analysis of tail genomic DNA.

Results: Less than 4% of F1-generation mice had germline transmission of transgenic (TG) human LPA2 as such only 3 F1 mice out of 72 genotyped had TG expression. These TG mice appeared anemic with hematochezia and died shortly after birth. TG mice were smaller in size compared with the wild type mice of the same age and sex. Morphological analysis showed that TG LPA2 colon had hyper-proliferation of IECs resulting in increased colonic crypt depth. Surprisingly, TG small intestine had villus blunting and decreased IEC proliferation and dysplasia. In both intestine and colon, TG immunohistochemical analysis revealed that expression of LPA2 compromised the terminal epithelial differentiation, consistent with epithelial dysplasia. Furthermore, we showed that epithelial dysplasia was observed in founder mouse intestine, correlating LPA2 overexpression with epithelial dysplasia.

Conclusion: We demonstrated that overexpression of LPA2 induces dysplasia in mouse intestine that alter IEC proliferation and differentiation. Our results reinforce the importance of the LPA-LPA2 axis in homeostatic regulation of IECs. The aim of this study is to determine whether increased LPA2 expression in intestinal epithelial cells (IECs) alone is sufficient to induce spontaneous transformation in the intestinal tract. In this study, we expressed human LPA2 in IECs under control of the villin promoter. The transgenic DNA was injected into the promulc of fertilized eggs of C57BL/6j mice. The transgenic mice were identified by PCR analysis of tail genomic DNA.

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

References:


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

References:

OP038 CELL-SPECIFIC ROLES OF CALCINEURIN IN INTESTINAL TUMOR DEVELOPMENT
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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 Apcþ/þ model. Antibiotic treatment of mice as well as backcrossing to a Myd88-deficient background revealed that the activation of oncogenic epithelial calcineurin leads to increased intestinal tumor growth in Apcþ/þ mice, which is consistent with an increased CRC incidence observed in patients receiving calcineurin inhibitors. In contrast, intestinal epithelial cell-specific deletion of calcineurin is associated with reduced intestinal tumor formation and growth in the Apcmin/þ and Apcmin/+ models of genetically induced intestinal tumor development as well as in the AOM/DSS model of colitis-associated cancer. For mechanistic studies, organoid cultures, immortalized IECs and CRC cell lines as well as samples of more than 700 CRC patients were studied.

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

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

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

OP039 ALIX POSITIVE EXOSOMES IN COLORECTAL ADENOMA-CARCINOMA SEQUENCE
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Introduction: During colorectal carcinoma (CRC) formation exosomes play important roles as intercellular regulators in conveying complex signals between epithelial/carcinoma cells and their abnormal microenvironment.

Aims & Methods: Our aim was to characterize changes in exosome-based communication in the colorectal adenoma-carcinoma sequence by determining ALIX 2-interacting protein X (ALIX) exosome marker production on mRNA and protein level. mRNA expression was analyzed using Affymetrix HG U133 Plus2.0 whole transcriptome data of healthy (n=49), adenoma (n=49) and CRC (n=49) samples. Immunohistochemistry was performed on healthy (n=27), adenoma (n=42), CRC (n=37) patients and stained for ALIX exosome, cytokerin (CK) epithelial, podoplanin (PDPPN) lymphatic vessel, Ki-67 proliferative and Musashi-1 (MSI1) stem cell markers. Slides were digitalized and analyzed with digital microscopy.

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

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

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

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Introduction: The Na+/H+ exchanger regulatory factor (NHERF) family of proteins is scaffolds that orchestrate interaction of receptors 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 the NHERF receptors. NHERF1 is reported to be a tumor suppressor. However, the role of NHERF2 in cancer progress has not been reported.

Aim & Methods: We investigated the role of NHERF2 in colon tumor progression. We first determined NHERF2 expression in human colorectal cancer (CRC) using a tissue microarray. Next, the role of NHERF2 on colon cancer growth and invasion was assessed by a loss-of-function approach (shRNA) and a gain-of-function approach (overexpression). We used xenograft model to investigate the molecular mechanism of NHERF2 in tumor growth, we also performed the transcriptional 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 mouse xenograft tumor model. Histologic analysis confirmed the reduction of cell proliferation by Ki-67 immunostaining. In addition, deletion of NHERF2 in ApcMin/+ (ApcMin/+;Nherf2-/-) mice resulted in decreased tumor growth in ApcMin/+ mice and increased lifespan. Blockade of 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-associated genes largely differ from LPA2-regulated genes.

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 CD44. 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 EMILIN Domain ENdowed (EDEN) protein family that exerts pleiotropic effects in the tumor microenvironment. It has been found to act as a tumor suppressor in mice (4). EMILIN2 knockdown or deletion 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.

Aim & 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). We investigated the molecular mechanisms of EMILIN2 in tumors from control mice and EMILIN2-deficient mice. Tumor development was assessed by colonoscopy. Histopathological and IHC analyses were performed on colon samples from treated mice. β-catenin activation was assessed by Western blot and qPCR. Multiplex serum cytokine analyses from the two mouse models were performed through Luminex Screening and peripheral blood cells were counted. The inflammatory infiltrate was analysed by flow cytometry.

Results: The EMILIN2 KO mice developed a significantly higher number of tumors compared to wt mice. Tumors from EMILIN2 KO mice were more undifferentiated and at an advanced stage compared to the tumors from control mice. 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. The EMILIN2 KO mice where characterized by a higher number of macrophages and granulocytes than those from WT mice. Similar alterations in the KO model were found during the acute phase of inflammation: mice subjected to DSS treatment alone developed a more severe colitis than WT mice. Accordingly, the infiltration of myeloid cells within the intestinal mucosa was altered and the serum level of a number of cytokines, including IL-1β, INF-γ, TNF-α and IL-10, was affected.

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:
OP042 THE ROLE OF MRNA-145 IN COLON CANCER STEM CELL- LIKE PROGENY
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Introduction: Cancer stem cells (CSCs) are thought to be responsible for tumour initi- ation, metastasis and relapse through their unlimited self-renewal and differ- entiation capacities. CSCs are able to form tumour xenografts in immunocompromised mice and tumour cell lines, and examined their ability to form colon spheres in ultralow-attachment plates and specific CSCC media. Colon spheres were dissociated to single cells and reseeded to yield the second and third generation of colon spheres. The number of spheres and cells per sphere were counted over 3 gen- erations. mRNA expression levels of stemness markers were evaluated by SYBR Real-Time PCR. CD44 and CD133 expression levels and aldehyde dehydrogenase 1 (ALDH1) activity were evaluated by flow cytometry.

Results: Forced miR-145 expression significantly decreased the proportion of CD44/CD133+ cells overexpressing miR-145 (p < 0.01). OCT4 mRNA levels were increased in HCT116 spheres overexpressing miR-145 (p < 0.05). In addi- tion, HT29 and SW620 cell line-derived colon spheres overexpressing miR-145 displayed reduced OCT4 mRNA levels. Furthermore, miR-145 overexpression significantly decreased the proportion of CD44/CD133+ cells and ALDH1 activity (p < 0.05). 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 186

OP043 PAN-EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): INTERIM ANALYSIS OF THE TREATMENT REGIMEN WITH BISMUTH, LEVOFLOXACIN AND AMOXICILLIN
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Introduction: H. pylori rescue therapy is still a major concern for clinicians treat- ing this infection. Although several rescue treatments have been proposed and tested, the selection of resistant strains or acquisition of resistance after failed eradication hinders the success rate of most proposed regimens. Traditionally rescue treatments in Europe have been divided in bismuth quadruple therapy or levofloxacin triple. Some authors have recently proposed a combination of both strategies in order to increase the traditionally low eradication rates of H. pylori. The aim of this study was to compare the different effects of rescue therapies with conventional PPIs. The aim of this study was to compare the different effects of rescue therapies with conventional PPIs. The aim of this study was to compare the different effects of rescue therapies with conventional PPIs.

Disclosure of Interest: A.G. McNicholl: Speaker for all the other authors have declared no conflicts of interest.

OP044 ERADICATION RATES OF HELICOBACTER PYLORI USING A NEW GASTRIC ACID SUPPRESSANT, VONOPRAZAN, COMPARED WITH AN ESOMEPRAZOLE REGIMEN
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Introduction: A proton pump inhibitor (PPI)-based triple regimen containing two antibiotics (amoxicillin, APPI, 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 due to increasing resistance of H. pylori. Insufficient acid inhibition during treatment also causes eradication failure. This is because the antimicrobial agents are unstable and degraded in the stomach. Esomeprazole (EPZ) is a new PPI available in Japan since September 2011. EPZ has an improved pharmacokinetic profile as regards CYP2C19 genotype; therefore, it shows less individual variability. Vonoprazan (VPZ) is a potassium-competitive acid blocker (P-CAB). P-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 has the potential to increase eradication rates compared with conventional PPIs. The aim of this study was to compare HP pylori eradication rates with EPZ-based and VPZ-based triple therapies with CAM and AMPC.

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

Results: The overall first-line eradication rate was 79.1% (341/431) for the EPZ regimen and 84.6% (318/373) for the VPZ regimen based on Intention to treat (ITT) analysis. The eradication rate evaluated by Par protocol (PP) analysis for the EPZ and VPZ regimens were 79.9% (341/427) and 85.3% (318/373) respectively.

Conclusion: In conclusion, VPZ has a rapid, sustained, and possibly more potent acid-inhibitory effect than EPZ, irrespective of CYP2C19 genotype. The rate of H. pylori eradication obtained using the first-line VPZ regimen was significantly higher than that for the first-line EPZ regimen. However, for the second-line...
OP045 STROMAL MYOFIBROBLASTS ORCHESTRATE GASTRIC EPITHELIAL WNT-SIGNALING AND STEM CELL KINETICS IN HEALTH AND DISEASE

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

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

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

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

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

Reference

Aims & Methods: Using gastric tissue from humans, rats treated with proton pump inhibitors and/or a cholecystokinin type B receptor (CCK-BR) antagonist (CCKBR) in rats and Mongolian gerbils. The oxyntic mucosa of H. pylori +/− infected mice contained distinct areas with CLU positive mucous cell hyperplasia, possibly representing SEM. 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 Interests: All authors have declared no conflicts of interest.

References

OP046 THE ANTI-APOPTOTIC FACTOR CLUSTERIN IS INVOLVED IN GASTROINTESTINAL TUMORIGENESIS AND STOMACH CANCER

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Introduction: A negative association exists between H. pylori infection and both gastrointestinal reflux disease and oesophageal adenocarcinoma and this may be due to the infection of intragastric acidity. To exert such a protective effect the reduced acidity would need to be evident in the majority of H. pylori-infected subjects. To investigate this we have examined the acid secretory capacity of H. pylori +/− infected mice in three different animal models. This shift was partly inhibited by antagonizing the CCKBR in rats and Mongolian gerbils. The oxyntic mucosa of H. pylori +/− infected mice contained distinct areas with CLU positive mucous cell hyperplasia, possibly representing SEM. In vitro, gastrin increased the secretion of CLU, and both gastrin and secretory CLU promoted survival of gastric cancer 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 Interests: All authors have declared no conflicts of interest.

References
3. Asaka M, et al. A multicenter, double-blind study on triple therapy with proton pump inhibitor and/or a cholecystokinin type B receptor (CCK-BR) antagonist (CCKBR) in rats and Mongolian gerbils. The oxyntic mucosa of H. pylori +/− infected mice contained distinct areas with CLU positive mucous cell hyperplasia, possibly representing SEM. In vitro, gastrin increased the secretion of CLU, and both gastrin and secretory CLU promoted survival of gastric cancer following starvation- and chemotherapy-induced stress.

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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 Interests: All authors have declared no conflicts of interest.
Conclusion: The majority of H. pylori-infected subjects have reduced intragastric acidity compared to the uninfected population and this is most marked close to the gastroesophageal junction. The density of parietal cells and chief cells is reduced in H. pylori infected subjects throughout the gastric mucosa. These findings raise the possibility that these play a role in reflux perception. We have recently demonstrated that, in healthy volunteers, there is a differential location of afferent fibre nerves within the distal and proximal oesophageal mucosa, and that these nerves are superficially and close to the lumen. In the distal oesophageal mucosa they lie much deeper and closer to the basal epithelium.

Aims & Methods: We aimed to investigate the location of distal and proximal oesophageal mucosal afferent nerves in H. pylori-infected patients with non-eroded reflux disease. We investigated mucosa from 10 patients with typical heartburn symptoms, normal macroscopic oesophageal appearances, and all had normal acid oesophageal exposure on reflux testing (oesophageal pH exposure > 4.2%).

In each patient, endoscopic mucosal biopsies were taken from 3 cm above the gastro-oesophageal junction (proximal) and at 20 cm from the incisors (proximal). Biopsies were fixed in 4% paraformaldehyde, cryoprotected, and 10 μm sections were cut on a cryostat and prepared on slides. Slides were examined immunohistochemically for presence and location of calcitonin gene-related peptide (CGRP) and protein gene product 9.5 (PGP) - immunoreactive nerve fibres. Where fibres were identified their location in the mucosa was recorded in terms of cell layers from luminal surface.

In control subjects and volunteers with NERD, afferent nerves were found a mean of 7.7 ± 1.3 cell layers from the surface. In the distal oesophageal mucosa these were found a mean of 8.9 ± 2.7 cell layers from the surface.

In most, healthy volunteers proximal nerves were found 12.3 ± 0.9 cell layers from the lumen in the proximal oesophageal mucosa, and 22.2 ± 2.7 cell layers from the lumen in the distal oesophageal mucosa. On ANOVA, the more superficial location of distal oesophageal nerves in patients versus healthy controls was statistically significant (p < 0.002). There was a non-significant trend to more superficial proximal nerves in NERD patients versus healthy volunteers.

Conclusion: Distal oesophageal afferent mucosal nerves are significantly closer to the lumen versus healthy controls and the usual differential location between proximal and distal fibre location is lost. This may be relevant for symptomatic acid perception in patients with reflux disease, and may represent a target for topical treatment of these patients.

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

Reference


Aims & Methods: This was carried out in 21 healthy volunteers (11 men, 25 ± 6 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 assess acid sensitivity and mucosal integrity of the proximal and distal esophageal segments separately in patients with gastroesophageal reflux disease (GERD) and to investigate the relationship between these parameters. We included patients with heartburn and evidence of GERD on ambulatory pH-impedance measurement. After PPI washout, an esophageal hydrochloric acid perfusion test measuring segmental acid sensitivity proximally and distally in the esophagus (3 and 18 cm above the Z-line) and an upper esophagitis with biopsies at both levels were performed. During endoscopy, electrical tissue impedance spectroscopy was performed at the two levels and biopsies were taken from macroscopically unaffected mucosa. Biopsies were used to measure the distribution of intercellular spaces with transmission electron microscopy and to assess morphological measure of impaired integrity and to investigate transepithelial electrical resistance and transepithelial fluorescence permeability in Oesoph. Pathol. Res. Pract. 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 9%, CI) 0.8 minutes (0.1–1.5) than after distal acid perfusion (3.9 minutes (CI) 2.4–5.4); log rank p = 0.002. In vivo electronic impedance measurement was lower in the distal esophagus (median (95% CI) 4563 ± 3640 (5429) compared to the proximal esophagus (8170 ± (7353–10110)) p = 0.02. Transepithelial fluorescence permeability was higher in the distal than the proximal esophageal segment (median 2051 nmol cm−2 hr−1 (IQR 1201–3708) and 368 nmol cm−2 hr−1 (IQR 138–592)), a more cellular space and transepithelial electrical

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

References


Aiming to explore the in vivo and in vitro effects of bile acids on duodenal mucosal permeability in healthy volunteers.

Aims & Methods: This study was carried out in 21 healthy volunteers (11 men, 25 ± 6 years). Duodenal biopsies were obtained by gastroduodenoscopy and used to measure the in vitro transepithelial resistance (TEER) using Ussing chambers. Meantime, fluorescein isothiocyanate dextran (FITC-dx4, MW 4kDa) was applied to assess paracellular permeability. After the gutoduodenectomy, an aspiration catheter was placed in the second part of the duodenum under fluoroscopic control. Duodenal fluid aspirates were collected at fixed time points during endoscopy with biopsies at both levels were performed. During endoscopy, electrical tissue impedance spectroscopy was performed at the two levels and biopsies were taken from macroscopically unaffected mucosa. Biopsies were used to measure the distribution of intercellular spaces with transmission electron microscopy and to assess morphological measure of impaired integrity and to investigate transepithelial electrical resistance and transepithelial fluorescence permeability in Oesoph. Pathol. Res. Pract. 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 9%, CI) 0.8 minutes (0.1–1.5) than after distal acid perfusion (3.9 minutes (CI) 2.4–5.4); log rank p = 0.002. In vivo electronic impedance measurement was lower in the distal esophagus (median (95% CI) 4563 ± 3640 (5429) compared to the proximal esophagus (8170 ± (7353–10110)) p = 0.02. Transepithelial fluorescence permeability was higher in the distal than the proximal esophageal segment (median 2051 nmol cm−2 hr−1 (IQR 1201–3708) and 368 nmol cm−2 hr−1 (IQR 138–592)), a more cellular space and transepithelial electrical

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

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Aiming to explore the in vivo and in vitro effects of bile acids on duodenal mucosal permeability in healthy volunteers.

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

References


mean RSI 0.5
GSI 22
in 64/86 (74%) LPR patients and in 54/59 (92%) HCs (p = 0.0039). PeptestTM had an accuracy of 47% (IC5 39%–55%) a sensitivity of 74% (IC5 65%–84%), a specificity of 7% (IC5 0%–13%), a positive predictive value of 54% (IC5 45%–68%) and a negative predictive value of 2% (IC5 0%–8%) in identifying LPR as diagnosed by RSI.

Conclusion: In this pilot study, PeptestTM was not able to discriminate among primary care patients with LPR from those without and therefore cannot be suggested as preliminary tool to select patients requiring pH monitoring. Further studies including investigated healthy controls are mandatory to elucidate the diagnostic utility of salivary pepsin measurement in primary care setting.

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

Aims & Methods: We aimed to investigate the usefulness of PeptestTM in primary care patients presenting with chronic laryngeal symptoms suggestive of LPR. In a prospective multicenter, controlled, pilot study, consecutive patients presenting with chronic laryngeal symptoms were enrolled by primary care physicians. Uninvestigated individuals with no gastrointestinal symptoms or disease (including GERD or dyspepsia) or history of surgery served as healthy controls (HCS). All subjects completed the validated reflux symptom index (RSI) questionnaire and in case of a score >13, a symptom-based diagnosis of LPR was made. Also the gastrointestinal symptom scale (GIS) questionnaire was completed to investigate reflux symptoms and Quality of Life. All individuals were asked to provide 2 samples of sputum collected one hour after lunch and dinner. A positive PeptestTM was considered in case of a concentration of pepsin higher than 25 mg/mL. A positive result was defined as a concentration of pepsin >25 mg/mL. A negative result was defined as a concentration of pepsin ≤25 mg/mL.

Results: Between February and April 2014 and during August 2015, 86 patients with LPR (37 Male:49 Female, age 54 ± 14, RSI>13, mean RSI 22 ± 6, mean GSI 22 ± 6.4) and 59 healthy controls (30M:29F, mean age 41 ± 15; RSI<5, mean RSI 3 ± 1.6; mean GSI 33 ± 5.6) were tested. In total 236 samples were examined, whereas 34 samples were discarded because of technical problems (i.e. unclear storage, poor/excessive quantity). At least one positive result was found in 64/86 (74%) LPR patients and in 54/59 (92%) HCs (p < 0.0095), whereas two positive results were observed in 34/70 (49%) LPR patients and 26/46 (57%) HCs (p = 0.4505). One (in case of a single test) or two negative tests were registered in 22/86 (26%) LPR patients vs 4/57 (7%) of HCs (p = 0.0039). PeptestTM had an accuracy of 47% (IC5 39%–55%) a sensitivity of 74% (IC5 65%–84%), a specificity of 7% (IC5 0%–13%), a positive predictive value of 54% (IC5 45%–68%) and a negative predictive value of 2% (IC5 0%–8%) in identifying LPR as diagnosed by RSI.

Aims & Methods: This study design was a randomized, placebo-controlled, double-blind, parallel-group, double-blind, multicenter study. The primary endpoint was symptom relief and the secondary endpoints were treatment success and the need for rescue medication. The study was conducted at 33 sites in Japan, with 450 patients randomized 1:1 to receive either acotiamide (10 mg thrice daily) or a matching placebo for 2 weeks. The study population consisted of 205 patients with chronic GERD (i.e. with heartburn and regurgitation), confirmed at impedance-pH (24-h MII-pH) monitoring at baseline and after 2 weeks. The acotiamide group showed a significant decrease in the number of total reflux events, acid and liquid reflux events (39.6 vs. 25.5, p = 0.028; 14.7 vs. 8.3, p < 0.0001) and acid reflux events (15.0 vs. 7.4, p = 0.009). The placebo group presented with chronic laryngeal symptoms were enrolled by primary care physicians. 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 symptoms 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 reflux medication. “Lost Patients” were defined as those with a score of 1 or 2 on a 5-point Likert scale (1: very satisfied; 2: satisfied; 3: doubtful; 4: dissatisfied; 5: very dissatisfied) at baseline.

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

Results: 200 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 32 months. 74% were dissatisfied or very dissatisfied on their current PPI therapy (score of 1 or 2), whereas 26% were satisfied or very satisfied (score of 3 or 4). PeptestTM had an accuracy of 49% (IC5 39%–61%) a sensitivity of 74% (IC5 65%–84%), a specificity of 7% (IC5 0%–13%), a positive predictive value of 54% (IC5 45%–68%) and a negative predictive value of 2% (IC5 0%–8%) in identifying LPR as diagnosed by RSI. PeptestTM had an accuracy of 47% (IC5 39%–55%) a sensitivity of 74% (IC5 65%–84%), a specificity of 7% (IC5 0%–13%), a positive predictive value of 54% (IC5 45%–68%) and a negative predictive value of 2% (IC5 0%–8%) in identifying LPR as diagnosed by RSI.

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

Disclosure of Interest: All authors have declared no conflicts of interest.
showed no significant change. In patients with a symptom index > 30% or total reflux events > 40, the effective rate was significantly different (p = 0.038) at 60 and 33% for the acitamidine and placebo groups, respectively. These results suggest that acotiamide may be effective in patients with associated reflux events. Co-administration of acitamidine 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 EFFICACY AND SAFETY OF ACO TIAMIDE FOR RESOLUTION OF GASTRO-ESOPHAGEAL REFLUX DISEASE SYMPTOMS IN NEWLY DIAGNOSED PATIENTS

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Introduction: Acotiamide is a new proton 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: Acotiamide was a single-placebo, 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] ≥ 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 resolution (GOS = 0) at 4 weeks. 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 frequency of side effects was lower in the EPZ group (10.9%) than in the VPZ group (27.9%) (p < 0.01).

Discussion: Acotiamide showed significant treatment efficacy and improved reflux symptoms in patients whose symptoms were associated with reflux events. Co-administration of acitamidine and PPIs may be a new strategy for PPI-refractory GERD patients.

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

References


OP055 EFFICACY AND SAFETY OF THE ENDOLUMINAL REMOVAL OF REFRACTORY GASTROESOPHAGEAL REFLUX WITH BAND LIGATION

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Introduction: Gastroesophageal reflux disease is characterized by reflux of the gastric contents causing troublesome esophageal and extraesophageal symptoms that could affect adversely the quality of life. About 10–40% of patients with GERD fail to show adequate symptomatic response to the standard dose of PPI. Severe complications could explain refractory GORD as improper PPI dose, patient non-compliance, esophageal hypersensitivity, residual acid reflux, alkaline or bile reflux, nocturnal acid breakthrough. Alternative therapeutic options included laparoscopic fundoplication, lower esophageal magnetic band, patients are expensive, and about 10% of patients experience persistence of heart burn, or develop dysphagia.

Aims & Methods: We aimed to evaluate the safety and efficacy of endoluminal rubber band ligation in the management of refractory GERD. 20 patients were enrolled in the study after informed consent was taken. They were treated with rubber band ligation and the cap used for ligation had a diameter of 11 mm and loaded with 6 rings. The main outcome is reduction of reflux symptoms measured by GERD health related quality of life Questionnaire. Patients were included if they were 18 years of age or older with typical symptoms of heartburn or regurgitation refractory or less responsive to maximally optimized dose of PPI therapy (given twice, 30 min before food) and after adding H2 receptor blocker before bedtime and baclofen 10 mg twice daily to the unsponsive patients. Patients excluded if they had lower esophageal ulcers, pregnancy, red flag signs as loss of weight, fever, dysphagia, odynophagia, bleeding. Large hiatal hernia more than 2 cm, paraesophageal hernia, active Helicobacter pylori infection, eosinophilic esophagitis were also excluded. Band ligation was performed in the four quadrants 5 mm distal to the Z-line which is measured before and after the sessions were completed.

Results: 13 males and 7 females were enrolled in the study. Their mean age 39.5 ± 6.2 with a range (31–49 years). The pre-endoscopic intervention characteristics were mean hemoglobin 10.6 ± 0.9 gm/dl, mean GERD related quality of life questionnaire (GERD-QLQ) value was 35.4 ± 6.9, depth of Z-line 34 ± 1.1cm, frequency of the sessions needed 1.6 ± 0.6 times over 4 months. After 6 months of follow-up, GERD-QLQ score had dramatically improved 15.4 ± 4.6 (t = 11.85, p = 0.000), depth of Z-line became 35 ± 0.9 cm (t = 3.25, p = 0.005), hemoglobin level showed non-significant increase (10.9 ± 0.8 gm/dl, p = 0.008). 5 patients experienced mild dysphagia which disappeared after 6 ± 2.4 weeks. 8 patients (40%) experienced transient epigastric pain which disappeared within 5.4 ± 1.5 days. 13 patients stopped PPI use (65%), 6 patients were on demand therapy (30%), and only one patient continued low dose PPI which was significantly reduced when compared to pre-endoscopic PPI intake.

Conclusion: Endoluminal band ligation is a safe, well tolerated and cost-effective therapeutic option for refractory GERD.

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

References
1. 1. Inadomi JM, McIntyre L, Bernard L and Fendrick AM. Step-down from multiple- to single-dose proton pump inhibitors (PPIs): a prospective study of patients with heartburn or acid regurgitation completely relieved with PPI. Am J Gastroenterol 2003; 98: 1940.


OP056 ENDOSTIM® LES STIMULATION THERAPY IMPROVES GERD IN PATIENTS WITH LAPAROSCOPIC SLEEVE GASTRECTOMY (LSG)
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Introduction: LSG is the most commonly performed bariatric procedure in the US and Canada and the Asia-Pacific region. However, LSG can result in new GERD and may worsen preexisting GERD.1 LSG patients with GERD not well controlled with PPI do not have good treatment options except for more invasive, anatomy-altering gastric bypass surgery. LES electrical stimulation is currently under investigation as a treatment option for patients with GERD not well controlled with PPI. Randomized controlled trials have shown that LES stimulator implant procedure and were enrolled in an international patient registry prospectively tracking outcomes in GERD patients treated with LES electrical stimulation. LES stimulation was delivered at 5mA, 215μsec, at 20Hz. Postop follow-up endpoints included clinical symptoms, endoscopy and reflux was diagnosed with Multichannel Intraluminal Impedance-pH testing (MII-pH). The LES Stimulation system (EndoStim, BM, The Hague, The Netherlands) was implanted using standard technique (Surg Endosc. 2013:27:1083–1092) and stimulation was delivered in 12, 30 minute sessions daily. GERD outcomes pre and post stimulation were evaluated.

Results: 12 patients, 66% (8/12) women at 8 centers have been treated. Median age was 51 [IQR = 34–55] years. All (12/12) were on daily double-dose PPIs. At their last follow-up (median = 12 months), 75% (9/12) were off PPIs and one each was using PPIs on < 50% of days and standard dose once a day. The latter patient had GI prophylaxis for chronic steroid therapy for kidney transplants and not GERD symptoms. Median esophageal pH at baseline was 16.4% (IQR 8.5–22.4), which improved to 1.3% (IQR 0.4–2.2) at last follow-up at 6 months post implant (n = 6; p = 0.01). All patients improved esophageal acid exposure compared to baseline (0.55) and had normalized acid exposure and 16 patients had >40% improvement in distal esophageal acid exposure. Median GERD-HRQL scores at baseline was 25 (IQR 18–31) which improved to 4 (IQR 3–10) at last follow-up (n = 6; p = 0.01). No SAEs related to the device or procedure were reported. No dysphagia or other GI side effects were reported.

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

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

References

Impact of LES-EST in this difficult group of patients.
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 SG-DV, SG-DLA or NASH were included on maximum dose PPI therapy as well as patients with Barrett’s (n = 5) either primary or in patient with prior lung transplant can be a challenge. Antireflux surgery for GERD associated with failed peristalsis, or lung transplant (n = 12) were on daily double-dose PPIs. At their last follow-up (median = 12 on daily double-dose PPIs. At their last follow-up (median = 12 months), 75% (6/8) were off-PPIs and 1/6 patients had >40% improvement in distal esophageal acid exposure. Median GERD-HRQL scores at baseline was 25 (IQR 18–31) which improved to 4 (IQR 3–10) at last follow-up (n = 6; p = 0.01). No SAEs related to the device or procedure were reported. No dysphagia or other GI side effects were reported.

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

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

**High-confidence cases was 93.5%. These values were higher than those for trai-

**Results:**

The overall accuracy of ECV-CAD was 87.8%, whereas the accuracy for

**Aims & Methods:** The aim of this study was to compare the diagnostic ability of

**Conclusion:** The overall accuracy of ECV-CAD was comparable to that of

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

**References:**


evaluation is a reliable new diagnostic method for colorectal lesions (with

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**OP060**

**Lymphoma in Patients with Inflammatory Bowel Disease: A French Nationwide Observational Cohort Study**

M. Lemaitre1, J. Kirchgeiner2, A. Rudnichi1, F. Carrat1, A. Racine2, M. Zureik1, R. Dray-Spira1, F. Carbonnel1

**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 test the risk of lymphoma in patients with inflammatory bowel disease (IBD) treated with thiopurines, anti-TNFs or the combination of both treatments (combotherapy).

**Results:** The cohort included 173 190 patients with IBD, followed for a median of 4.9 years, accounting for 522 487 person-years (PY) unexposed to thiopurines or anti-TNFs, 111 113 PY exposed to thiopurines, 60 736 PY exposed to 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.

**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.

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**Table:** Diagnostic Abilities

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**OP060 INCIDENT CANCER IN INFLAMMATORY BOWEL DISEASE: RISK FACTORS IN A LONG TERM MULTICENTER NESTED CASE-CONTROL IG-IBD STUDY AT 4 YEARS**

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Introduction: the author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Astra Zeneca, Chiesi, Ferring, MSD, Otsuka, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lily, MSD, Sofar; A. Armuzzi: The author declares no conflicts of interest specifically related to the study. Financial support for research not related to the study from Abbvie, MSD; Merck & Co, MSD, Otsuka; M. Daperno: No conflicts of interest specifically related to the study. Financial support for research not related to the study from Abbvie, MSD, Hospira, Mundipharma, Takeda, Sofar, Chiesi, Ferring; C. Papi: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Consultant for Abbvie, Takeda, Asian, MSD, Chiesi, Kishin, Ferring; A. Orlando: No conflicts of interest specifically related to the study. Consultant for Abbvie, MSD, Ferring; 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 Abbvie, MSD, Hospira, Ferring; G. Riegler: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, MSD, Hospira, Ferring.

**Abstract No:** OP060  
**Table:** Hazard ratio for lymphoma in thiopurines, anti-TNFs monotherapy and comotherapy exposed patients compared to unexposed patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cases</th>
<th>Persons-years</th>
<th>Cases Crude Hazard Ratio (95% CI)</th>
<th>Cases Adjusted Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiopurines</td>
<td>111 113 PY</td>
<td>1.39 (1.02–1.90)</td>
<td>1.64 (1.08–2.26)</td>
<td>31</td>
</tr>
<tr>
<td>Anti-TNFs monotherapy</td>
<td>522 487 PY</td>
<td>1.59 (0.96–2.66)</td>
<td>2.31 (1.49–3.65)</td>
<td>21</td>
</tr>
<tr>
<td>Comotherapy</td>
<td>60 736 PY</td>
<td>2.99 (1.69–5.29)</td>
<td>4.83 (2.51–9.16)</td>
<td>21</td>
</tr>
</tbody>
</table>

**OP061 INCIDENT CANCER IN INFLAMMATORY BOWEL DISEASE: RISK FACTORS IN A LONG TERM MULTICENTER NESTED CASE-CONTROL IG-IBD STUDY AT 4 YEARS**


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166 56 1.39 (1.02–1.90) 1.64 (1.08–2.26) 31 1.30 (0.88–1.93) 1.87 (1.15–3.03) 13 2.99 (1.69–5.29) 4.83 (2.51–9.16)
150 45 1.19 (0.85–1.68) 1.56 (0.98–2.48) 25 1.10 (0.71–1.70) 1.94 (1.05–3.05) 9 2.19 (1.11–4.31) 4.09 (1.93–8.64)
16 11 3.32 (1.54–7.18) 2.41 (0.86–7.23) 6 3.31 (1.28–8.54) 2.52 (0.78–8.20) 4 11.50 (3.82–35.99) 9.09 (2.46–33.66)

**TOPICS**


**References**

J Crohns Colitis. 2016; pii: jjw048. [Epub ahead of print].
and 438 patients at the five, ten and 20 years follow up, respectively. Of these patients, 199 (139 UC, 60 CD) and 191 (133 UC, 58 CD) answered the SF-36 at every follow-up visit, respectively. We could not register clinical 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, 54 (38.9%) and 17 (28.3%) had stable scores. Of 133 UC patients and 58 CD patients, who answered the SF-36 at all follow-up visits, 31 (23.3%) and 13 (22.4%) had stable scores.

Table 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>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>10</td>
<td>20</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>All patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NBDQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean scores</td>
<td>108</td>
<td>140</td>
<td>113</td>
<td>72</td>
</tr>
<tr>
<td>SD</td>
<td>62</td>
<td>77</td>
<td>35</td>
<td>21</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean scores</td>
<td>104</td>
<td>138</td>
<td>110</td>
<td>73</td>
</tr>
<tr>
<td>SD</td>
<td>66</td>
<td>72</td>
<td>63</td>
<td>56</td>
</tr>
<tr>
<td>GH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean scores</td>
<td>68</td>
<td>70</td>
<td>62</td>
<td>64</td>
</tr>
<tr>
<td>SD</td>
<td>24</td>
<td>22</td>
<td>24</td>
<td>27</td>
</tr>
<tr>
<td>Patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>participating</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>in every follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBQD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean scores</td>
<td>191</td>
<td>191</td>
<td>183</td>
<td>182</td>
</tr>
<tr>
<td>SD</td>
<td>23</td>
<td>26</td>
<td>29</td>
<td>28</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean scores</td>
<td>104</td>
<td>110</td>
<td>81</td>
<td>76</td>
</tr>
<tr>
<td>SD</td>
<td>66</td>
<td>63</td>
<td>63</td>
<td>57</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Medication to which exposed</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiopurines or anti-TNFs</td>
<td></td>
</tr>
<tr>
<td>18–64 years</td>
<td>5.30 (4.13–6.81)</td>
</tr>
<tr>
<td>65 years</td>
<td>0.89 (0.74–1.06)</td>
</tr>
<tr>
<td>Opportunistic infections, all</td>
<td></td>
</tr>
<tr>
<td>18–64 years</td>
<td>4.31 (3.48–5.36)</td>
</tr>
<tr>
<td>65 years</td>
<td>0.94 (0.81–1.10)</td>
</tr>
<tr>
<td>Serious infections, all</td>
<td></td>
</tr>
<tr>
<td>18–64 years</td>
<td>1.31 (1.20–1.42)</td>
</tr>
<tr>
<td>65 years</td>
<td>1.31 (0.87–2.10)</td>
</tr>
<tr>
<td>Serious infections, excluding GI infections</td>
<td></td>
</tr>
<tr>
<td>18–64 years</td>
<td>2.38 (1.41–3.99)</td>
</tr>
<tr>
<td>65 years</td>
<td>2.38 (1.41–3.99)</td>
</tr>
</tbody>
</table>

OP965 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 suboptimal and prognostic factors for real-life long-term efficacy are insufficiently studied.

Aims & Methods: The aim of this study was to identify patient- and disease-related factors influencing the real-life long-term response of infliximab in CD in 1994 and January 2016 at a tertiary centre, were 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) presence of persistent antibodies towards infliximab (ATI), and 3) the need for IBD related surgery. Since 2010-2011, IFX and ATI serum concentrations at trough were measured in all patients with an house-developed and clinically validated drug sensitive bridging enzyme-linked immunosorbent assay (ELISA). Therapeutic drug monitoring (TDM) was used to identify predictors of IFX failure-free survival using Cox proportional hazards model and Kaplan-Meier analysis. Internal validation of the Cox regression analysis was performed with bootstrapping with 1000 replications.

The c-statistic was used to assess the predictive accuracy of the regression model.

Results: A total of 261 CD patients were included in the final analysis. Median time on IFX was 2.4 [IQR 1.4–4.7] years, and 65 (24.9%) patients experienced IFX failure. Median age at start of IFX was 32.8 [22.6–44] years, after a median disease duration of 3.4 [0.7–13.6] years. In total, 59 (14.9%) patients received anti-TNF prior to IFX start (adalimumab or certolizumab pegol). TDM was used in 202 (77.4%) patients. Estimated 1, 5, and 10 year IFX failure-free survival was 93.7% (95% CI 90.7–96.7), 65.9% (58.3–73.5) and 58.2% (45.6–70.9), respectively. When combining all available IFX measurements during the follow-up of the study, median IFX concentrations were lower in patients who experienced IFX failure (3.1 [0.3–7.5] μg/mL) compared to patients who did not fail IFX (5.3 [3.1–8.4] μg/mL, p < 0.0001). Multivariate Cox regression identified disease duration <1 year (hazard ratio (HR) 2.5 [95% CI 1.2–5.2], p = 0.02), isolated IL1 disease location (HR 2.0 [1.1–3.5], p = 0.02), prior anti-TNF use (HR 2.3 [1.1–4.8], p = 0.03), hemoglobin < 13.5 g/dL (HR 2.3 [1.2–4.4], p = 0.02), absence of TDM use (HR 8.0 [4.1–15.6], p = 1x10^-8), and first IFX dose optimization within first year (HR 3.7 [2.1–6.6], p = 5x10^-6) 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 93.3% (95% CI 92.4–96.4) for the low risk group (0 or 1 risk factor), 79.3% (78.4–80.2) for the medium risk group (2–3 risk factors), and 26.3% (8.4–44.0) for the high risk group (4 or more risk factors) (p = 6x10^-15). IFX concentrations at...
OP066 CIRCULAR ENTERAL NUTRITION FOR THE MAINTENANCE OF REMISSION IN PEDIATRIC CROHN’S DISEASE PATIENTS
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3Paris-Pitié Hospital, Université Sorbonne, Paris/France
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Introduction: Enteral nutrition (EN) is a well-established treatment in pediatric Crohn’s disease (CD) for induction of remission. Stratifing patients according to the amplitude 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: Nineteen 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 IB, patients who came into complete CRP-negative remission were proposed to continue on cyclic EN therapy as sole treatment in an open manner. Cyclic EN consists of a 6 weeks phase of normal feeding followed by a 2 weeks phase of exclusive enteral nutrition, without any concomitant CD-related medication. Patients were followed on a fixed scheme (3 months visits) with collection of anthropometric, clinical and biological data.
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±9.2) and 5 of 6 patients (wPCDAI 5.7±3.2), respectively were in clinical remission. Concomitant 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 (p = 0.05) and albumin normalization with 33.8±3.8 g/L at M0, 41.5±3.0 g/L at M6 (p = 0.05) and 42±2.9 at M12 (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>
</tr>
</thead>
<tbody>
<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 cyclic enteral nutrition. Cyclic EN can be an efficacious non pharmacological treatment of Crohn’s disease patients potentially acting ahead of the inflammation cascade in the intestinal mucosa. A sufficiently power randomized controlled trials is currently conducted by the GETAID pédiatrique to confirm these pilot data.
Disclosure of Interest: F. Rueemmele: Nestle Nutrition Institute, Nestle Health Science
All other authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016 14:00-15:30
OP067 CHANGES IN MUCOSAL-ASSOCIATED INTESTINAL MICROBIOTA AND FECAL FERMENTATION IN INFILTRATING BOWEL DISEASE Patients and healthy subjects: a pilot study
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Introduction: The existing literature on 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 adhesion 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 (phylootyping, PH). Fecal specimens were collected from 14 IBD patients [10 Crohn’s disease (CD), 4 ulcerative colitis (UC)], and from 11 healthy subjects. Mucosal specimens were 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 locus was amplified on a 454-Juino Genome Sequencer. Reads were analyzed by Quantitative Insights into Microbial Ecology (QIIME, v.1.8.0), grouped into operational taxonomic units (OTUs) at a sequence identity level of 97 % by PAST for taxonomic assignment, and aligned by LUST 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 predominant presence of Enterobacteriaceae in IBD and a predominant presence of Ruminococcaceae, Rikenellaceae and Prevotellaceae in CTRLs were prevalent (P < 0.05). Patient pathology findings, according to intestinal sampling site, the analysis revealed that only Ruminococcaceae resulted statistically increased in the colon. Tackling in account only colon biopsy samples, a significant reduction of Rikenellaceae, Proteobacteria markedly increased in the colon. Roseburia, Ruminococcaceae was observed in patients and an increment of Enterobacteriaceae was observed in CTRLs. Finally, stratifying the analysis based on the base of disease activity a decrease of Ruminococcaceae, Peptostreptococcus and Paraprevotella and an increase in Enterobacteriaceae 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, phylum Proteobacteria was significantly more represented, while phylum Firmicutes and Actinobacteria were reduced. The profiles of fecal microbiota partially replicate those of the mucosal microbiota being more similar between controls and patients. It appears that microbiota adhesion 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 tissue.
Disclosure of Interest: All authors have declared no conflicts of interest.

OP068 BACTERIOPHAGE THERAPY: A NEW STRATEGY TO TARGET ADHERENT-INVASIVE ESCHERICHIA COLI BACTERIA IN THE GI TRACT OF CROHN’S DISEASE PATIENTS
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2Université d’Auvergne Inserm U1101, Clermont-Ferrand/France
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Contact E-mail Address: adeline.sivignon@u-clermont1.fr
Introduction: Adherent-invasive Escherichia coli (AIEC) are abnormally predominant on Crohn’s disease (CD) ileal mucosa. AIEC are pathobiont bacteria able to promote inflammatory responses that could initiate or perpetuate the chronic gut inflammation. Antimicrobial treatments, such as bacteriophages (viruses infecting bacteria) represent a way to eliminate these bacteria from the GI tract without disturbing the microbiota-homogenous balance. Here, we report in this pilot study the efficacy of bacteriophages to reduce AIEC colonization associated to intestinal mucosa.
Aims & Methods: Three bacteriophages were selected to efficiently target AIEC isolated from CD patient. Efficacy of this bacteriophage cocktail was investigated using two in vivo experimental models: transgenic mice expressing CEACAM6 colonized by AIEC strain LF82 and the DSS chemically-induced colitis model infected with AIEC strain LF82.
Results: In LF82-colonized CEACAM6-expressing mice, 24 hours after the oral administration of the AIEC 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 colonisation level of LF82 bacteria through the entire gut. In addition, bacteriophage treatment reduced colitis symptoms in the DSS-induced model, with a reduction of LF82 bacteria levels in feces, compared to the control group. Then, we showed that bacteriophages were driving a long-term digestive tract decolonization of AIEC LF82 bacteria which in turns reduces colitis symptoms.

Conclusion: Bacteriophages targeting all 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 proves therefore a new “microbiota friendly” way to efficiently target gut pathogens.

Disclosure of Interest: All authors have declared no conflicts of interest.
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 rRNA gene sequencing performed using 2x300 bp Illumina MiSeq chemistry (F27 & 519R). Raw sequences were analysed using MOTHUR, and statistical tests performed on counts and relative abundances.

**Results:** Faecal and colonic samples were collected from 70 study patients. 14 donors contributed to 21 donor batches. 314 patient and 113 donor (individual + batch) faecal samples along with 160 patient colonic samples were analysed. 2697 ± 540 clean sequences per faecal sample and 2093 ± 881 per colonic biopsy were obtained with rarefaction curves suggesting sampling had reached saturation. In both faecal and colonic samples α-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. LESA 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 microbial α-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 remission across both faecal and colonic samples: taxa within Barnesiella were associated with remission, while OTUs within Fusobacterium 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 are associated with remission of UC which are associated with FMT 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 marketing and synthesized for selective detection of chemically reactive molecules of thiols 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. After sacrificing the animals, unfixed liver tissues were collected and incubated with each probe at the final concentration of 50 to 100 μmol for 10min, and then imaged using multiphoton microscopy (JenLab GmbH, Jena, Germany).

**Results:** Each probe exhibited a strong positive fluorescent response only in the presence of its specific chemically reactive molecule, whereas negligible fluorescent signals were observed upon the additions of other reactive oxygen/nitrogen species and metal ions. There was a good linear relationship between the probe response 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 diseases, 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**

**MONDAY, OCTOBER 17, 2016**

**14:00-15:30  FREE PAPER SESSION: THE FUTURE OF DIAGNOSTIC IN HBP AND UPPER GI – ROOM N1**

**OP072 RELAXIN-COADED IRON-OXIDE MAGNETIC NANOPARTICLES AS A NOVEL THERANOSTIC APPROACH FOR DIAGNOSIS AND TREATMENT OF LIVER FIBROSIS**

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**Introduction:** Hepatic fibrosis is a growing health problem with no effective and clinically approved therapy. Hepatic stellate cells (HSCs) are the key cells involved in the pathogenesis of liver fibrosis. Upon activation, HSCs undergo morphological and functional changes, and are transformed into contractile myofibroblasts leading to scar tissue formation. HSCs are key pathogenic cells involved in liver fibrogenesis, for the diagnosis and monitoring of cellular microenvironment in human diseases.

**Aims & Methods:** In this study, we aimed to develop a nanoparticle-based delivery system 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. After sacrificing the animals, unfixed liver tissues were collected and incubated with each probe at the final concentration of 50 to 100 μmol for 10min, and then imaged using multiphoton microscopy (JenLab GmbH, Jena, Germany).

**Results:** Each probe exhibited a strong positive fluorescent response only in the presence of its specific chemically reactive molecule, whereas negligible fluorescent signals were observed upon the additions of other reactive oxygen/nitrogen species and metal ions. There was a good linear relationship between the probe response 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 diseases, and can be readily extended to examination of diseases and injury of other organs. We anticipate that in the near future this quantitative imaging platform will be evaluated from bench to bedside, leading to real-time monitoring of cellular microenvironment in human diseases.

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

**References**

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

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1Gastroenterology/medicine, UCLA, Los Angeles/United States of America/CA
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Introduction: For decades, stigmata of recent hemorrhage (SRH) in ulcers & NVUGIH have been used to guide endoscopic hemostasis. Arterial blood flow underlying SRH is rarely monitored, yet determines rebleed risk after treatments.

Aims & Methods: In a RCT, our primary aim was to compare 30-day rebleed rates of index lesions for patients treated with Standard vs. DEP guided endoscopic hemostasis. In a 2-center study, patients were resuscitated & consented. They & managing medical-surgical teams were blinded to endoscopic treatments. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic instability) were followed prospectively by research coordinators who recorded routine 30 day outcomes. All blood flow detected by DEP was reproducible & arterial. For 148 consecutive patients (84 Chinese: 17 Malay: 9 Indian: 9 others) underwent WS with SV for evaluation of (i) dysphagia (n = 56 [47.4%]); (ii) reflux symptoms (n = 45 [38.1%]) and (iii) atypical chest pain (n = 17 [14.5%]). HRM with WS was performed in 114 (96%) patients. Compared to WS alone (n = 2/119 [1.7%]), more patients were diagnosed with esophageo-gastric junction (EGJ) outflow obstruction during a ST (n = 8/114 [7.0%]; p = 0.05). The study was well tolerated in all patients.

Conclusion: The use of additional physiological stimuli during routine esophageal manometry improves diagnostic yield and symptom reproducibility. Methodologies: Prospective series of patients referred for esophageal HRM between November 2014-April 2016. All patients had undergone prior endoscopy with findings of normal or mild (LA grade A esophagitis). WS and STM studies were performed in the upright seated position. Diagnosis of major and minor esophageal motility disorders were based on CC version 3.0 for water swallows (2) and modified for solid swallows as appropriate (3). All medications known to interfere with GI motility were stopped for at least one week prior to the study.

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

References
1. Fox et al., NGM 2014.

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Introduction: The Chicago Classification (CC) of esophageal motility disorders for high resolution manometry (HRM) is based on ten 5 mLs water swallows (WS). We have previously reported the use of a solid test meal (STM) in patients undergoing HRM to improve diagnostic sensitivity(1). We further validate the use of a STM in a multicentric cohort.

Aims & Methods: We aimed to determine if the use of a STM during routine esophageal manometry improves diagnostic yield and symptom reproducibility.

Methods: Prospective series of patients referred for esophageal HRM between November 2014-April 2016. All patients had undergone prior endoscopy with findings of normal or mild (LA grade A esophagitis). WS and STM studies were performed in the upright seated position. Diagnosis of major and minor esophageal motility disorders were based on CC version 3.0 for water swallows (2) and modified for solid swallows as appropriate (3). All medications known to interfere with GI motility were stopped for at least one week prior to the study.

Symptoms reported by the patients during HRM study were analyzed for any corresponding manometric abnormalities. Symptom associated dysfunction (SAD) was defined as a symptom event reported during or up to 10 seconds after concurrent esophageal dysmotility during ST.

Results: In 119 (56 Male [47.4%]; more TRICE translocations were randomization at unrelated endoscopy may be seen, particularly among patients & Dieulafoy’s lesions or Mallory Weiss tears- MWT (with active bleeding or NBVV). For Standard treatment, hemoclip-and/ or multipolar probe electrocoagulation (MPEC-large probe) with or without dilute epinephrine injection was used without DEP & visual end points were control of bleeding, flattening VVs, & a foot-print at the SRH. For the DEP group, SRH & lesion base were interrogated for underlying blood flow at < 4 mm deep settings with an FDA approved control unit & disposable DEP probe (Vascular Technology, Nashua, NH). Then Standard RX was applied on & out from the SRH, where the artery was traced. DEP was used to recheck & if residual blood flow was detected, further hemostasis was performed until no blood flow was detected. Standard group patients with flat spots were not treated endoscopically, but DEP patients were if they had blood flow detected. All patients with ulcers & Dieulafoy’s lesions received high dose PPI infusion X 72 hours & then BID for 30 days. MWT patients were treated with anti-emetics & BID PPI. Rebleeding was determined by a 2 gm decrease of Hgb, with clinical signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic instability) were followed prospectively by research coordinators who recorded routine 30 day outcomes.

Results: All blood flow detected by DEP was reproducible & arterial. For 148 patients randomized, see the Table (for 30 day rebleed rates by SRH. There was a significant difference in rebleed rates (15.2%) in Standard group vs. DEP group (p = 0.02138) & surgery (4/76 vs. 0/72 - p = 0.0484). 1 perforation occurred in the Standard group & none in the DEP group.

Conclusion: In a RCT of patients with severe NVUGIH, use of Doppler probe as a guide to endoscopic hemostasis significantly reduced 30 day rebleed & surgery rates compared to Standard, visually guided hemostasis. We now recommend DEP (along with SRH) as a new guide for risk stratification & definitive endoscopic hemostasis in patients with severe NVUGIH. RCT was supported by a VA Career Development Award (1IK08CX000172-01A1) and in part by NIH-NIDDK, AM 41301 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.
Aim & Methods: When we use AIM, indigocarmine accumulates in pit of the duct, and histopathology with an endoscopic image intuitively, so we believe that a magnifying endoscopy with LCI mode, we discovered that the magnifying images of early gastric adenoma. The differentiation ability of a cancer and the non-cancer (adenoma vs. normal) that was clearly demonstrated. 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 are indicated of the endoscopic submucosal dissection (ESD), and were given pre-ESD endoscopy in our hospital from September 2014 to February 2016. Firstly we observed the lesions by magnifying endoscopy with LCI+AIM method and diagnosed using VS classification 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 a significant difference between the BLI mode and the LCI+AIM method. In the classification of visualization ability, 12 lesions were Clear, 22 lesions were Visible, 35 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 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.


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

Results: Of the 6,300 survey completers, 5,931 were retained for analysis (49.2% females; mean age 47.4, range 18–92; 1,949 US, 1,994 UK, 1,988 Canada) after inconsistent responders were eliminated. Due to the quota-based sampling, ROME IV IBS show that IBS prevalence and demographic distribution is equivalent in all 3 countries to measure and compare ROME IV vs. Rome III IBS. It is unknown how this will affect Rome IV criteria are used than with Rome III, and the new criteria also change IBS subtype distribution, marked reducing the IBS-M proportion. [Support: National Institute of Diabetes and Digestive and Kidney Diseases; National Institute of Mental Health; National Institute of Diabetes and Digestive and Kidney Diseases].


Introduction: Gastric cancer (GC) is the second most common malignancy and the cause of the second leading cancer death worldwide. The current diagnostic methods for GC are not enough to identify incurable factors including peritoneal metastasis and local invasion. We have previously reported the usefulness of urinary biomarkers for diagnosis of GC. With the goal of discovering non-invasive biomarkers for pre-
Aims & Methods: Our aim was to assess the prevalence of IBS as well as anxiety and depression in UC patients subdivided into typical reflux symptoms sub divided into GERD and FH by means of upper GI endoscopy and MII-PH monitoring. We also aimed to assess the prevalence of various clinical and endoscopic characteristics in IBD. We compared FH and IBS 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 four major diagnostic criteria for GERD (ERD) and IBS (IIRAO). Depression and anxiety were assessed by the HADS. Upper GI endoscopy and 24h MII-PH off-therapy monitoring were performed in all cases. In patients with IBS, fecal calprotectin was measured and colonooscopy was scheduled for values > 100 μg/kg to exclude organic disease. Multivariate logistic regression analysis was performed to identify independent risk factors for FH. A predictive model for FH diagnosis based on clinical and endoscopic findings was developed by applying the purposeful selection of covariates. The coefficients estimated in the multivariate logistic regression analysis were used to predict FH diagnosis. The performance of the predictive model was then assessed by examining measures of discrimination and calibration. Discrimination was considered as the ability of the predictive model to differentiate between patients with FH diagnosis and patients with GERD diagnosis and was quantified by calculating the area under the ROC curve (AUC). A calculator to help clinicians in automatically computing the predicted probability of FH versus GERD in patients presenting with heartburn was built.

Results: Of the 701 consecutive heartburn patients who entered the study, 458 (65%) had GERD whereas 243 (35%) had FH. IBS was found in 143/458 (31%) GERD but in 187/243 (77%) FH patients (p < 0.001). At multivariate analysis IBS, anxiety, and smoking resulted independent risk factors for FH whereas hiatial hernia resulted protective. We developed a predictive model based on clinical and endoscopic characteristics (IBS, Smoking, Anxiety, Age ≥ 45, HADS > 8, and positive ROC curve in an external validation cohort of 51 patients was 0.920. Considering the previously established cut-off, sensitivity and specificity of the predictive model in diagnosing FH against GERD were 84.3% and 78.9%, respectively. A calculator to help clinicians in automatically computing the predicted probability of FH versus GERD in patients presenting with heartburn was built (URL: http://app.calculed.com/#/ calculation/2012).

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

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

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

<table>
<thead>
<tr>
<th>Symptom persists</th>
<th>Probability</th>
<th>95% CI</th>
<th>Symptom subsides</th>
<th>Probability</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>22%</td>
<td>18-26%</td>
<td>23%</td>
<td>16-28%</td>
<td></td>
</tr>
<tr>
<td>Sense of coherence</td>
<td>21%</td>
<td>18-24%</td>
<td>17%</td>
<td>13-22%</td>
<td></td>
</tr>
<tr>
<td>Coping resources</td>
<td>19%</td>
<td>18-21%</td>
<td>20%</td>
<td>17-23%</td>
<td></td>
</tr>
<tr>
<td>GI-specific anxiety</td>
<td>16%</td>
<td>14-18%</td>
<td>27%</td>
<td>23-31%</td>
<td></td>
</tr>
<tr>
<td>Quality of life</td>
<td>16%</td>
<td>14-18%</td>
<td>27%</td>
<td>23-31%</td>
<td></td>
</tr>
<tr>
<td>GI symptom severity</td>
<td>12%</td>
<td>10-14%</td>
<td>44%</td>
<td>40-50%</td>
<td></td>
</tr>
<tr>
<td>GI symptom severity</td>
<td>8%</td>
<td>7-9%</td>
<td>47%</td>
<td>41-50%</td>
<td></td>
</tr>
</tbody>
</table>

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


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

M. Simrén: Unrestricted research grants from Danone, and Ferrering Pharmaceuticals.

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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 poorly understood.

Aims & Methods: The aim of this study was to determine the probability of IBS-related symptoms to persist or subside over time. The study consisted of three parts. First, we addressed the question which factors can determine the probability of a symptom to 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 (VSI), 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: The main result 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 hiatial hernia (23% 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 role emotional (10 and 79%). The QOL domains physical role, social role, and food were intermediate.

Conclusion: IBS overlaps more frequently with FH than with GERD, suggesting common pathways and treatment. The score derived from ISAIAH predictive model allows a high level of suspicion for FH and can be useful in clinical practice.
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. Simmer: Unrestricted research grants from Danone and Ferring Pharmaceuticals; Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Albireo, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall. B. Jonéfil: 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 America USA. H. Törnbom: Consultant/Advisory Board member for Almirall, Danone and Shire. L. Ohman: Unrestricted research grant from AstraZeneca; Consultant/Advisory Board member for Genetic Analysis; Speaker for Takeda and Abbvie. H. Strid: Consultant/Advisory Board member for Takeda, Abbvie, Ferring Pharmaceuticals, Tillotts, MSD Speaker for Takeda, Abbvie, Ferring Pharmaceuticals, Tillotts, MSD and Shire.

OP083 ENHANCED DIAGNOSTIC PERFORMANCE OF SYMPTOM-BASED CRITERIA FOR IRRITABLE BOWEL SYNDROME BY INTEGRATING CLINICAL HISTORY AND COLONOSCOPY

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1 Leeds Gastroenterology Institute, Leeds Teaching Hospitals NHS Trust, Leeds; United Kingdom
2 Clinical Enteric Neurosensory Translational and Epidemiological Research (C.E.N.T.E.R.), Mayo Clinic, Rochester; United States of America

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, colonoscopy, and histology 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 symptoms, 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>
<th>Positive LR (95% CI)</th>
<th>Negative LR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rome III criteria and normal Hb and CRP</td>
<td>49.0% (34.4%–63.4%)</td>
<td>89.2% (83.2%–93.6%)</td>
<td>4.32 (2.67–7.66)</td>
<td>0.59 (0.46–0.72)</td>
</tr>
<tr>
<td>Rome III criteria and HADS score ≥8</td>
<td>47.2% (35.3%–59.9%)</td>
<td>89.1% (84.2%–92.9%)</td>
<td>4.32 (2.67–7.66)</td>
<td>0.59 (0.46–0.72)</td>
</tr>
<tr>
<td>Rome III criteria and high somatisation</td>
<td>69.6% (54.0%–83.4%)</td>
<td>93.2% (87.9%–96.7%)</td>
<td>5.04 (2.48–10.2)</td>
<td>0.71 (0.53–0.84)</td>
</tr>
<tr>
<td>Rome III criteria, normal Hb and CRP, and high somatisation</td>
<td>42.4% (22.7%–61.1%)</td>
<td>96.8% (92.0%–99.1%)</td>
<td>7.36 (2.63–21.7)</td>
<td>0.76 (0.63–0.90)</td>
</tr>
<tr>
<td>Rome III criteria, no nocturnal passage of stool, and HADS score ≥8</td>
<td>69.0% (51.6%–84.3%)</td>
<td>95.4% (91.7%–98.5%)</td>
<td>4.84 (2.33–10.0)</td>
<td>0.82 (0.70–0.91)</td>
</tr>
<tr>
<td>Rome III criteria, no nocturnal passage of stool, and high somatisation</td>
<td>18.2% (9.8%–29.6%)</td>
<td>99.0% (86.3%–99.9%)</td>
<td>17.3 (4.45–67.6)</td>
<td>0.83 (0.72–0.90)</td>
</tr>
</tbody>
</table>
Table

<table>
<thead>
<tr>
<th></th>
<th>Diagnosed IBS-D (n = 859)</th>
<th>Undiagnosed IBS-D (n = 370)</th>
<th>Controls (n = 56,932)</th>
<th>p-value: Diagnosed vs. controls</th>
<th>p-value: Diagnosed vs. undiagnosed</th>
<th>p-value: Undiagnosed vs. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any provider visits</td>
<td>7.23 (0.31)</td>
<td>5.17 (0.35)</td>
<td>4.14 (0.02)</td>
<td>&lt; 0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Gastroenterologist visits</td>
<td>19 (0.62)</td>
<td>0.01 (0.01)</td>
<td>0.03 (0)</td>
<td>0.001</td>
<td>0.001</td>
<td>0.012</td>
</tr>
<tr>
<td>General practitioner visits</td>
<td>2.69 (0.12)</td>
<td>2.06 (0.15)</td>
<td>1.70 (0.01)</td>
<td>&lt; 0.001</td>
<td>0.001</td>
<td>0.007</td>
</tr>
<tr>
<td>Emergency room visits</td>
<td>0.22 (0.04)</td>
<td>0.12 (0.03)</td>
<td>0.17 (0)</td>
<td>0.002</td>
<td>0.012</td>
<td>0.264</td>
</tr>
<tr>
<td>Hospitalisations</td>
<td>0.14 (0.03)</td>
<td>0.08 (0.03)</td>
<td>0.11 (0)</td>
<td>0.099</td>
<td>0.148</td>
<td>0.430</td>
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Monday, October 17, 2016 14:00–15:30
What is New in Gastro Endoscopic Submucosal Dissection (ESD) – Room L7

OP084 Long-term outcomes of Endoscopic Submucosal Dissection (ESD) and Gastroscopy based on Indications for ESD

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

Aims & Methods: This study aimed to compare long term outcomes between ESD and gastroscopy, 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 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 (AC), expanded criteria (EC) and beyond expanded criteria (BEC group).

Conclusion: The recurrence rate was neither significantly different between ESD and gastrectomy patients, nor was significantly different between criteria groups in terms of ESD criteria. 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 gastro 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 patient and lesions’ factors. However, the knowledge of risk factors alone is not readily accessible, 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 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 (AC), expanded criteria (EC) and beyond expanded criteria (BEC group).

Conclusion: The recurrence rate was neither significantly different between ESD and gastrectomy patients, nor was significantly different between criteria groups in terms of ESD criteria. 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.

Reference
OP087 LONG-TERM OUTCOMES OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION: FOCUS ON METACHRONOUS AND NON-CURATIVE RESECTION MANAGEMENT

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Introduction: Endoscopic submucosal dissection (ESD) is an effective treatment for gastric superficial neoplasms, being curative in 80–85%. Identification of risk factors for a non-curative resection is of utmost importance to improve patient selection. Furthermore, it is important to evaluate the management after an unsuccessful treatment in order to assess the clinical outcomes of each option, that is, surveillance or surgical treatment. Moreover, patients with an early neoplastic lesion are at risk of developing metachronous lesions and endoscopic surveillance will still be needed after endoscopic resection. The identification of risk factors for metachronous development is also important to adequate surveillance.

Aims & Methods: The aims of this study were to identify risk factors for non-curative resection and metachronous development and to evaluate management and outcomes after non-curative resection. Methods: Single centre assessment of a cohort of consecutive patients submitted to gastric ESD, with a minimum follow-up of 18 months. The Japanese Gastric Cancer Treatment Guidelines criteria already used in clinical practice: recurrences were also classified with the recently published European Society of Gastrointestinal Endoscopy guidelines. Univariate analysis (independent t-test, Mann-Whitney U test or chi-square test as appropriate) and multivariate logistic regression were performed to identify risk factors. Odds ratios (OR) were computed with 95% confidence intervals (CI). Survival was analysed with Kaplan-Meyer curves and log-rank test. Significance level was defined as p < 0.05.

Results: Long procedure time and more advanced histology in pre-resection biopsies were associated with non-curative resection (p < 0.05) but only intramucosal carcinoma on pre-resection biopsies was identified as a significant risk factor on multivariate analysis (adjusted OR 3.04, 95% CI 1.02–9.86). Histological upgrade (from low-grade dysplasia to high-grade dysplasia or from high-grade dysplasia to carcinoma) occurred in 49.5% of the cases. Metachronous lesions occurred in 18.4% and the incidence rate was 4.7 lesions (95% CI 3.0–6.7) per 100 patient-years. The median time to metachronous detection was 24 months (interquartile range 9–56.25 months). Older age at diagnosis was identified as the only predictor of metachronous development in logistic regression (OR 10 years 1.68, 95% CI 1.03–2.74). Overall survival was 94.5% and 89.5% at 1 and 3 years, respectively; disease-specific survival was 99.4%, with only one patient dying of gastric cancer. Survival was significantly higher in patients with curative resections (log-rank 4.538, p = 0.033). In the non-curative resection group, patients submitted to surgery were significantly younger (mean age 66.7 ± 9.4 versus 73.6 ± 7.5 in the follow-up group, p = 0.037) and were less frequently classified as ASA III/IV (23.1% versus 31.1%, p = 0.62). However, survival was significantly worse in the different in the two groups (log-rank 0.929).

In gastrectomy specimens, there was no residual neoplasia in 75%. Comparing criteria. The median follow-up time was 40 months. End-bloc and complete resection rates were 93.3% and 93.8%, respectively. Overall adverse events occurred in 13%. Majority of adverse events were location (lower third or the other), tumor size (≥30 or ≤≤30 mm), tumor depth (submucosal invasion ≤500 μm (SM2) or shallower than SM2), histopathological type (undifferentiated or differentiated), lymphatic invasion, vascular invasion, ulceration (scar), positive vertical margin and lymph node metastasis (LNM). In this study, recurrence was defined as the metastatic one, and curative resections were defined with a median follow-up period of 67 months. LNM was found in 89 patients (8.4%) and 14 patients (1.3%) developed recurrence. All recurrent sites at the time of initial diagnosis were patients with local-risk resection (log rank 5.445, p < 0.001). Kaplan-Meier analysis showed that the independent risk factors for recurrence were LNM (hazard ratio [95% confidence interval] = 28.2 [7.12–112, p < 0.001) and vascular invasion (4.37 [1.25–15.3, p = 0.021). The 3-year and 5-year OSs were 96.8% and 92.6%, respectively, and the 3-year and 5-year DSSs were 99.4% and 98.8%, respectively.

Conclusion: This multicenter study with the largest cohort revealed that additional radical surgery for patients who do not meet the current curative criteria for ESD of EGC has a low recurrence rate and excellent prognosis. Submucosal operation during ESD for EGC does not make risk of LNM and prognosis worse.

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

References
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Introduction: Endoscopic full-thickness resection (EFR) is a minimally invasive method for an en bloc resection of GI lesions originating from the muscularis propria layer. Successful closure of the wall defect is a critical step. Aim & Methods: The aim was to evaluate the safety 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 2015, among 10 patients undergoing EFR, 11 gastrectomy specimens with an intramucosal 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 lighted gently (with videos). Patient characteristics, tumor size, end 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 lesser curvature in the fundus. The endoscopic Gralus 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 significant differences were location (the size of the lesion was 1.3 cm (range 0.5–3.5 cm). Pathological diagnosis of these lesions were 11 gastrointestinal stromal tumors (GISTs) and 2 leiomyomas. No major adverse events occurred during or after the procedure. All lesions were discharged at 24 hours. Further resection and information regarding the probability of success. Metachronous incidence is significant, being older patients at increased risk for its development. In the non-curative resection group, survivors, who underwent radical surgery after having failed to meet the curative criteria to gastrectomy. An individualized decision is adequate after a non-curative resection and surveillance seems to be an adequate option in selected cases.

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

References
Disclosure of Interest:
confirming the incision line from the inside of the stomach without exposure the
gastric cancer, because it was possible to incise all-layer of the stomach while
patients were preserved QOL without postoperative complications such as small
tumor, silicon sheet and PGA sheet are removed through oral cavity. Finally, the
for tumor cells, standard gastrectomy with D2 lymphadenectomy is performed.
for malignancy, EFTR is performed. On the other hand, when they are positive
ing the bright nodes are dissected laparoscopically and subjected to rapid intrao-
sentinel nodes emitting fluorescence are identified. The lymphatic basins contain-
submucosal layer around the lesion. Using an infrared fluorescence laparoscope,
solution (5
Laparoscopic sentinel node biopsy. On the day before surgery, indocyanine green
the ethical standards of the institution's Committee on Human Experimentation.
obtained from each patient. All procedures were conducted in accordance with
9 patients with clinical T1 gastric cancer, who were outside of indication of ESD,

Aims & Methods:

Introduction:
Endoscopic full-thickness resection (EFTR) and laparoscopic and
submucosal tumors with purse-string sutures. 

Aims & Methods: We introduced a sealed EFTR technique and describe a clinical study of EFTR in patients with submucosal invasive gastric cancer who were diagnosed as negative for lymph node metastasis by laparoscopic sentinel lymph node biopsy. Patients: Between December 2012 and April 2013, 9 patients with clinical T1 gastric cancer, who were outside of indication of ESD, were enrolled in this study. Before surgery, written informed consent was obtained from each patient. All procedures were conducted in accordance with the ethical standards of the institution's Committee on Human Experimentation. Laparoscopic sentinel node biopsy. On the day before surgery, indocyanine green solution (5ug/ml) is injected at a volume of 0.2ml each into 4 points in the submucosal layer around the lesion. Using an infrared fluorescence laparoscopic sentinel nodes emitting fluorescence are identified. The lymphatic basins containing the bright nodes are dissected laparoscopically and subjected to rapid intraoperative pathological examination. When the sentinel lymph nodes are negative for malignancy, EFTR is performed. On the other hand, when they are positive for tumor cells, standard gastrectomy with D2 lymphadenectomy is performed. Sealed EFTR At first, circumferential mucosal incision is performed in the same manner as ESD. Continuously, silicon sheet and polyglycolic acid (PGA) sheet are put on the serosa of the lesion and pasted with fibrinogen, thrombin solution. Then, full-thickness incision is performed by Hook knife and/or FT knife. The tumor, silicon sheet and PGA sheet are removed through oral cavity. Finally, the defect of gastric wall is closed laparoscopically using hand-sewn sutures.

Results: Seven patients (78%) were negative for sentinel node metastasis, and were performed EFTR. Four patients who were enrolled after 2014 were performed EFTR and laparoscopic sealing method (sealed EFTR). In sealed EFTR, it was possible to incise all-layer of the stomach with keeping good endoscopic view without collapse of the stomach by covering the serosa using silicon sheet and PGA sheet. The condition of the patients was almost the same as before surgery. All patients were preserved QOL without postoperative complications such as small stomach syndrome or early satiety. During follow-up of 1 to 4 years, all patients except one, who died of other cancer, are alive without recurrence or metastasis.

Conclusion: Sealed EFTR is considered to be useful technique as one of the minimally invasive surgeries for lymph node negative gastric cancer, because it was possible to incise all-layer of the stomach while confirming the incision line from the inside of the stomach without exposure the tumor to the abdominal cavity.

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

Reference

cosa-infiltrating gastric cancer without sentinel node metastasis: a pilot study of laparoscopy-assisted endoscopic full-thickness resection in an in vivo por-
OPI094 INFLAMMATORY AND ANTIOXIDANT RESPONSE FOLLOWING STANDARD MEAL CONSUMPTION IN PATIENTS WITH FUNCTIONAL DYSPEPSIA AND HEALTHY VOLUNTEERS
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1Department Of Internal Medicine, IRCCS S. Matteo Hospital Foundation, University of Pavia, Pavia/Italy
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Introduction: The Rome III criteria recognize two distinct subgroups of functional dyspepsia (FD): the postprandial distress syndrome (PDS) and the epigastric pain syndrome (EPS). The underlying pathophysiologic mechanisms of these syndromes are partially known. Recently, the worsening of hypersensitivity in the postprandial period was shown in PDS (1–2) and an impairment of gastric compliance was detected in EPS (2). Moreover, in FD patients an altered permeability of intestinal mucosa, an altered expression of cell adhesion proteins and the presence of mucosal infiltration of mast cells and eosinophils were shown (1), suggesting a role for inflammation and permeability alterations in the pathogenesis of this condition.
Aim: Our aim was the evaluation of postprandial modification of both inflammatory and antioxidant markers in a group of PDS patients in comparison with healthy volunteers (HV). 14 consecutive, non-smoking patients (9 females, mean age 42.8 ± 11.2 years) affected by FD, subtype PDS, according to Rome III criteria and a group of 13 HV comparable for age and gender were enrolled.
Methods: Chronic inflammatory and autoimmune diseases were excluded. Serum levels of inflammatory cytokines (IL-1, IL-6 and TNFα), insulin, glucose, uric acid (UA) and lipopolysaccharide (LPS) were evaluated at fast and every 30 minutes after the ingestion of a standard meal (proteins 15.7%, lipids 28.3%, carbohydrates 56.0%), and after 30 min recording, patients performed to assess oesophageal function. After 30 min recording, patients performed to assess oesophageal function. After 30 min recording, patients performed to assess oesophageal function. After 30 min recording, patients performed to assess oesophageal function.
Results: The IGP drop but it significantly delayed the GE t1/2 (p = 0.007 and 0.005 respectively). Similarly, the duodenal MI was also lower after LG for both phases III and IV, while the antral MI was lower only after LG for phase III. Hunger or satiation ratings (JT3) were not affected by LG treatment in PDS and HV, similarly for OPI scores (JT3).
Conclusion: 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 role of the antioxidant system in functional dyspepsia.
Disclosure of Interest: All authors have declared no conflicts of interest.
References

OPI095 A DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSS-OVER STUDY USING BACLOFEN IN THE TREATMENT OF RUMINATION SYNDROME
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Introduction: Rumination syndrome and supra-gastric belching are two conditions with limited treatment options. Baclofen, a γ-aminobutyric acid (GABA) agonist, increases 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 x 1 day) 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, which were collected at the end of each 2 week intervention period. In total, an overall treatment evaluation (OTE) on -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: Baclofen significantly reduced the number of rumination and/or supra-gastric belching events compared with placebo (p = 0.0007 and 0.0167 respectively).
Conclusion: Baclofen is effective in reducing rumination and supra-gastric belching events compared with placebo.
Disclosure of Interest: All authors have declared no conflicts of interest.
Disclosure of Interest: An effective GES reduced significantly the frequency of refractory gastroparesis, was not associated with a better QoL, and was significantly faster during the “ON” period. The greater symptomatic effect with an effective GE was not associated with a change in LOS sphincter (LOS) pressure, to confirm or not the efficacy of GES.

Introduction: Prospective, patients were implanted with an ENTERRA (R) device with reverse recording, to confirm or not the efficacy of GES. We enrolled 20 patients (mean age 42y (range 18–61), 13f). Lower oesophageal sphincter (LOS) pressure was significantly higher in the baclofen treatment arm compared to the placebo arm (17.8±1.4 vs. 12.8±1.4 mmHg, p = 0.001). The number of transient LOS relaxations was lower (6 ± 1 vs. 8±2, p = 0.07), without any difference in strainings episodes between placebo and baclofen arm, but the percentage of strainings episodes associated with rumination was significantly lower in the baclofen arm (16.4±3.8 vs. 31.29±5.96, p = 0.0005). The number of postprandial regurgitation symptoms marked by the patients tended to be lower in the baclofen treatment arm (p = 0.09), OTE was superior after baclofen compared to placebo (1 (0–2) vs. 0 (1–0), p = 0.04).

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

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

Background: Gastroparesis (GP) is a neuromuscular disorder resulting from a failure of gastrointestinal (GI) motility, and is commonly associated with delayed gastric emptying (GE) (1). In the absence of a gold standard treatment, options are usually empirical and based on symptom control. The implementation of novel therapeutic strategies is of interest.

Methods: A multicenter, double-blind, randomized controlled cross-over trial was performed in a single center, including 20 patients with idiopathic delayed GE (average GE half-time >5h, LOS sphincter (LOS) pressure >20 mmHg). Patients were randomized to receive baclofen or placebo for 3 months, followed by 4 months “OFF”. During the cross-over phase, both patients and physicians were blinded to the treatment arm. The primary endpoint was an increase in GE half-time and an improvement of the global symptom score (GSS), defined as the sum of the score of each symptom on a 1–4 scale. Secondary endpoints were an increase of the GE rate (2), and the number of episodes of rumination and oesophageal transient lower oesophageal sphincter relaxations (OTE).

Results: We enrolled 20 patients (mean age 42y (range 18–61), 13f). Lower oesophageal sphincter (LOS) pressure was significantly higher in the baclofen treatment arm compared to the placebo arm (17.8±1.4 vs. 12.8±1.4 mmHg, p = 0.001). The number of transient LOS relaxations was lower (6 ± 1 vs. 8±2, p = 0.07), without any difference in strainings episodes between placebo and baclofen arm, but the percentage of strainings episodes associated with rumination was significantly lower in the baclofen arm (16.4±3.8 vs. 31.29±5.96, p = 0.0005). The number of postprandial regurgitation symptoms marked by the patients tended to be lower in the baclofen treatment arm (p = 0.09), OTE was superior after baclofen compared to placebo (1 (0–2) vs. 0 (1–0), p = 0.04).

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

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

References:

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

Introduction: Despite numerous efforts to develop novel therapies, pancreatic ductal adenocarcinoma (PDAC) has remained one of the most devastating and lethal malignancies worldwide. The poor outcomes of patients suffering from PDAC can be attributed to the presence of desmoplastic stroma. PDAC is an atypical member of the ankyrin repeat-containing IκB family of NFκB inhibitors that was first identified as a candidate proto-oncogene in chronic lymphocytic leukemia. Although a recent study provides evidence that deletion of Bcl-3 expression results in increased cell proliferation, cell survival and malignant potential. However, the functional role of Bcl-3 in pancreatic cancer has not been elucidated so far. In this study, we aim to identify whether Bcl-3 impacts pancreatic cancer development and progression in mice and humans.

Aims & Methods: PDAC tissues and cell lines obtained from humans and a KrasG12D mouse model (KC) of pancreatic cancer were investigated for Bcl-3 expression. The overall survival of human PDACs expressing high and low levels of Bcl-3 was compared. Further, Bcl-3 was deleted in a KrasG12D mouse model (KC) and tumor incidence, metastases as well as proliferation, and apoptosis in tumor-bearing mice and primary tumor cells was examined. Pancreatic Intraepithelial Neoplasia (PanIN) in KC and KCM mice at 13 and 24 weeks was analyzed.

Results: We show that Bcl-3 is highly expressed in human PDACs and in a KC mouse model of pancreatic cancer correlating with prognosis and overall survival. 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 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.

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

Introduction: Gastrointestinal electrical stimulation (GES) has been used for refractory vomiting, as a result of a prospective multicenter, double-blind, randomized controlled cross-over trial. The aim of this study was to assess the efficacy and safety of an electric stimulation device for the treatment of nausea and vomiting associated with gastroparesis in 133 patients with diabetes lasting from 5.1 years, associated with gastroparesis in 133, 5.9 years, associated with gastroparesis in 133, 5.9 years, associated with gastroparesis in 133.

Methods: A total of 149 patients were evaluated at 9 months. Among the 172 patients, 149 patients were evaluated at 9 months. Among the 172 patients, 149 patients were evaluated at 9 months.

Results: We enrolled 20 patients (mean age 42y (range 18–61), 13f). Lower oesophageal sphincter (LOS) pressure was significantly higher in the baclofen treatment arm compared to the placebo arm (17.8±1.4 vs. 12.8±1.4 mmHg, p = 0.001). The number of transient LOS relaxations was lower (6 ± 1 vs. 8±2, p = 0.07), without any difference in strainings episodes between placebo and baclofen arm, but the percentage of strainings episodes associated with rumination was significantly lower in the baclofen arm (16.4±3.8 vs. 31.29±5.96, p = 0.0005). The number of postprandial regurgitation symptoms marked by the patients tended to be lower in the baclofen treatment arm (p = 0.09), OTE was superior after baclofen compared to placebo (1 (0–2) vs. 0 (1–0), p = 0.04).

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

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: In conclusion, the present study reveals ITGA5 as a novel prognostic and therapeutic target in pancreatic tumor stroma. These data make a strong case to utilize this target for developing novel diagnostic and therapeutic strategies against pancreatic tumors.

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

References

OP099 MICRORNA-622 INHIBITS EPITHELIAL-MESENCHYNAL TRANSITION BY TARGETING LONG NON-CODING RNA HULC IN HUMAN PANCREATIC CANCER
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Introduction: Transforming growth factor (TGF)-β1-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-β-induced lncRNA during EMT and reveal contributions of the inter-relationship between the TGF-β-induced lncRNA and miRNA to the regulatory mechanisms of EMT in human pancreatic cancer. We used human pancreatic cancer (Panc-1, BxPC-3, MiaPaCa-2, QGP-1 and KP-3) and non-malignant pancreatic ductal (hTERT-HPNE) cells. Expression profiling of 90 lncRNAs and 2565 miRNAs were performed using qPCR and miRNA microarray. lncRNA targets were predicted by miRanda. Cells were treated with 10 ng/ml of TGF-β 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-β in Panc-1 cells by 1.4-fold. From these, HULC was amongst the top most significantly up-regulated. HULC expression was induced by TGF-β by 1.5-2.7-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-β compared to control. Of these, miR-622 was predicted to target HULC by miRanda. miR-622 expression was reduced by TGF-β by 0.5 to 0.9-fold in a panel of pancreatic cancer cells. Overexpression of miR-622 using miRNA mimic 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-β, (b) demonstrating that HULC promotes EMT, (c) identifying that miR-622, as a down regulated miRNA by TGF-β, can target HULC, and (d) showing a functional role for miR-622 in EMT via targeting HULC. These observations implicat 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, PI3-K-Akt-mTOR, NF-kB...). Thus, for instance, SHP-2 plays a role in cellular responses to growth factors (IGF, EGF, FGF, IGF-1...), cytokines (IL-5, 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 (Ptf1a-Cre SHP-2f/f) with or without Pancreas specific deletion (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 results in progressive reduction of the exocrine compartment in the growing pancreas is impaired. In adult mice, organ weight is reduced by about 50%, compared to uncombined littermate-controls. In the organ growth phase, centro-acinar cells display enhanced cell death (necrosis and apoptosis) which is accompanied by markedly reduced proliferation. In aged SHP-2f/f mice acinar lobuli are consecutively replaced by adipocytes. Lineage-tracing experiments provide insight into the origin of this cell population (invasion vs. transdifferentiation) and will be presented. Interestingly, introduction of mutated Kras (Lsl-KrasG12D) into the model fully compensates for the deletion of SHP-2. Finally, in the pancreas, we not only observe an essential role of SHP-2 in adequate activation of the RTK-Ras-Raf-MEK-ERK-signaling axis but also in positive regulation of RTK-expression levels.

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

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

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

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

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

References:
3. Maniati E, Bossard M, Cook N, Candido JB, Emami-Shahri N, Nedospasov S, deryakabacaoglu@gmail.com
4. Kabacaoglu D. Chronic Inflammation and Cancer, German Cancer Research Center, Heidelberg / Germany.
colonic of CDEIS responding patients. The molecular profile appears to be different from anti-TNF treatment.


J. Panis: Julián Panis: Personal fees from Boehringer Ingelheim, during the conduct of the study, personal fees from Abbvie, Galapagos, Genentech Roche, Pfizer, Takeda, TiGenix and Topvetre, outside the submitted work.

**OPI04 EFFICACY OF USTEKINUMAB FOR INDUCTION AND MAINTENANCE OF ENDOSCOPIC HEALING IN PATIENTS WITH CROHN'S DISEASE**


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Introduction: Ustekinumab (UST) has been shown to induce & maintain clinical remission & endoscopic healing of the mucosa in CD. The endoscopy substudy primary endpoint was met; a single IV dose of UST induced significantly greater reduction in SES-CD activity vs PBO, despite a relatively early evaluation at Wk8. Results in the 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
S. Hanauer: Investigator for Janssen Research and Development, LLC
D. Wolf: Investigator for Janssen Research and Development, LLC
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J. Johanns: Employees of Janssen Research and Development, LLC
P. Szapary: Employee of Janssen Research and Development, LLC
B.G. Feagan: Investigator for Janssen Research and Development, LLC
W. Sandborn: Investigator for Janssen Research and Development, LLC

**OPI05 FILGOTINIB, A SELECTIVE JAK1 INHIBITOR, INDUCES CLINICAL REMISSION IN PATIENTS WITH MODERATE-TO-SEVERE CROHN'S DISEASE: FINAL ANALYSIS OF THE PHASE 2 FITZROY 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, disease duration ≤8 years, ≥1 corticosteroid tapering after Week 10 are presented. On Week 10 clinical response, patients continued to receive filgotinib (200 mg or 100 mg QD) for an additional 10 weeks. Patients who demonstrated clinical response (CDAI-100) underwent corticosteroid tapering after Week 10. Anti-TNF naïve as well as anti-TNF non-responders were included. Immunosuppressants were to be discontinued prior to treatment initiation. Final data for the primary endpoint of clinical remission (CDAI < 150) at Week 10 are presented.

**Results:** Baseline characteristics were comparable in both groups, including mean disease duration (8.3 y), mean CDAI score (293), mean CRP (15.6 mg/L, 41% >10 mg/L), oral corticosteroids (51%, mean daily dose 21.6 mg/day). Primary endpoint of the study was met: Filgotinib induced clinical remission in 47% of the patients, compared to placebo recipients (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:77%, PBO:41%) and showed an improvement of at least 50% in CDAI (FIL:52%, PBO:19%), compared to placebo (p = 0.05).

**Table 1:** Key efficacy parameters

<table>
<thead>
<tr>
<th>Variable/unit/population</th>
<th>Placebo</th>
<th>Filgotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=44</td>
<td>n=128</td>
<td></td>
</tr>
<tr>
<td>Clinical remission</td>
<td>23</td>
<td>47</td>
</tr>
<tr>
<td>(CDAI &lt; 150), %, IIT-NRI</td>
<td>0.0077</td>
<td></td>
</tr>
<tr>
<td>PRO2, mean change</td>
<td>-15.6</td>
<td>-21.9</td>
</tr>
<tr>
<td>from baseline, IIT-LOCF</td>
<td>0.0321</td>
<td></td>
</tr>
<tr>
<td>17.6</td>
<td>33.8</td>
<td>0.0045 (c)</td>
</tr>
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</table>

A44 United European Gastroenterology Journal 4(5S)
Table 1  Continued

<table>
<thead>
<tr>
<th>Variable/unit/population</th>
<th>Placebo</th>
<th>filgotinib</th>
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</thead>
<tbody>
<tr>
<td>n</td>
<td>44</td>
<td>128</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total IBDQ score, mean change from baseline, ITT-LOCF  
SAS-CD improvement by at least 50%, N, ITT-LOCF  
overall total histopathology score, mean change from baseline, ITT-LOCF

CDAI: Crohn’s Disease Activity Index; ITT: Intent-to-treat; NRI: Non-responder imputation; LOCF: Last observation carried forward; PR2: Patient Reported Outcome = 7x (mean daily number of liquid or very soft stools) + 7x (mean daily abdominal pain score); IBDQ: Inflammatory Bowel Disease Questionnaire; SF-36: Short Form 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 its favourable risk/benefit profile, showing its potential as an oral treatment with a novel mechanism of action for the treatment of CD.


OPI06 TOFACITINIB HAS INDUCTION EFFECT IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS, REGARDLESS OF PRIOR TNF INHIBITOR THERAPY
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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). Two phase 3 randomised placebo (PBO)-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01458951) demonstrated efficacy of tofacitinib 10 mg twice daily (BID) vs PBO as induction therapy for patients (pts) with moderate to severe UC.

Aims & Methods: We investigated the effect of prior tumour necrosis factor inhibitor (TNFi) therapies or disease activity (baseline Mayo score) on clinical efficacy endpoints and patient-reported outcomes (PROs) in pooled data from OCTAVE Induction 1 and 2. Adults with moderate to severely active UC (baseline Mayo score ≥2, rectal bleeding subscore ≥1 and endoscopic subscore ≥2) and prior failure/intolerance to ≥1 of corticosteroids, thiopurines or TNFi were randomised (4:1) to receive tofacitinib 10 mg or PBO BID 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 of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1). All endpoint scores were measured 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 ≥ or < 9; Table). For all three endpoints, greater effects were observed when comparing secondary vs primary TNFi failure subpopulations and baseline Mayo score < 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>Placebo N = 234</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission, n (%)</td>
<td>159 (17.6)</td>
</tr>
<tr>
<td>Prior TNFi exposure</td>
<td>14 (6.0)</td>
</tr>
<tr>
<td>No prior TNFi exposure</td>
<td>99 (23.7)</td>
</tr>
<tr>
<td>Prior TNFi failure</td>
<td>53 (11.4)</td>
</tr>
<tr>
<td>No prior TNFi failure</td>
<td>106 (24.1)</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)</td>
<td>19 (7.5)</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)</td>
<td>31 (16.6)</td>
</tr>
<tr>
<td>Baseline Mayo score &lt;9</td>
<td>91 (28.3)</td>
</tr>
<tr>
<td>Baseline Mayo score ≥9</td>
<td>68 (11.7)</td>
</tr>
<tr>
<td>Mucosal healing, n (%)</td>
<td>271 (29.9)</td>
</tr>
<tr>
<td>Prior TNFi exposure</td>
<td>32 (13.7)</td>
</tr>
<tr>
<td>No prior TNFi exposure</td>
<td>159 (23.1)</td>
</tr>
<tr>
<td>Prior TNFi failure</td>
<td>103 (22.2)</td>
</tr>
<tr>
<td>No prior TNFi failure</td>
<td>168 (32.8)</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)</td>
<td>38 (15.0)</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)</td>
<td>57 (30.5)</td>
</tr>
<tr>
<td>Clinical response, n (%)</td>
<td>212 (23.6)</td>
</tr>
<tr>
<td>Prior TNFi exposure</td>
<td>45 (20.0)</td>
</tr>
<tr>
<td>No prior TNFi exposure</td>
<td>268 (28.8)</td>
</tr>
<tr>
<td>Prior TNFi failure</td>
<td>254 (52.0)</td>
</tr>
<tr>
<td>No prior TNFi failure</td>
<td>284 (64.5)</td>
</tr>
<tr>
<td>Prior TNFi failure (primary non-responder)</td>
<td>116 (45.8)</td>
</tr>
<tr>
<td>Prior TNFi failure (secondary non-responder)</td>
<td>102 (54.5)</td>
</tr>
<tr>
<td>Baseline Mayo score &lt;9</td>
<td>205 (63.9)</td>
</tr>
<tr>
<td>Baseline Mayo score ≥9</td>
<td>316 (54.3)</td>
</tr>
</tbody>
</table>

Full analysis set, non-responder imputation 99Not significant; p < 0.05; ** p < 0.01; *** p < 0.0001 vs placebo 95% confidence interval was based on normal approximation for the difference in binomial proportions 99N = 488 for tofacitinib 10 mg BID and N = 130 for placebo; 99N = 417 for tofacitinib 10 mg BID and N = 104 for placebo/N = 465 for tofacitinib 10 mg BID and N = 124 for placebo; 99N = 440 for tofacitinib 10 mg BID and N = 110 for placebo; 99N = 253 for tofacitinib 10 mg BID and N = 74 for placebo; 99N = 187 for tofacitinib 10 mg BID and N = 43 for placebo; 99N = 321 for tofacitinib 10 mg BID and N = 82 for placebo; 99N = 582 for tofacitinib 10 mg BID and N = 151 for placebo; 99statistical 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

Disclosure of Interest: G.R. Daëns: Study-related disclosures: Dr. Daëns received speaker fee from and is an advisor for Pfizer Inc B.E. Sand: Grants(G), Personal Fee(P), Non-Financial/Pfizer G, P.Amgen, TNFi failure, reason for TNFi failure (primary or secondary) or disease severity; CIBERehd, Barcelona/Spain

BMS P.Bi, Salix, Lupinoid, Shire, Lilly, TGenix, Immune, Arena, Akros, Forward, Theravance, Receptos, Vedanta, Synergy, Topivert W.J. Sandborn: Study-related disclosures: Dr. Sandborn received grant support, personal fees and non-financial support from Pfizer during the conduct of the study; grant support from Pfizer T. Hibi: Grants, personal fees: Mitsubishi Tanabe Pharma, Ajinomoto Pharma, Abbvie Personal fees: Eizai, Takeda Pharma
T. Knittel5, J. Kowalski5, M.F. Neurath6, C.J. Hawkey7

mucosal remission in combination with mucosal healing (MH) defined as endo-

and 12. As endoscopic examination was performed at week 4 and 12 sympto-

mucosa at baseline (week 0) and after 4 weeks (week 4). For this post-hoc

be taking sulphasalazine, aminosalicylates, or thiopurines at stable doses.

therapeutic efficacy in ulcerative colitis (UC) patients refractory to conventional

cobitolimod (formerly known as DIMS0150, Kappaproct

In the COLLECT study the Toll like receptor (TLR-) 9 agonist

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Introduction: In the COLLECT study the Toll like receptor (TLR)-9 agonist
cobitolimod (formerly known as DIMS0150, Kappaproct3) was evaluated for its
therapeutic efficacy in ulcerative colitis (UC) patients refractory to conventional
therapy.

Aims & Methods: In this post-hoc analysis the therapeutic effects were analysed with
respect to disease activity of the patients at baseline. Cobitolimod was studied in a
randomized, double blind, placebo-controlled, multicentre, pan-
European study (COLLECT) in 191 patients with moderate to severe
active ulcerative colitis. Patients were on mandatory steroid therapy and could be
taking sulphasalazine, aminosalicylates, or thiopurines at stable doses.

Patients were randomly assigned to receive two single doses of cobitolimod (30
mg or placebo) at 2-week intervals through the endoscope to the inflamed
mucosa at baseline (week 0) and after 4 weeks (week 4). For this post-hoc
analysis efficacy was studied using the secondary endpoint symptomatic remis-
sion (CAI ¼ 0) in patients who received placebo or ozanimod 0.5 mg in the TOUCHSTONE trial with a change in pMS at Week 44 of 2.6, 2.7 and 
1.3 in the placebo, 0.5 mg and 1 mg groups.

Results: At entry into the OLE, the partial Mayo Score (pMS) for patients on
placebo, ozanimod 0.5 mg, and 1 mg were 4.6, 4.5, and 3.3 respectively. At
the time of the data-cut in the OLE, the PMS had improved in all groups (1.7, 1.7, and 1.9) at Week 44. The greatest improvement was reported in patients who
received placebo or ozanimod 0.5 mg in the TOUCHSTONE trial with a change
in pMS at Week 44 of 2.6, 2.7 and 1.3 in the placebo, 0.5 mg and 1 mg groups.

Conclusion: Long-term treatment with ozanimod continues to be safe and well
tolerated with good compliance and evidence of durable efficacy.

Disclosure of Interest: W.J. Sandborn receives financial support for research and consultancy fees from Celgene, Inc. 
B.G. Feagan receives consulting fees from Celgene, Inc. 
F. G. D’Haens receives consulting fees from Celgene, Inc. 
S. Hanauer: Richard Hanauer is an employee of Celgene, Inc. 
P.A. Frohna: Paul A. Frohna is an employee of Celgene, Inc. 
R. Aranda: Richard Aranda is an employee of Celgene, Inc.

MONDAY, OCTOBER 17, 2016
15:55-17:15
NON-BLEEDING EMERGENCIES OF THE OESOPHAGUS - ROOM E20

OP109 SELF-ASSEMBLING PEPTIDE MATRIX FOR THE PREVENTION OF
ESOPHAGEAL STRICTURE AFTER ENDOSCOPIC RESECTION:
A RANDOMIZED CONTROLLED TRIAL IN A PORCINE MODEL

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Introduction: Esophageal stricture formation after extensive endoscopic resection
is a frequent complication of endoscopic therapy for early esophageal neoplasia.
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. Esophageal diameter, endoscopic and esophagogastroscopy, weight variation, and histological measurements of fibrosis, granulation tissue, and neopithelium were assessed in each animal.

**Results:** The rate of esophageal stricture at day 14 was 40% in the group treated with self-assembling peptide vs. 100% in the control group (p = 0.04). Median (IQR) esophageal diameter at day 14 was 8 mm (2.5–9) in the self-assembling peptide group vs. 4 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 +2.7 (–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**

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

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

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

The proposed classification is based in a Retrospective study of 130 patients were studied, (retrospective: 87 / prospective: 43); 30 female, mean age 61 (48–72) years old. 13/23 cases were malignant and 10/23 benign. The macroscopic classification all patients’ records were evaluated. 315 images were analyzed and classified as benign or malignant by an expert with more than 140 POCS cases, and compared to histology. Based on the morphological and vascular pattern the lesions were classified as follows:

Benign lesions: Type 1 “Villosus pattern” (micronodular or villous pattern without out-visibility). Type 2 “Polypoid pattern” (adenoma or granuloma pattern without visibility) and Type 3 “Inflammatory pattern” (regular or irregular fibrous and congestive pattern with regular visibility). Malignant lesions: Type 1 “Flat pattern” (flat and smooth or irregular surface with irregular or spider vascularity); Type 2 “Polypoid” (polypoid or mass with fibrosis and irregular or spider vascularity). Type 3 “Ulcerated” (irregular pattern ulcerated and infiltrative with or without fibrosis with irregular or spider vascularity) and type 4 “Honeycomb-pattern” (fibrous honeycomb pattern with or without irregular or spider vascularity). Inter-observer and intra-observer agreement was calculated using 40 random images of lesions for 1 expert and 2 non-expert in POCS. Finally a prospective, non randomized, double blind evaluation of diagnostic accuracy, sensitivity, specificity, PPV, NPV using the new classification was performed for consecutive tissular lesions detected from Oct-2015 to April-2016 correlated with histology.

Results: 130 patients were studied, (retrospective: 87 / prospective: 43); 30 female, mean age 61 (50–74). Absence of statistical difference in gender (p value = 0.606) or age (p = 0.017) between groups. For retrospective evaluation 46/87 patients were evaluated, 21 female, mean age 61 (52–73). 18/46 cases were malignant and 28/46 benign. The overall interobserver agreement was substantial when lesions were classified as benign or malignant (K = 0.75 – CI 0.46–0.89) and when lesions were classified by sub-types (K = 0.71 – CI 0.39–0.88). The intraobserver agreement was almost perfect when lesions were classified as benign and malignant (K = 0.88 – CI 0.66–1.0) and when lesions were classified by sub-types (K = 0.90 – CI 0.71–1.0). For the prospective evaluation 23/43 patients were evaluated, 9 female, mean age 61 (48–72) years old. 13/23 cases were malignant and 10/23 benign. The accuracy was 86.9%, sensitivity 100%, specificity 70%, PPV 81.3%, NPV 100%.

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

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

Reference

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

Reference
**OPI15 PREVENTION OF POST-SPHINCTEROTOMY BLEEDING BY PROTON PUMP INHIBITOR: A PROSPECTIVE RANDOMIZED TRIAL**

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

**Aims & Methods:** The aim of this study was to study the role of high-dose PPI in patients undergoing EST. It was a prospective randomized open-label study performed in the endoscopy centre of a university teaching hospital. Consecutive patients who were scheduled to have ERCP and EST were enrolled. We excluded patients who had previous EST, prior gastric surgery, or were taking PPIs. Antplatelet therapies were continued as usual. Anti-coagulants (warfarin or heparin) were stopped with coagulopathy corrected prior to the procedure. All the patients were followed up for 30 days. Secondary outcomes were severity of PEP (defined as epigastric pain plus either amylase or lipase levels more than 3 times the upper limit of normal at 24h). Secondary outcomes were severity 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 including indications for EST, patient and procedure-related factors were comparable. Immediate bleeding was noted in 9 (15%) patients in the PPI group and 4 (6.2%) in the SC group (P = 0.14). Overt delayed ES bleeding was respectively seen in 4 (3.5%) and 3 (7.7%) in SC and PPI group (P = 0.44). There was no significant difference in the proportions of patients with hemoglobin drop of > 2 g without overt bleeding (Day 10: 13.3% in PPI group and 9.2% in SC group; P = 0.57). Other outcomes including hospital stay (13.1 vs 11.8 days; P = 0.69), transfusion requirement (5% vs 7.7%; P = 0.72) and 30-day mortality (3.3% vs 1.5%; P = 0.61) were also comparable between the two groups.

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

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

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**OPI16 IMPACT OF INTENSIVE HYDRATION ON THE INCIDENCE OF POST-ERCP PANCREATITIS: A DOUBLE-BLIND 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 during the procedure, 20 mL/kg bolus after the procedure, and 3 mL/kg/h for 8 hours after the procedure). A blood panel including serum levels of amylase and lipase was obtained at 4 and 24 hours after ERCP. Primary outcome was the incidence of PEP (defined as epigastric pain plus either amylase or lipase levels >3 times the upper limit of normal at 24h). Secondary outcomes were severity of PEP, incidence of volume overload, patient and procedure-related factors associated with PEP, and the predictive values of serum amylase/lipase at 4 hours after ERCP for PEP development.

**Results:** Included were 75 patients, 38 in the intensive hydration arm, and 37 in the standard hydration arm. Both groups were homogeneous for patient and procedure-related factors. PEP incidence was 9.3% (n = 7), and was lower in the intensive hydration arm (5.3% versus 13.5%, p = 0.204). Additionally, both PEP in the intensive hydration arm were mild, while out of the 5 PEP in the normal hydration arm, two patients presented with moderate and severe PEP, respectively. Contrast injection of the Wirsung was significantly associated with PEP (28.6% versus 7.1%, p = 0.016), while no other patient or procedure-related factors associated with PEP incidence. Finally, both amylase levels <2 times and lipase levels <3 times the upper limit of normal at 4 hours demonstrated a
Milkshake intake was significantly lower after QHCl administration, compared to placebo. Significantly lower prospective food consumption ratings, circulating octanoylated ghrelin levels and hedonic food intake at 24 hours, displaying a negative predictive value of 100%.

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

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

OP117 INTRAGASTRIC BITTER TASTANT ALTERS BRAIN ACTIVITY IN HOMEOSTATIC AND Hedonic REGIONS AND DECREASES OCTANoyLATED GHErLIN 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) control of feeding.

Aims & Methods: The aim of this project was to study the effect of intragastric administration of the bitter tastant Quinine Hydrochloride (QHCl) on brain activity in homeostatic and hedonic regions and on circulating ghrelin plasma levels. Furthermore, to test the hypothesis that lower hunger and prospective food consumption ratings, and lower hedonic food intake after QHCl administration compared to placebo. Fifteen healthy women were studied after an overnight fast. Brain activity before and up to 50 minutes after infusion of QHCl (10mM/ kg rat weight) (n=5 per group) and placebo (n=5) was recorded using functional magnetic resonance imaging (fMRI). Hunger and prospective food consumption scores were assessed every 10 min using Visual Analogue Scales. Blood samples were taken at the same time points. Hedonic food intake was measured immediately after scanning using an ad libium chocolate milkshake drink test. fMRI processing and analysis was conducted using SPM12. Brain responses to time over QHCl versus placebo infusion were compared in a priori defined regions of interest (ROI) at both voxel- and cluster-level threshold of pFWERcorrected < 0.05. The interaction effect was tested on hunger and prospective food consumption scores with mixed models. Hedonic food intake was compared between infusions using a one-tailed paired T-test. Blood plasma was analysed for circulating ghrelin levels using radioimmunoassays.

Results: Compared to placebo, intragastric QHCl infusion significantly increased neural activity in 5 different clusters within the ROIs, with local maxima in the fasted state. At 24 hours, displaying a negative predictive value of 100%.

Conclusion: Intragastric administration of the bitter tastant Quinine Hydrochloride (QHCl) on brain activity in homeostatic and hedonic regions and on circulating ghrelin plasma levels. Furthermore, to test the hypothesis that lower hunger and prospective food consumption ratings, and lower hedonic food intake after QHCl administration compared to placebo. At 24 hours, displaying a negative predictive value of 100%.

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: The gut-brain axis has been indicated as major substrate of pathophysiology in patients with functional gastrointestinal disorders, with no severe pancreatitis being observed in this group. Wirsung contrast injection at Kings College London - ISS on November 25, 2016ueg.sagepub.comDownloaded from ueg.sagepub.com at Kings College London - ISS on November 25, 2016

Disclosure of Interest: All authors have declared no conflicts of interest.
TNF-α and iNOS) was evaluated by Western Blot analysis. Extracellular record-
ing from CA3 and CA1 regions 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 and a significant increase in IL-1β, TNF-α and iNOS expression, associated with a depressive-like behavior and a reduced social interaction. Altered behavior was accompanied by significant changes CA3 pyramidal neu-

Conclusions: We found that, in mice, dysbiosis induced gut inflammation and sickness behaviors associated with biochemical and electrophysiological alter-

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

References


The mean LES pressure induced by PWS was 33.0 ± 1.6 mmHg, and did not differ significantly from that using HLES (32.7 ± 2.0 mmHg). Acamitamide was confirmed to address severe symptoms in six out of 13 patients with EGJOO. Acamitamide normalized impaired receptive LES relaxation and substantially improved symptoms.

Contact: Patients subjects have receptive LES relaxation, but this is impaired in EGJOO. Acamitamide normalizes IR in EGJOO, mainly by restoring LES receptive relaxation.

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

Reference

ENDOSCOPIC MANAGEMENT OF UPPER GASTROINTESTINAL CANCER – ROOM U7

OP123 EFFICACY AND SAFETY OF ESD FOR SUPERFICIAL CANCER OF THE CERVICAL ESOPHAGUS
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Introduction: It is a difficult to observe a lesion in the cervical esophagus because of the difficulty in spreading the tumor. It is a challenge not only to find esophageal cancers at an early stage, but also to successively treat them by ESD compared with lesions located at the thoracic esophagus.

Aims & Methods: The aim of this study was to clarify the efficacy and safety of ESD for superficial cancer located at the cervical esophagus. Patients who met the following criteria (case group) were enrolled in this retrospective study: 1) ESD was performed from January 2006 to December 2015; 2) the lesion was located at the cervical esophagus; and 3) squamous cell carcinoma (SCC) was proven histologically. Forty-five patients met those criteria. As a control group, 379 patients with 405 lesions of SCC which were located at the middle thoracic esophagus were enrolled. The lesions with entire circumferential mucosal defect, recurrent lesions after radiotherapy, and the lesions located near the scar were excluded in both groups. We evaluated advanced in both structure and 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 29.6%. 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 under general anesthesia in 32 patients and under local anesthesia in 32 patients (71%). 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 4 patients. No local recurrence was observed during an average duration of follow-up of 34 months. In the control group, the average age was 66.2 years old, and the male-to-female ratio was 84.1%. The average maximum size of lesions was 24.2 mm, and the histological depth of invasion was EP/LPM, MM/SM1, and SM2 in 306, 67, and 32 cases, respectively. The en bloc resection rate and R0 resection rate was 100% and 99%, 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 ESOPHAGOGASTRIC JUNCTION
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Introduction: Small gastrointestinal submucosal tumors (SMTs) are asymptomatic and undetectable, while patients with larger tumors have symptoms, and require intervention. Previously, thoracoscopy submucosal tunneling endoscopic resection (STER) was used for the resection of upper gastrointestinal SMTs. Recently, reports about STER are increasing. However, it is unclear whether STER is feasible for large SMTs. Moreover, studies about comparison of STER and surgery for upper gastrointestinal SMTs are still limited.

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 1.6 cm and irregular shape were excluded in both groups. We evaluated adverse events including stricture and recurrent lesions after radiotherapy, and the lesions located near the scar were excluded in both groups. We evaluated advanced in both structure and 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 33.4:45. The average age at initial ESD was 72 (range, 56–82) years. The male to female ratio was 25.8%. The transverse diameter and irregular shape is feasible, but associated with a relatively high risk of difficulty in retrieval of tumors.

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

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

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

Results: The median age at initial ESD was 72 (range, 56–82) years. The male to female ratio was 23.4. On endoscopy, all patients were found to have atrophic gastritis of the open-type according to the Kimura-Takemoto classification. Helicobacter pylori testing was positive in 18 patients (66.7%), negative in 8 (25.8%), and not done in 1 (3.7%). Of 18 patients, 17 underwent H. pylori eradication therapy after initial ESD, and it was successful in 16 (94.1%). The median duration from initial ESD to the detection of a metachronous lesion was 25.9 (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, 1 lesions (3.7%) were M, and 17 lesions (58.6%) were L. The gross type was 0 in 1 lesion (3.4%), 0-IIa in 15 lesions (51.7%), 0-IIc in 12 lesions (41.4%), and 0-IVa in 1 lesion (3.4%). The median tumor size was 6 (range, 2–10) mm. En bloc resection was performed for 28 lesions (96.6%). Aspiration pneumonia occurred in one patient after ESD, but the patient was successfully treated by intravenous antibiotics. There were no treatment-related deaths. On pathological examination, 21 were tubular adenomas, 8 were tubular adenocarcinomas, and 8 were signet ring cell carcinomas. 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 (31.6%), 0-IIb in 1 lesion (3.2%), 0-IIc in 13 lesions (41.9%), and 0-IIa–IVb in 1 lesion (3.2%). The median tumor size was 4 (range, 1.5–23) mm. En bloc resection was performed for 28 lesions (90.3%). Aspiration pneumonia occurred in one patient, he recovered with conservative treatment. One patient was successfully treated by intravenous
This procedure is known to have several disadvantages such as greater technical difficulty, increased procedure time, and increased risk of related complications.

Aims & Methods: The aim of this study is to find the best method for treating early gastrointestinal neoplasia. Fifty-one patients (mean patient age 71, range 32-92 years, male: female ratio 25:26) including 19 involved adenoma with low-grade was analyzed. Three minute submucosal cancers, 6 submucosal deep cancers and 2 carcinoid tumors subsumed to ESD, were compared to 98 patients (mean patient age 62.7, range 20-80 years, male: female ratio 52:48) who underwent EMR (20 involved adenomas 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 1-80 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 rate, recurrence rate, post-operative bleeding and perforation rate were compared with the use of the chi-square test.

Results: En-bloc resection rate (ESD: 82.4%, 42/51 vs EMR: 51%, 50/98; p < 0.001) 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 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 rate, recurrence rate, post-operative bleeding and perforation rate were compared with the use of the chi-square test.

Conclusion: This scoring system predicted cancer-specific survival, which may be helpful to value the risk of LNM in patients after ESD that does not meet the curative criteria.

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


OP128 LONG-TERM OUTCOME OF THE INCIDENCE RATE OF METACHRONOUS GASTRIC CANCERS AFTER HELICOBACTER PYLORI ERADICATION – A FOLLOW-UP AND ANALYSES OF JAPAN PIETTE STUDY GROUP ENROLLED PATIENTS

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Introduction: The author and Japan Gast Study Group (JGSG) reported that the eradication of Helicobacter pylori reduced the incidence of metachronous gastric cancers (GC) after endoscopic mucosal resection significantly in the Lancet paper (1). The exact rates of GC in Japan have not been compared. EMR is associated with local recurrences, especially for high-risk patients or when performed by less experienced endoscopists. Based on these aspects, an ESD was found to be the best method for early gastrointestinal cancers; EMR would be a good alternative to an ESD, especially for risk-patients when performed by less experienced endoscopists.

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

MONDAY, OCTOBER 17, 2016 15:45–17:15
HEPATIC CYSTS AND HEPATO-BILIARY TRACT DISORDERS – ROOM L8

**OP129 THE EFFECT OF PASIREOTIDE IN CYST REDUCTION OF ASPIRATION SCLEROTHERAPY IN PATIENTS WITH LARGE SYMPTOMATIC HEPATIC CYSTS, A RANDOMIZED CONTROLLED TRIAL**

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**Introduction:** Aspiration sclerotherapy is a therapeutic option for large symptomatic hepatic cysts. However, inadequate cyst reduction is frequently reported. Somatostatin analogues are able to curtail cyst volume. We hypothesized that 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 administered two weeks prior and twice after aspiration sclerotherapy. Primary endpoint was proportional cyst diameter reduction after six weeks, as measured by ultrasonography. Secondary outcomes included long-term diameter reduction at 26 weeks, symptomatic change at 26 weeks, and safety during the study. Symptomatic change was evaluated using the polycystic liver disease-questionnaire (PLD-Q) that assesses frequency and severity of 14 disease-specific symptoms leading to a total PLD-Q sum score.

**Results:** Thirty-four patients (32 females (94%); mean age 53.6 ± 7.8 years) were randomized between pasireotide (n = 17) and placebo (n = 17). Pasireotide did not improve efficacy of aspiration sclerotherapy at six weeks compared to controls (23.6% [IQR 9.6–31.8%] versus 21.8% [IQR 9.6–31.8%], respectively; p = 0.98). Long-term cyst diameter reduction was similar in both groups (49% [IQR 27.0–73.6%] and 45.5% [IQR 29.2–59.6%]; p = 0.90). Mean PLD-Q scores improved significantly in both groups (p < 0.01) indicating symptomatic relief, but there were no differences between groups (p = 0.92). Transient hyperglycaemia was seen in all patients allocated to pasireotide.

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

**Disclosure of Interest:** J.P.H. Drenth: Novartis provided the study drug and partially funded this investigator-initiated study. Novartis did not have any influence on the execution of the trial or the preparation of the manuscript. All other authors have declared no conflicts of interest.
exposure. Exogenous estrogens are used extensively to alleviate symptoms of menopause on biliary tract cancer after menopausal hormonal therapy (MHT). The National Prescribed Drug Register was used to identify MHT exposed women during the study period. For each exposed woman, three unexposed women were randomly selected from the same study base. Unexposed individuals were exactly matched for history of delivery, thrombotic events and hysterectomy, creating 8 strata (women combined with the MHT regimen (estrogen or estrogen/progestogen) and cancer status). Targeted matched women were included in the logistic models. 

Results: The positive cells rates of MUC3A in ECC specimens were significant compared with CEA, CA19–9 in 20 patients with ECC and 20 patients with chronic obstruction of the extrahepatic bile ducts (OR 0.8, 95% CI 0.6–1.2). There were no clear differences when the analyses were stratified for estrogen or estrogen/progestogen combinations. Adjusting for clinically manifest gallstone disease attenuated the odds of gallbladder cancer in MHT-exposed women (OR 0.8, 95% CI 0.6–1.2). Additionally, MHT exposure significantly increased the risk of gallstone disease (OR 7.0, 95% CI 6.6–7.3). 

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

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

References

**OP132 MUCIN3A, A PROMISING TUMOR MARKER FOR DIAGNOSIS OF EXTRAHEPATIC CHOLANGIOCARCINOMA**

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Introduction: The expression of extracellular mucin (MUC3A) was poor for early diagnosis due to their anatomical location and insidious onset, and little effective tumor markers. Our previous study showed Mucin3A (MUC3A) was the main differential protein in bile with proteomics technology using isobaric tags for relative and absolute quantitation (iTRAQ) in patients with ECC and 20 patients with cholangitis or patients with cholecystectomy.

Aims & Methods: Aim: To validate the histologic expression of MUC3A in ECC and explore diagnosis value of serum MUC3A as a potential tumor marker for diagnosis of ECC. Methods: (1) The expression of MUC3A was detected in 15 specimens of ECC and 20 normal bile duct tissue specimens by immunohistochemistry method. The relationship between MUC3A and the clinicopathologic features of ECC were investigated. (2) Serum MUC3A were detected in 16 preoperative patients with ECC and 15 preoperative patients with SOD. Serum MUC3A in 16 patients with ECC were compared preoperative and postoperative one month. (3) The clinical diagnosis application of serum MUC3A was compared with CEA, CA19-9 in 20 patients with ECC and 20 patients with SOD.

Results: (1) The positive cells rate of MUC3A in ECC specimens were significant higher than in normal bile duct tissue specimens (83.3% vs. 35.0%, P < 0.01). The expression of MUC3A was significant correlated with metastasis of lymph nodes (P = 0.038) and pathological stage of carcinoma (P = 0.005). (2) The preoperative serum values of MUC3A in patients with ECC were significant 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 the 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 than 90% sensitivity over the period of 6 months and 85% sensitivity (90% specificity) 12 months after the surgery. SOD was distinguished 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 exclusions concerning primary gallbladder surgery containing a polyp or (focal) wall thickening > 5 mm were included. These exceptions were regarded as nonpeptic (adenoma, dysplasia, carcinoma or other malignancies) or nonpeptic (all other types of polyp). If both neoplastic and nonneoplastic lesions were present, the lesion was classified as neoplastic. Prevalence of gallbladder
polyps and the attribution of neoplastic polyps and nonneoplastic polyps was calculated. From 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 4349 patients. A total of 337 patients were excluded due to primary non-gallbladder surgery, leaving 4012 unique cholecystectomies. In 2003 cholecystectomies (0.9%), a polyposidal lesion was present. Which results in a calculated prevalence of polyps in 94/100,000 patients who undergone cholecystectomy. Of the polyps, 1172 (56.3%) had adenomas, 378 (13.5%) adenocarcinomas, and 57 (2.7%) other malignancies. Nine hundred and ten (43.7%) polyps were nonneoplastic; 375 (18%) cholesterol polyps, 334 (16%) adenomyomas, 70 (3.7%) hyperplastic polyps, 54 (2.6%) mucosal polyps, 45 (2.2%) inflammatory polyps, 18 (0.9%) papilloma’s and 17 (0.8%) other types of polyps.

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

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

References

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

OP135 CHANGES IN CIRCULATING MICRONORA AFTER TREATMENT: MICRONORA 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 prevents the opportunity for individualized treatment.

Aims & Methods: 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: 15 consecutive patients with early-intermediate stage HCC were enrolled and treated according to the ESSL/ASLSD practice guidelines. Patients were staged (CT scan and/or MRI) at time 0 (T0, before treatment), 1 month (T1) and 6 months (T6) from therapy. Pax-gene Blood RNA tubes and Vacuette tubes where used to collect total blood and serum at T0, T1, T6. Small RNAs were isolated and hybridized on Affymetrix GeneChip miRNA arrays 3.0. QR-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: 80 single miRNA profiles have been analyzed using a microarray approach. We analyzed 1733 miRNAs over the 6 months period. The analysis yielded different profile in serum and blood identifying the two bioluids as two distinctive sources of miRNA carrying the same message. Only a small portion of the circulating genome remained significant at 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 decrease. In serum, mir-4649-3p, 3148, 371 increase while mir-103b decrease. The hierarchical clustering revealed four clusters distinguished patient with a complete response from those having only a partial response to therapy. Further validation of mir-106b showed a correlation between increased serum levels and treatment response (P < 0.0001) and the longer DFS (P < 0.0038). MRNA-106b was also significantly correlated with the with ICLC staging A1 and A2 (P = 0.01).

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.
Aims & Methods: We attempted to investigate the mechanism of liver atrophy by portal vein obstruction and clarify the role of autophagy and apoptosis. As pig lobule structures were well-defined as compared with human specimen, we performed percutaneous transhepatic portal embolization (PTPE) in 5 pigs. And then sacrificed them at day 0, week 2, or 4 and 6 (d0, w2, w4, w6, respectively). In specimens of embolized lobe (E) and non-embolized lobe (control, Cont), we measured the distance between the portal vein and central vein (PV-CV) area, and hepatocyte number per lobule and apoptotic activity. Immunohistochemistical reactions of microwave-associated-protein-light chain 3 beta (LC3) as autophagy and glutamine synthetase (GS) and cytochrome 2E1 (CYP2E1) as zonation were evaluated.

Results: PV-CV and lobule area showed no significant difference between E and Cont at d0, but were lower in E than in Cont at w2, w4 or w6 (P < 0.001). Hepatocyte number was not significantly reduced in E at d0 and w2 but was reduced in w4 and w6 (P < 0.05). Apoptotic activity was highest in E in Cont at d0 and w4. LC3 staining peaked in E at w2, with no significant difference between E and Cont at w4 and w6. GS and CYP2E1 areas in E at w2, w4 and w6 were narrower than those in Cont.

Conclusion: Our morphological study focused on changes in the lobules over time, and we observed two distinct phases of liver atrophy following portal blood flow disruption. The first (the autophagic phase) was characterized by 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

OP1040 EFFECT OF CHRONIC THIOACETAMIDE TREATMENT ON HEPATIC HEMODYNAMIC PARAMETERS IN RATS:
EVALUATION BY MAGNETIC RESONANCE IMAGING (MRI) D. Schaffner1, D. Elverfeldt2, P. Deibert1, A. Lazaro1, I. Merfort1, L. Lutz1, M. W. Baumstark1, W. Kreisel1, W. Reichardt2
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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. (3) To evaluate the change in the arterial blood flow volume, hemodynamic parameters as a result of the hepatic steatosis and overall liver weight change in the TAA-induced liver injury model. (4) To compare differences in the blood flow distribution between healthy and steatotic liver.

Methods: We used 1.5 T MRI. T2-weighted spin echo sequence was used to assess the liver size and morphology. A 3D HASTE sequence was used to measure the blood flow volume. We further used a 3D reconstruction of the portal vein branches to measure the blood flow volume in the portal vein branches.

Results: The blood flow volume was significantly reduced in the TAA-induced liver injury model. The portal vein area and blood flow volume were reduced in the steatotic liver as compared to the healthy liver. The blood flow volume in the portal vein branches was reduced in the steatotic liver as compared to the healthy liver.

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

References
received TAA for 16 weeks, 46% (11/24) developed liver fibrosis with a Desmet score of 1–3 (group 12w/fib) and 54% (13/24) had liver cirrhosis with a Desmet score of 4 (group 16w/cir). The untreated rats (15/54) served as control group (group con). Mean portal vein area showed no significant differences among all groups. However mean portal flow velocity was reduced by 15% in group 12w/fib and 31% in group 16w/cir compared to group con. In contrast mean portal flow volume per body weight was significantly lower than that of group con. Thus flow volumes were adjusted according to the body weight in order to eliminate weight-induced changes in hemodynamics. Mean aortal flow volume per body weight did not show significant differences among all groups. In contrast mean portal flow volume per body weight was significantly reduced in group 12w/fib by 23% compared to group con. On the other hand, in group 16w/fib and group 16w/cir there was no further reduction of mean portal flow volume per body weight. This might indicate that in the majority of TAA-induced liver injury the development of fibrosis is sufficient to cause a significant decrease in portal flow volume. There were no significant differences between group 12w/fib and 16w/fib in terms of all parameters, in particular portal flow volume.

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

Disclosure of Interest: All authors have declared no conflicts of interest.
Table (OP144): Clinical and serological evolution after dose de-escalation

<table>
<thead>
<tr>
<th>COHORT</th>
<th>Median (IQR) time from T0</th>
<th>Median (IQR) serum albumin 44.5 g/L (42.6–47.0)</th>
<th>Median (IQR) PRO2 UC 0.0 (0.0–0.0)</th>
<th>Median (IQR) time from T0 18.0 weeks (13.5–26.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-1 (n = 33)</td>
<td>18.0 weeks (13.5–26.1)</td>
<td>44.5 g/L (42.6–47.0)</td>
<td>0.0 (0.0–0.0)</td>
<td>18.0 weeks (13.5–26.1)</td>
</tr>
<tr>
<td>T0 (n = 43)</td>
<td>14.0 weeks (12.3–19.0)</td>
<td>44.1 g/L (42.2–47.0)</td>
<td>0.0 (0.0–0.0)</td>
<td>14.0 weeks (12.3–19.0)</td>
</tr>
<tr>
<td>T1 (n = 43)</td>
<td>30.5 weeks (26.8–34.5)</td>
<td>43.7 g/L (41.6–47.2)</td>
<td>0.0 (0.6–5.1)</td>
<td>30.5 weeks (26.8–34.5)</td>
</tr>
<tr>
<td>T2 (n = 26)</td>
<td>7.2 µg/mL (5.4–8.6)</td>
<td>0.0 (0.6–4.1)</td>
<td>0.217</td>
<td>7.2 µg/mL (5.4–8.6)</td>
</tr>
</tbody>
</table>

**Aims & Methods:**

In this retrospective cohort analysis, the outcome of dose de-escalation (ADM 40 mg ETW) after a median of 28 months was assessed. All patients included were on INF therapy for inflammatory bowel disease (IBD) who are in clinical remission. Dose de-escalation may not only have beneficial economic repercussions, it may possibly also decrease the occurrence of adverse events.

**Conclusion:**

Median PRO2 UC was 0.0 (0.0–0.0) for all three cohorts at the time of inclusion (T0). A significant reduction in PRO2 UC was observed in all three cohorts after dose de-escalation (T1, n = 43), 4 months after dose de-escalation (T1, n = 43) and 8 months after dose de-escalation (T2, n = 26).

**Disclosure of Interest:**

All authors have declared no conflicts of interest.

**OP145 EFFICACY AND SAFETY OF BIOSIMILAR INFLIXIMAB AFTER ONE-YEAR: RESULTS FROM A PROSPECTIVE NATIONWIDE COHORT**


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**Introduction:**

The aim of this prospective, nationwide, multicenter, observational study was to evaluate the efficacy and safety of biosimilar infliximab (BF-20) after one-year of use in patients with inflammatory bowel disease (IBD), including Crohn’s disease (CD) and ulcerative colitis (UC), treated in 214 gastroenterology and pathology centers in Hungary.

**Methods:**

A total of 521 patients treated with ADM for CD or UC were included in the study. The primary endpoint was the percentage of patients achieving clinical remission at week 52, defined as a recorded CDAI score ≤ 150 and an improvement of ≥ 70% compared to baseline. Secondary endpoints included the percentage of patients achieving other remission criteria (ATI and B) as defined by a decrease of TRI ≤ 6 pmol/L and/or need to change the original therapeutic regimen because of adverse events. Trough levels of IFX (TRI) and antibodies (ATI) were measured before each infusion.

**Results:**

At the time of inclusion (3.65 vs 3.45 p = 0.02), four patients in Cohort A, four patients in Cohort B (14.8%), and 11 in Cohort C (42.3%) experienced an unfavorable evolution of IFX pharmacokinetic defined by a decrease of TRI ≤ 6 pmol/L (p = 0.022 between A and C, p = 0.039 between B and C, p = 0.87 between A and B). By ROC analysis (AUROC: 0.93), a threshold of 6-TGN levels < 105 pmol/L was associated with an unfavorable evolution of IFX pharmacokinetics.

**Discussion of Interest:**

Elena Del Tedesco has been a consultant for Merck, Janssen Biologics, and does consultancy for Abbvie, MSD, and Takeda.

**Disclosure of Interest:**

All authors have declared no conflicts of interest.
mab sequences ranged from higher cost-utility ratio. ICURs of biosimilar infliximab-adalimumab-vedolizumab-infliximab was dominant relative to originator infliximab-standard care strategy. Undiscounted health gain was 0.3 QALY per patient. In all countries, biosimilar Results: and a five-year time horizon. Discount rates for both costs and benefits complied estimated based on randomised controlled trials and cohorts. Country-specific Transition probabilities of moving between health states were designed to examine the efficacy and safety of CT-P13 infliximab biosimilar in Europe. The efficacy and safety of CT-P13 infliximab biosimilar in the maintenance treatment of Crohn’s disease (CD) 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 1 day to 72 years (median 22.1 and 22.9) in CD and 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. 83.59% of UC patients had proctitis/left-sided colitis/extension colitis. 25.14% of patients had received previous anti-TNF therapy in CD and UC, respectively. 60/52% of CD/UC patients received concomitant immunosuppressors 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 in both CD (p < 0.001) and UC (p <0.041/0.05 and p < 0.02/0.01) 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 14.0 to 8.8 mg/L in CD and from 29.5 to 14.7 and W4: 8.29 to W14: 8.5, W30: 13 and W54: 12.3 mg/L in UC). 21 (6.6%) patients had infection reactions, 23 (7.9%) patients had infections and 1 death occurred. Conclusion: This prospective nationwide cohort shows that CT-P13 is effective and 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.
3.8-fold (p<0.01) and MT2, which were co-localized with survivin, IGF-1 and IGFR-1 structures from full thickness wall specimens of a normal rat stomach was assessed: 1) cell injury under confocal microscopy, 2) survival and apoptosis by Western blotting and immunostaining. For comparison, 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 (IGFR-1) 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 IGFR-1 in these cells. In in vitro study, the cultured normal rat gastric mucosal epithelial cells (RGM1) were pretreated with vehicle or melatonin (10 -6) 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 IGFR-1 by Western blotting and immunostaining. For comparison, the quantitative expression of MT1 and MT2 in gastric epithelial and submucosal structures from full thickness wall specimens of a normal rat stomach was evaluated.

Results: Rat gastric mucosa expressed both MT1 and MT2 (1.8-fold more MT1 than MT2; p<0.01) in gastric epithelial progenitor cells, endothelial cells of blood vessels, and in enteric neural elements. RGM1 cells expressed both MT1 and MT2, which were co-localized with survivin, IGF-1 and IGFR-1. IND treatment produced extensive cell injury and reduced RGM1 cell viability by 38.5% (p<0.01). In cells pretreated with melatonin (ND) the IND induced cell injury and death was dramatically reduced by 82.4±4% (p<0.001) reflecting a direct protective action of melatonin.

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 RGM1 cells express melatonin receptors MT1 and MT2 that are co-localized with survivin, IGF-1 and IGFR-1 indicating a spatial relation to factors promoting cell survival, and 3) binding of melatonin derived from pineal gland, this indolamine 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.
Aspirin is a potent anti-platelet agent used for the prevention of cardiovascular and cerebro-vascular diseases. However, gastrointestinal (GI) bleeding is the most frequently reported serious adverse events for the long term use of aspirin.

Aims & Methods: The objective of this study is to investigate whether the risk of proven aspirin usage on increasing ulcer bleeding would outweigh its benefit on the prevention of CRC. The present study investigated the electronic medical records from 42 publically funded hospitals, which serves a 7 million population in Hong Kong. All hospital admissions from 2000 to 2004 and their outcome in the follow-up period were extracted until 2014. Aspirin users were matched with control 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 year. 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 were described in Table 1. The mean ages of aspirin users and non-aspirin users are 68.4 (SD = 13.1) and 66.4 (SD = 13.2) respectively. In the aspirin group, 78,316 patients (30.7%) had aspirin prescribed for 10 years or more, and 54,011 of them (69.0%) were routinely prescription during the years of clinic visits. Medium 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 = 0.89; 95% CI = 0.86 to 0.92). Whereas, patients in aspirin group showed significantly higher incidence of GI bleeding (OR = 1.74; 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 linear after more than 10 years of aspirin use.

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.

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

OP153 COMPREHENSIVE ANALYSIS OF ADVERSE EVENTS ASSOCIATED WITH PER ORAL ENDOSCOPIC MYOTOMY (POEM) IN 826 PATIENTS: AN INTERNATIONAL MULTICENTER STUDY

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Introduction: POEM was introduced as a minimally invasive and effective therapeutic modality for the treatment of achalasia and spastic esophageal disorders. POEM is not widely used in single-center studies and small case series suggest effective in reducing the incidence of colorectal cancers (CRC) in many previous studies. However, gastrointestinal (GI) bleeding is the most frequently reported serious adverse events for the long term use of aspirin.
POEM as a safe alternative to Heller Myotomy. However, the safety of POEM is still under comprehensive analysis and 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. Methods: Patients who underwent POEM performed for the treatment of achalasia and SEDs at 12 tertiary-care centers (5 US, 4 Europe, 2 Asia and 1 Australia) between 2011 and 2015 were used in a case-control study. Cases were defined by the occurrence of any AEs related to POEM procedure. Control patients were selected for each AE case by matching for age, gender, disease classification (type I&II vs. type III/SEDS). All pertinent data including AEs were collected and their severity was graded according to the ASGE lexiorn’s severity grading system.

Results: A total of 1826 patients underwent POEM during the study period. Overall, the incidence of AEs was 33.2% (577 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 (6.5%) severe AEs (type IV: perforation), 1 aspiration pneumonitis, 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 knife used, extent and length of myotomy, and operator training. The median time of procedure was significantly longer in cases as compared to controls (123 ± 49 vs. 103 ± 33 min, p = 0.002). Length of stay was significantly higher in patients who experienced AEs (4.9± vs. 2.7 d, p < 0.001). Conclusion: POEM can be considered as a safe therapeutic modality with an overall 7.5% incidence of AEs. Severe AEs are rare. AEs result in prolongation of hospital stay. Longer procedural times (indicative of technically complex procedures) are associated with increases of occurrences of AEs.

Disclosure of Interest: M. Khshab: Consultant of Boston Scientific and Xlumena

All other authors have declared no conflicts of interest.

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

Aims & Methods: We aimed to study (1) clinical outcome of patients with a minimum post-POEM follow-up of 2 years and (2) factors associated with long term clinical failure after POEM. Methods: We conducted a retrospective review of consecutive patients with achalasia who underwent POEM with a minimum follow-up of 2 years at 10 tertiary-care centers (3 US, 4 Europe, 3 Asia) and clinical response was defined by decrease in primary Eckardt score to ≤2 at 2 years. Results: A total of 179 patients (82 males (45.8%); mean age 49 yr) underwent POEM for the treatment of achalasia (type I1, type I1, type III, unspecified type III). Of these, 16 patients (8.9%) had prior Heller myotomy, 65 (36%) had prior pneumatic dilatation (PD), 3 patients (1.6%) had prior botulinum injection. POEM was successfully completed in all patients. A total of 18 adverse events occurred in 8 (4.4%) patients (8 mucosotomies, 1 delayed bleeding, 1 esophageal leak, 2 DVT/PE, 1 pneumothorax, 2 symptomatic pleural effusion, 2 aspiration pneumonia and 1 mediastinitis). Per-oral endoscopic myotomy (POEM) was successfully completed in all patients.

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OP155 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.

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

Results: A total of 347 patients underwent POEM (mean age 47 years, 48% males). Seventy-eight patients (22.5%) had type 1 achalasia, 174 type II (50.1%), 40 type III (11.5%), 2 Jackhammer esophagus (0.6%), 4 distal esophageal motor segment (1.1%), and 1 nitratercker 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, 3 received no treatment because of mild symptoms. Clinical success slightly decreased with time, being 97%, 97%, 93%, 95%, 92% and 67% after 6, 12, 24, 36, 48 and 60 months, respectively. However, almost 50% of recurrences (6/13) occurred during the first 25 cases (learning curve). No associations were found between preoperative manometric pattern and clinical outcomes: the success rate of POEM was similar in patients with type I, type II and type III achalasia (94%, 96% and 91%, respectively; p>0.05). A total reflux time > 5% was diagnosed in 50% of the patients (111/223) who underwent pH-study. Esophagitis was seen in 28% of patients, 22% of patients received PPI because of heartburn. Esophagitis healed completely with proton pump inhibitors (PPI) in all the patients. GERD symptoms were effectively controlled with PPI in all the patients but 2 who complained with heartburn and regurgitations.

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

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

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

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

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

Results: A total of 55 patients (3.3%, 95% confidence interval [CI] 2.5-4.2%) suffered mAE, distributed as follows: delayed mucosal barrier failure, 13 (0.8%, 95% CI 0.4-1.3%); delayed bleeding, 3 (0.2%, 95% CI 0.04-0.5%); hydrothorax, 8 (0.5%, 95% CI 0.2-0.9%); pleural effusion, 25 (1.5%, 95% CI 1.0-2.2%); and miscellaneous, 6 (0.4%, 95% CI 0.1-0.8%). Four patients (0.2%) required ICU admissions. No surgical conversions occurred, and 30-day mortality was zero. In stepwise multivariate regression, experience (OR = 3.85, 95% CI 1.49-9.9), air insufflations (OR = 3.41, 95% CI 1.37-9.50), and mucosal edema (OR = 2.01, 95% CI 1.14-3.53) were identified as related risk factors. After introducing CO2 insufflation, mAE rate declined to 1.9% (95% CI 1.2-2.7%) and seemed to plateau after 3.3 years at ~1%.

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

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

References

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

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Table (OP154)

<table>
<thead>
<tr>
<th>Age ≤ 50 50-64 65-79 &gt; = 80</th>
<th>Aspirin Group (n = 254,887)</th>
<th>Non-Aspirin Group (n = 491,852)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex – Male</td>
<td>136,534 (53.8%)</td>
<td>260,933 (53.1%)</td>
</tr>
<tr>
<td>Duration of Aspirin Prescribed 1 month to ≤ 6 months 6 months to &lt; 3 years years to &lt; 5 years years to ≥ 5 years years to &gt;10 years more</td>
<td>48,591 (19.1%) 44,516 (17.5%) 34,013 (13.3%) 49,451 (19.4%) 78,316 (30.7%)</td>
<td>24,067 (9.4%) 59,289 (23.3%) 121,671 (47.7%) 49,360 (19.6%) 57,690 (11.7%) 129,196 (26.3%) 232,319 (47.2%) 72,047 (14.8%)</td>
</tr>
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</table>

*Not Applicable for the Patients in Non-Aspirin Group.
In this large multicenter study, POEM was safe and effective for achalasia. The presence of reflux esophagitis and abnormal pH acid exposure was marginally associated with clinical failure after POEM. Post-POEM symptoms (vomiting, nausea, abdominal pain) were significantly associated with clinical failure. Post-POEM symptoms were comparable to that of patients with no prior HM. This is a case consecutive report on 23 patients operated for achalasia who underwent POEM with and without prior HM. Methods: We conducted a retrospective review of achalasia patients who underwent POEM at 11 tertiary centers (4 US, 4 Europe, 3 Asia). Patients were divided into two groups: (1) patients who had prior HM (HM group) and (2) those without prior HM (control group). Control patients were selected for each HM case by matching for age, achalasia subtypes (type I&II vs type III), and baseline Eckardt scores (ES) [Stage II (ES 4–6) or Stage III (ES ≥ 6)]. Clinical response was defined by decrease in ES to ≥ 3. Adverse events (AEs) were graded according to the ASGE lexicon. Technical success, clinical success and AEs were compared between the two groups.

Results: A total of 181 patients (91 HM, 90 controls) were included. There was no difference between the groups in baseline demographics, ES and 4sIRP. The HM group demonstrated a higher proportion of patients with prior PD (44% vs 26%; p = 0.01). The length of myotomy was similar between the two groups. Technical success rates were comparable between HM group (89; 91; 2% failed due to extensive submucosal fibrosis) and control group (100%) in control group (p = 0.26). Postoperative outcomes between the two groups were comparable. The mean follow-up was 8.5 months (IQR 3.2–14.7) and was similar in both groups. 20 AEs occurred in 19 patients (7% in HM group and 12% in control group, p = 0.23). For HM and control respectively, the rate of mild (5% vs 10%, p = 0.28) and moderate (1% vs 3%, p = 0.34) AEs were similar. Two severe AEs occurred in the HM group. Follow-up data were available in 153 patients. Clinical response was significantly lower in the HM group as compared to the control (80% vs 94%, p = 0.02). Mean post-POEM ES was also higher in the HM group (2.09 ± 2.5 vs 1.04 ± 1.2, p = 0.00). On univariate analysis, post HM (OR 3.5, p = 0.02) and prior PD (OR 3.36, p = 0.01) were significantly associated with clinical failure. Multivariate analysis demonstrated prior HM (adjusted OR 2.91, p = 0.05) was marginally associated with clinical failure after POEM. Post-POEM symptoms (vomiting, nausea, abdominal pain) and gastritis were similar between the two groups.

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

Disclosure of Interest: S. Roman: Sabine Roman is a consultant for Medtronic and Sandhill Scientific. F. Mion: Francois Mion is a consultant for Medtronic. M. Khashab: Mouen Khashab is a consultant for Boston Scientific All other authors have declared no conflicts of interest.

OP158 GASTRIC PERORAL ENDOSCOPIC ANTRAL-PYLORIC MYOTOMY FOR THE TREATMENT OF REFRACTORY GASTROPARESIS: LARGEST SERIES WITH CLINICAL AND SCINTIGRAPHIC FOLLOW-UP
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Introduction: Gastroparis is an invalidating motility disorder and the available treatments remain disappointing. Recently, a novel approach has been performed by performing a myotomy of the pylorus after creating a tunnel, with promising results [1–3]. We report the largest retrospective clinical experience in 23 consecutive patients treated by gastric peroral endoscopic myotomy (G-POEM). The aim was to document the results of this novel technique.

Aims & Methods: This is a case consecutive report on 23 patients operated for severe refractory gastroparesis, between January 2014 and April 2016, with a rigorous prospectively designed follow-up. The inclusion criteria were patients with severe refractory gastroparesis refractory to currently available treatment means (Swallow Coag, 35W, Effect 2) until reaching the pyloric arch, which had a consistent aspect; retrograde antro-pyloromyotomies of 3cm length; closure of the mucosal flap with clips. The primary objective was improvement of quality of life (visual analog scale ~5). The secondary objectives were to document the GES evolution at 2 months and the procedure complications.

Results: The procedure was completed on all the patients. We observed a significant improvement of GES score at POD 5, 1 month and 3 months (3.5 ±0.8 vs. 0.8 ± 0.8; 0.9 ± 0.9; 1.1 ± 1.5; p < 0.001). Regarding the severity of symptoms analyzed separately, it was observed a significant improvement of each of them, except dysphagia. The overall clinical efficacy was 70% with a mean overall quality of life improvement > 65%. The GES normalized in 75% of cases, showing a significant improvement of the mean half emptying time (222 ± 90 min. vs. 133 ± 90; p = 0.03) and of retention at 2 hours (76 ± 20% vs. 44 ± 26%; p = 0.009). Two patients underwent complications related to the procedure: one was a bleeding due to an ulceration along the tunnel path (coagulation necrosis) treated by endoscopy, while the second was a perforation of the gastric wall, which was managed endoscopically by a nasogastric drain and fasting, with excellent outcomes. All the other patients could be refeed at POD2-3, and discharged at POD5-6, with PPI treatment.

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

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

References

TUESDAY, OCTOBER 18, 2016 08:30–10:00

LIVER FIBROSIS: FROM MECHANISM TO THERAPY – ROOM 1.61/1.62

OP159 EXPRESSION OF CONSTITUTIVELY ACTIVE IKK2 LEADS TO LIVER FIBROSIS AND INCREASED CARCINOGENESIS IN THE BACKGROUND OF LIVER SPECIFIC TRP53 DELETION
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Introduction: Liver carcinoma is of particular importance, since it is a leading cause of cancer-related deaths worldwide. Most frequently liver tumors are arising in the context of a cirrhosis due to chronic liver diseases. Another circumstance contributing to liver cancer formation is the disruption of the immune response independent of the p53 status. During ageing, the inflammatory response decreases, the liver fibrosis increases, and the tumor incidence at the age of 9–12 month in CAIKK2 mice is significantly higher (67%) compared to CAIKK2 mice with wild-type Trp53 (25%). Mice with induced liver-specific Trp53 deletion did not show intrahepatic cholangiocarcinoma (ICC) (81%)

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

Aims & Methods: To investigate the sequence of inflammation and Trp53 deletion, we combined two transgenic mouse models. For modulation of an inflammatory response, we used an inducible mouse model (Tet-Off system) with a permanent expression of a constitutively active IKK2 isoform (CAIKK2). The expression of CAIKK2, starting from birth, leads to a continuous activation of the NF-kB pathway, simulating chronic inflammation. For the modulation of a p53 deletion, the inducible Cre-ERT2 transgenic expression line AlfpCre-ERT2 was crossed with a conditional Trp53 knockout mouse. Tamoxifen treatment at the age of four weeks induces liver-specific deletion of Trp53.

Results: Expression of the constitutively active IKK2 isoform leads to liver fibrosis development, increased proliferation in the liver and elevated expression of inflammatory markers independent of the p53 status. During ageing, the CAIKK2 expression and the inflammatory response decreased, the liver fibrosis was still reversible. The tumor incidence at the age of 9–12 month in CAIKK2 mice with wild-type Trp53 (25%). Mice with induced liver-specific Trp53 deletion did not exhibit liver tumor formation at the same age. The majority of liver tumors in CAIKK2 mice with p53 deletion (53%) were show intrahepatic cholangiocarcinoma (ICC) (91%) next to hepatocellular carcinoma (2%) and combined HCC/ICC (17%). In contrast, CAIKK2 mice with wild-type Trp53 developed mainly HCC (50%), but also ICC (25%) and HCC/ICC (25%) at lower level.

Conclusion: The study shows that liver-specific Trp53 deletion in combination with an inflammatory background results in elevated tumor incidence and leads to an increased occurrence of ICCs in the liver.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP160 EXPRESSION OF CD161 ON CD4+ T CELLS PROMOTES HBV-DIRECTED INFLAMMATION AND PROLIFERATION OF HEPATIC STEM CELLS THROUGH CD4+ T-CELL AND SPHINGOMYELINASE AND CD161-LECTIN-LIKE TRANSIENT-1 INTERACTION

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Introduction: Hepatitis B virus (HBV)-related liver fibrosis always progresses from inflammation to fibrosis. CD4+ T cell immune responses play a pivotal role in the process. Recently, CD161 is considered to be a costimulatory molecule on T cells and an important phenotypic marker of human Th17 cells. Aims & Methods: This study was designed to investigate the roles of CD161 in the pathogenesis of HBV-related liver fibrosis. Methods: A total of 54 CHB patients who underwent liver biopsy and 20 healthy controls (HC) were enrolled. CHB patients were further categorized according to the disease phase: immune-tolerant (IT, n = 12), immune-active (IA, n = 30), or inactive CHB (n = 12). Peripheral blood mononuclear cells (PBMCs) and flow cytometry sorted CD4+ CD161+ and CD4+ CD161- T cells were prepared for further flow cytometric and real-time PCR analyses. Flow cytometry sorted CD4+ CD161+ and CD4+ CD161- T cells were also cultured alone or co-culture with primary hepatic stellate cells (HSCs) in vitro experiments. Results: Compared to HC, the percentage of CD4+ CD161+ T cells significantly increased among IA patients while dramatically decreased among IT patients, but there was no significant difference between inactive CHB patients and HC. Besides, CD161 showed a positive correlation with histological inflammation grades and advanced histological fibrosis stages. In the PBMCs of CHB patients, CD4+ CD161+ T cells exhibited a CD45RO+ memory phenotype and secreted more interferon-gamma (IFN-gamma), tumor necrosis factor (TNF)-alpha, 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/Akt/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-gamma and IL-17, especially for IL-17. HSCs express lectin-like transcript-1 (LTL1), the only ligand of human CD161. HICs-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-gamma production of CD4+ CD161+ T cells as well. Knocking down of CD1 and on CD4+ T cells or LTL1 on HSCs could partly reverse the aforemen- tioned 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 might promote HBV-related liver fibrosis through CD161-LTL1 interaction to activate HSCs and through raising aSM to enhance the proinflammatory functions of CD4+ T cells.

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

References

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

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

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

Aims & Methods: This study aims to assess FUSE versus FVC in dysplasia surveillance in an IBD population. The dysplasia yield of targeted versus random colon biopsies will also be assessed. Methods: A prospective, single-center, randomized, order, back-to-back crossover tandem colonoscopy study was conducted comparing FUSE versus FVC in an IBD surveillance population. Crohn’s disease (CD) and ulcerative colitis (UC) subjects were recruited from the IBD Sydney Cohort population-based database, all of whom met the inclusion criteria of published IBD surveillance guidelines. Subjects not due their surveil- lance colonoscopy were excluded. The primary outcome was the per-dysla- procession miss rate of the first colonoscopy identified by the second colonoscopy with chromoendoscopy. Secondary outcomes were per-subject dysplasia miss rate, mean dysplasia lesions found, procedural times, and dysplasia yield of targeted-random colon biopsies. The trial was registered with the Australia New Zealand Clinical Trials Registry (ACTRN126160000047943).

Results: In total 104 tandem (52-paired) colonoscopies were conducted with 27 subjects randomized to FVC first and 77 to FUSE first. Both arms were not statistically significantly different for age, IBD duration, CD versus UC, and additional dysplasia risk factors. The dysplasia prevalence rate of the cohort was 30.8%. The dysplasia miss rates for FVC and FUSE were 71.4% versus 81.2% respectively (P = 0.046). FUSE identified a mean of 0.37 dysplastic lesions versus 0.12 for FVC (P = 0.007). Targeted biopsies increased dysplasia identification (26/163, 16.0% versus random biopsy yield of 8/50, 16.0%, P < 0.0001). Chromoendoscopy identified 10/28 (35.7%) of dysplastic lesions. The total colonoscopy times were similar (21.2 minutes versus 19.1 minutes, P = 0.32) but colonoscope withdrawal time was significantly longer (15.8 minutes versus 12.0 minutes, P = 0.03) for FUSE and FVC respectively.

Conclusion: Full Spectrum Endoscopy outperformed conventional forward view- ing colonoscopy in inflammatory bowel disease subjects undergoing dysplasia surveillance. A high dysplasia prevalence was identified most likely due to multiple colonoscopy passes and the use of multiple advanced imaging modalities comprising white-light colonoscopy, FUSE and chromoendoscopy. Improved dysplasia identification rates may reduce colorectal cancer mor- tality and increase interval colonoscopies. Improved dysplasia yield of targeted biopsies versus random colon biopsies was confirmed.

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

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Introduction: Optical biopsies of colon 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 and discarded (or left intact) without adverse clinical impact. The sec- ondary aim was to compare the real time diagnostic performance of WavSTAT version 4 with NBI and a combination of endoscopic and WavSTAT assess- ments. Patients attending the endoscopy unit for lower gastrointestinal endo- scopy as requested by their responsible physician were approached to participate in the study. Adult patients aged above 18 years were included.

Table (OP162): Diagnostic performance of WavSTAT, 4Endoscopic assessment and combined algobhimic assessment for characterization of 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 0.44-0.48)</td>
<td>77.2% (95% CI 0.61-0.82)</td>
</tr>
<tr>
<td>NPV</td>
<td>96.8% (95% CI 0.85-0.91)</td>
<td>91% (95% CI 0.73-0.84)</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 coded correctly)</td>
<td>81.2%</td>
<td>97%</td>
</tr>
<tr>
<td>Surveillance interval (% of patients called earlier)</td>
<td>18.8%</td>
<td>3%</td>
</tr>
</tbody>
</table>

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Patients known to have inflammatory bowel disease or colorectal cancer were excluded from the study. Polyps sized <10 mm were assessed in real time by high definition white light, NBI and WavSTAT version4 optical biopsy forceps. Standard techniques were used for polypectomy. Histopathological specimens were read separately by two expert GI pathologists blinded to the results of the WavStat4 assessments. The primary outcome measures were 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: were <10 mm and 10 were >10 mm were found in 70 patients (Males-44, females-27). Average age of the patients was 65 years (range 29–95 years). 16 polyps were not included in the final analysis due to discrepancy in histological analysis between two pathologists. We failed to retrieve 5 polyps. 28 patients were excluded from the study (No polyps seen in 17 patients, polyps <10 mm were not seen in 3 patients, and device failure in 4 patients). A total of 126 polyps <10 mm were included in final analysis. The diagnostic performance for WavStat version 4 and endoscopic assessment is detailed in the table. WavStat4 had a NPV of 96.8% and predicted 100% of surveillance intervals in the recto-sigmoid area. This combined algorithmic approach met the PIVI proximal to the recto-sigmoid junction. We classed them according to the endoscopic classification only if Wavstat4 prediction was as an adenomatous polyp in the recto-sigmoid area. This combined algorithmic approach met the PIVI thresholds and had a NPV of 95.8% and predicted 100% of surveillance intervals in the recto-sigmoid area. The primary outcome measures were 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.

Conclusion: WavStat version 4 has a high NPV for characterizing colorectal polyps less than 10 mm in size but only predicts surveillance intervals correctly in 81.2% of patients. An algorithmic approach combining Wavstat4 and endoscopic assessment had a high NPV with accurate prediction of surveillance intervals.

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 distend the intestinal lumen. Small intestine contrast ultrasound (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, site and extent of SB disease and in assessing strictures in pediatric CD. Children with suspected CD or relapse of known CD were prospectively enrolled. All underwent SICUS, MRI and ileocolectoscopy, performed by different operators blinded to other results. The SB was subdivided into 3 sections: jejunum, ileum, terminal ileum (TI). 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 ileocolectoscopy 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; range 7–18), 23 suspected, 43 known CD were included. The overall concordance (k) between SICUS and MRI for presence of SB disease was 0.94 (ES 0.06; 95% CI 0.85–0.99). The k for segments was: jejunum 0.67 (ES 0.1; 95% CI 0.54–0.8), ileum 0.91 (ES 0.06; 95% CI 0.77–0.96); TI 0.91 (ES 0.06; 95% CI 0.82–0.98). SE and SP (%)) of SICUS and MRI for TI lesions were 98, 100 and 93, 92, 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 0.4–0.8). SE and SP (%) of SICUS and MRI for TI strictures were 100, 100 and 92, 87, 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
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 from patients under aseptic conditions from cancers and adjacent non-cancerous 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 data-base was created using Rapid Evaporative Ionisation Mass Spectrometry (REIMS) from pure cultures of the target microbes. Desorption Electrospray Ionisation Imaging Mass Spectrometry (DESI-MSI) was then performed to provide a spatially resolved map of the mucosal microbial liposome. Tissue samples were then processed onto microscope slides for using chemical spectra identified by REIMS. Candidate microbial lipids were validated using cell co-culture experiments and analysis with REIMS. Multivariate analysis was performed using Matlab (Mathworks) and R. Both unsupervised Principal Component Analysis and supervised Linear Discriminant Analysis were performed. ANOVA was used to perform statistical analysis of single lipid species.

Results: 26 patients with sporadic colorectal cancer were recruited (17 women, median age 68, range 35–84, median BMI 27 kg/m2). Eight tumours were right sided, eleven were left sided and seven were rectal. Two patients had neo-adjuvant chemoradiotherapy. Histology showed six adenomas, one T1, six T2, ten T3 and three T4 cancers. Using DEI-MSI it was possible to geographically identify different lipids and metabolic regions based on co-regulation of the chemical data which independently validated H+E stained tissue. Using leave one patient out cross validation, DEI-MSI was able to diagnose cancer from normal colonic mucosa with ROC AUC = 0.73. Increased long chain fatty acids were seen in malignant tissues whereas glycerophospholipids 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, Bifidobacteria and Enterobacteria. These were positively validated using cell culture REIMS.

Conclusion: Chemical mapping of the colonic liposome permits spatially resolved analysis of the cancer microbiome and its metabolic functions, and this has diagnostic value. DEI-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.

OPI66: 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 effective 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 aim to identify the most extensively explored method for defining molecular heterogeneity in a manner independent of known biology.

Aims & Methods: Whole-genome transcriptomic data was generated for colonic biopsies from a total of 165 UC (93 treatment naïve, 72 controls) and 14 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/mucocytes, mucosa/pro-regulatory, T cells/metabolism and mitochondria/metabolism. Patients belonging to the subgroup characterized by the highest enrichment for the inflammation/mucocytes module cluster trended towards lower response to anti-TNF therapy. Conversely, the highest response rates to anti-TNF therapy were observed in the subgroup characterized by the lowest enrichment for the inflammation/mucocytes module cluster. These subgroups also contained normal healthy controls. Enrichment values for the top module cluster as well as the subclusters (r = 0.49) with enrichment values for the inflammation/mucocytes 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 heterogeneity is related to 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.


OPI67: COMPREHENSIVE CIRCULATORY TRANSCRIPTOMOME AND PROTEOMIC PROFILING IN NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASES: A MULTI-CENTRE COHORT STUDY

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Introduction: There is an unmet need to gain functional insights into pathways that are relevant to 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 (Illumina AmpSeq Transcriptome Human Gene Expression platform) and Olink multiplex protein panels (Olink Proteomics). Treatment-naïve newly diagnosed IBD and healthy symptomatic controls were included in the study. Phenotypic data were captured including demographics and disease classification. Statistical analysis was performed using R. Differentially expressed transcriptomes were correlated with serum protein expression to obtain a circulating profile at diagnosis.

Results: RNA expression profiles were available in 639 patients (351 IB, 288 controls). A total of 5078 genes were differentially expressed between IB and controls. Using hscRP to adjudicate for inflammatory status, 1440 remained significant. The most differentially expressed genes were CD-177 (Bonferroni corrected p = 2.3x10−11), VBI1 (p = 2.90x10−4) and S100 proteins (S100A9, S100A12, S100A14 and S100A1). Protein expression profiles were available in 635 patients (152 CD, 159 UC, 26 IB-D, 298 non-IBD) Multivariate analysis identified 59 protein markers that were significantly associated with IBD. The top significant protein upregulated in IBD included MMP12 (Homo- sapiens 14.1.0.0.04) and CXCL9 (p = 1.7x10−4) while other markers such as CXCL9 showed 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 = 0.69, AUC 0.64, p for comparison = 2.7×10−4 vs. MMP12) and albumin (AUC 0.66, p = 0.004 vs MMP12). 6 proteins differentially upregulated from CD including MMP12 (p = 4.6x10−3). 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 = 5.8x10−3).

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

Disclosure of Interest: R. Kalla: Funded by IBD Character Biering Speaker Fees J. Jahnsson: I have served as a speaker, a consultant and a advisory board member for MSD, Tillot, Ferring, AbbVie, Celltrion, Orion Pharma, Takeda, Napp Pharm, Meda, AstroPharma, Hikma and Pfizer. F. Gomollon: Advisor: Grifols, Abbvie, MSD. Travel Grants: Abbvie, MSD. Research funding (Department) MSD F. Gomollon: Advisor: Grifols, Abbvie, MSD. Travel Grants: Abbvie, MSD. Research funding (Department) MSD J. Satsangi: JS has served as a speaker, a consultant and an advisory board member for MSD, Ferring Abbvie and Shire, consultant with Takeda, speaking fees from MSD and has received research funding from Abbvie All other authors have declared no conflicts of interest.
Table 1 (OP168): Demographics, procedural outcomes, bowel cleanliness and adenoma detection.

<table>
<thead>
<tr>
<th>P value</th>
<th>WE vs WI</th>
<th>WE vs AI</th>
<th>WI vs AI</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females, n (%)</td>
<td>184 (45.1)</td>
<td>183 (44.9)</td>
<td>0.888</td>
<td>0.990</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>224 (54.9)</td>
<td>225 (55.1)</td>
<td>1.0</td>
<td>0.092</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>61.4 (6.2)</td>
<td>60.9 (6.2)</td>
<td>0.261</td>
<td>0.350</td>
</tr>
<tr>
<td>Body Mass Index, mean (SD)</td>
<td>26.4 (4.1)</td>
<td>26.4 (4.4)</td>
<td>0.753</td>
<td>0.775</td>
</tr>
</tbody>
</table>

Indications for colonoscopy, n (%)

| Overall ADR, n (%) | 201 (49.3) | 177 (43.4) | 165 (40.4) | 0.395 |
| Right colon ADR, n (%) | 63 (25.9) | 32 (17.2) | 26 (13.7) | 0.0007 |

Screening FIT+, n (%) | 242 (59.3) | 222 (54.4) | 1.0 | 0.597 |

Screening FOBT+, n (%) | 18 (4.4) | 19 (4.7) | 0.865 | 0.982 |

Family history of colorectal cancer, n (%) | 47 (11.5) | 45 (11.0) | 0.920 | 0.968 |

Primary colonoscopy, n (%) | 101 (24.8) | 101 (24.5) | 0.909 | 0.143 |

Procedural outcomes

| Cecal intubation rate (final), n (%) | 402 (98.5) | 399 (97.8) | 0.590 | 0.734 |
| Cecal intubation time, mean (SD), min | 10.1 (5.4) | 9.7 (6.7) | 0.059 | 0.188 |
| Withdrawal time without polypectomy, mean (SD), min | 24.8 (11.7) | 24.6 (12.0) | 0.842 | 0.084 |
| Overall Boston Bowel Preparation Scale (BBPS) score, mean (SD) | 29 (1.5) | 7.5 (1.7) | 0.981 | 0.128 |
| Right colon BBPS score (SD) | 2.6 (0.6) | 2.4 (0.6) | 0.842 | 0.128 |
| Infused water during insertion, median (range), mL | 550 (50-6500) | 500 (50-10000) | - | - |
| Aspirated water during insertion, median (range), mL | 500 (50-6500) | 500 (10-1000) | - | - |

Adenoma detection

| Overall ADR, n (%) | 201 (49.3) | 177 (43.4) | 165 (40.4) | 0.395 |
| Right colon ADR, n (%) | 63 (25.9) | 32 (17.2) | 26 (13.7) | 0.0005 |

<table>
<thead>
<tr>
<th>Demographics</th>
<th>WE N = 408</th>
<th>WI N = 408</th>
<th>AI N = 408</th>
</tr>
</thead>
</table>

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| Introduction: Adenoma detection rate (ADR, proportion of patients with at least one adenoma) is the primary quality indicator of colonoscopy, due to its correlation with the risk of post-colonoscopy interval cancer and mortality [1,2]. Data from U.S. male veterans [3,4], patients in Taiwan [5] and Europe [6], suggest that water exchange (WE, infusion of clean water in an airless lumen and removal of dirty water during insertion), but not water immersion (WI, infusion of water as adjunct to insufflation and removal of residual water during withdrawal) significantly increases ADR in the proximal (cecum-splenic flexure) and right (cecum-ascending) colon, when compared with standard air insufflation (AI). Limitations of these studies were their retrospective analysis and/or investigators unblinded to the insertion method. |

Aims & Methods: In a prospective, multi-site randomized controlled trial we tested the hypothesis that WE, but not WI, significantly increases ADR (primary outcome measure) compared with AI. The study population was represented by 50–70 years-old asymptomatic subjects, undergoing colonoscopy as primary screening test or after positive fecal occult blood test. A total of 1224 (672 males) patients were enrolled at three centers and randomly allocated 1:1:1 to WE, WI and AI. Split-dose bowel preparation was adopted to ensure optimal pre-procedure cleansing. To overcome the limitation of previous reports of unblinded colonoscopist performing withdrawal inspection, after reaching the cecum another investigator blinded to the insertion method performed the withdrawal. 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. Compared with AI (40.4%), WE (49.3%) but not WI (43.4%) achieved significantly higher overall ADR (p = 0.011 and 0.092, respectively). Compared with AI (16.9%), WE (24%) but not WI (19.1%) achieved significantly higher advanced adenoma detection (p = 0.049 and 0.249, respectively). In the right colon, WE (24%) but not WI (19.1%) achieved significantly higher ADR than AI (16.9%) (p = 0.012 and 0.413, respectively). Even after split-dose preparation, WE was associated with higher overall and right colon BBPS scores. The impact was most notable in patients with excellent BBPS, adjusted entire and right colon ADR of WE were significantly higher than those of AI and WE. Multivariate logistic regression showed that WE, compared with AI, was an independent predictor of adenoma detection in the entire colon [OR (95% CI), 1.18 (1.03–1.36)] and in the right colon [1.24 (1.04–1.47)], respectively. |

Disclosure of Interest: S. Cadoni: Recipient of the 2013 ESGE Research Grant All other authors have declared no conflicts of interest. References

OP169 EFFICACY OF ENDOCUFF-ASSISTED COLONOSCOPY IN THE DETECTION OF COLON POLyps: A MULTICENTER PROSPECTIVE STUDY

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Introduction: Colonoscopy is the gold standard for detecting colorectal adenomas and colon cancers. It can improve survival rates; however, its high cost and long duration have limited its use. The Endocuff is a new device that can be attached to the colonoscope to hold the colonic folds away from the field of view during withdrawal. The aim of this study was to compare the polyp and adenoma detection rates between Endocuff-assisted colonoscopy and standard colonoscopy. We conducted a randomized prospective study conducted at two academic endoscopy departments in Japan. The results were 446 patients who underwent a complete colonoscopy examination from April 2015 to September 2015. The Endocuff group included 239 patients. Cecal intubation rate, insertion time, withdrawal time, pain score, 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 COLON 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 and Methods: Primary objective was to develop and validate a simple classification system allowing differentiation of hyperplastic and adenomatous colorectal polyps. 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 85.9% of patients with high-confidence. Sensitivity ranged from 92% to 96% and specificity 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 98% 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 malignant and premalignant lesions. There is potential to improve the prognosis of patients with LNPcPs. The aim of this study was to examine the frequency of LNPcPs in clinical practice, endoscopic and histopathologic features and predictors for advanced histology.

Aims and Methods: We previously studied 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-pedunculated (flat and depressed) colorectal neoplasms using lectures, videos and individual feedback. Phase 2: Training in endoscopic resection techniques using videotraining and hands-on training with experienced colonoscopists. Then, we embarked in a prospective study of all consecutive colonoscopies performed at our institution from February 2008 to February 2012. Quality indicators (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 showing up- or downwards. We conducted a logistic regression analysis to identify predictors for advanced histopathology, defined as high-grade dysplasia or early colorectal cancer (pT1).

Results: A total of 7166 neoplasms were identified in 9353 patients (mean age 59.9 years, 46.0% male), of which 176 (1.9%) 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 more low-grade dysplasia adenoma (29.8%), 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 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 polyp detection rate to surgeon was decreased from 92% in the first half of the study period to 16.7%. Delayed bleeding occurred in 6 (5.6%) cases after endoscopic resection, none requiring surgical intervention. No perforations were recorded.

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 predictors for advanced histology is critical to optimize the outcomes of endotherapy for LNPcPs.

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 and Methods: The aim of this study was to estimate the loss of health and economic burden due to CRC-diagnosis due to PCCRC in Sweden. A
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 0–36 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 1351 life-years or, expressed differently, 1275 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 £1305.

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.

OPT173 COMPARISON OF COLONOSCOPY, Sigmoidoscopy AND MULTIPLE ROUNDS OF FIT-BASED COLORECTAL CANCER SCREENING: LONG-TERM FOLLOW-UP

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Introduction: Several methods for colorectal cancer (CRC) screening are available; the most often used include colonoscopy, sigmoidoscopy and fecal immunochemical testing (FIT). To date, comparison between these screening methods was mainly focused on one-time endoscopic screening to one-time FIT screening. A fair comparison of diagnostic yield (DY) of FIT would comprise cumulative DY after multiple rounds of FIT screening. The aim of our study is to compare the DY of multiple rounds of FIT-screening to one-time screening by sigmoidoscopy and colonoscopy.

Aims & Methods: Demographic data of 30,007 randomly chosen individuals aged 50–74 were obtained from municipal population registers in The Netherlands (2004–2010); of these 15,046 were invited for four rounds of FIT, 8,407 for one-time sigmoidoscopy, and 6,600 for one-time colonoscopy screening. We compared 2 rounds of FIT to one-time sigmoidoscopy and 4 rounds of FIT to one-time colonoscopy. Cumulative (cum.) participation rate, positivity rate, number of colonoscopies, and diagnostic yield were calculated for each method. The DY was calculated relative to eligible invitees and participants. Between-group differences for participation, number of colonoscopies and DY were evaluated using multivariable logistic regression analysis adjusted for age and gender.

Results: In total, 28,515 eligible persons (median age 60 years, IQR 55–66; 50% males) were invited. Cum. participation was significantly higher for FIT (77%) than for sigmoidoscopy (31%; p<0.001) and colonoscopy (24%; p<0.001). Number of colonoscopies performed relative to eligible invitees was highest for colonoscopy (24%) compared to FIT (13%; p<0.001) and sigmoidoscopy (3%; p<0.001). For invitees, the DY for advanced neoplasia (AN) was significantly higher after two rounds of FIT compared to one-time sigmoidoscopy (3.1% vs 2.3%; p<0.001) and after four rounds of FIT compared to one-time colonoscopy (4.5% vs 2.2%; p<0.001). For participants, DY for AN was significantly higher for 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 invitee compared to one-time sigmoidoscopy and colonoscopy screening, and with significantly fewer colonoscopies needed. Colonoscopy detected more advanced neoplasia per participant. However, due to low participation in colonoscopy screening, FIT seems most effective in population-based CRC screening.

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

TUESDAY, OCTOBER 18, 2016 08:30–10:00
Surgery in IBD – Room L7

OPT174 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 (JD): OR 0.70 (95% CI 0.53–0.92), an increase in the rate of prescription of anti-TNF therapy on admission from 3.9% to 8% and a fall in surgery from 23% to 18%.

Aims & Methods: Hospital Episode Statistics (HES) is an administrative database of data on all elective and emergency care episodes in hospitals in England. Using HES, patients aged between 18 and 60 years coded with a first emergency admission with CD were identified. The influence of demographic factors, comorbidity and infused anti-TNF therapy on mortality, surgery and emergency readmissions was examined using multivariate logistic regression.

Results: Between 2004 and 2014, 24,830 patients (55% female, mean age of 35 (IQR 25–44) were identified. Mortality was 0.22% at 30 days, 0.29% in hospital and 0.81% within 1 year. During admission, 19.2% of patients underwent surgery (median time to surgery 2 days (IQR 1–6)) and 1.9% received infused anti-TNF therapy. Surgery during admission rose from 16.1 to 22.9% (OR 1.52 (95% CI 1.17–2.00)) and 1.9% received infused anti-TNF therapy during admission. Mortality was 0.22% at 30 days, 0.29% in hospital and 0.81% within 1 year. During admission, 19.2% of patients underwent surgery (median time to surgery 2 days (IQR 1–6)) and 1.9% received infused anti-TNF therapy. Surgery during admission rose from 16.1 to 22.9% (OR 1.52 (95% CI 1.17–2.00)) and 1.9% received infused anti-TNF therapy.
TP175 IS THE ‘RESET’ SURGERY EFFECTIVE FOR CROHN’S DISEASE PATIENTS REFRACTORY TO ANTI-TNF THERAPY?

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Introduction: Anti TNF-alpha agents (anti-TNFα) are currently the most effective therapies for Crohn’s disease (CD). Some of CD patients under anti-TNFα therapy, however, need surgery because of disease progression. Surgical resection (‘Reset’) usually leads to the elimination of the intestinal regions with active inflammatory regions and contributes to the improvement of the CD activity. This study was to evaluate the efficacy of anti-TNFα therapy for CD patients who underwent surgery due to the refractoriness to previous anti-TNFα.

Aims & Methods: From July 2005 to November 2015, 65 CD patients underwent intestinal resection at Okayama University Hospital. Of these, 34 patients received anti-TNFα refractory surgery or preoperative anti-TNFα therapy. The efficacy of anti-TNFα therapy was evaluated. The evaluated factors were clinical backgrounds, duration of TNFα therapy, concomitant medications before and after surgery, laboratory data before surgery, and the residual of the affected intestine after surgery, etc. as historical as minimally invasive surgery, hospitalization, or surgery due to worsening of abdominal symptoms, CRP elevation with the evidence of endoscopic recurrence.

Results: Patients of the TNFα-refractory group showed significantly higher rate of ileoceleal valve resection (69% vs. 3%, p < 0.05). In the evaluation of factors predicting relapse in patients with retreatment after anti-TNFα surgery, only the residual of the affected intestine after surgery was identified as a risk factor. The CRP elevation with the evidence of endoscopic recurrence was also observed in patients with more residual of the affected intestine. At univariate analysis, total CGQL score was better in the laparoscopic group patients. At multivariate analysis, only surgical method was identified as a risk factor. In addition, clinical factors predicting relapse in patients with anti-TNFα refractory surgery after precedent surgery were evaluated. The evaluated factors were clinical backgrounds, duration of TNFα therapy, concomitant medications before and after surgery, laborat}

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

TP176 IMPACT OF MINIMALLY INVASIVE SURGERY ON QUALITY OF LIFE AFTER SURGERY FOR CROHN’S DISEASE TERMINAL ILEITIS

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Introduction: Crohn’s disease (CD) is a chronic disease that interferes with the daily life of those affected. Surgical treatment is required in about 70% of CD patients during the course of disease and risk of surgery is among the highest rated concerns among them. Quality of life is often worsened by intestinal surgery.

Aims & Methods: The aim of the study is to assess the impact of minimally invasive surgery on quality of life after surgery for Crohn’s disease terminal ileitis. From June 2010 to December 2015, one hundred patients underwent surgery for Crohn’s disease terminal ileitis were enrolled. Patients were interviewed by telephone and responded to the generic European Global Quality of Life (CQGQL) 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 CQGQL score and its single items (quality of life and body image) were significantly higher (and thus, better) in the laparoscopic 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 CQGQL score was directly correlated with minimally invasive surgery (rho = 0.44, p < 0.001) and inversely correlated with disease activity at the moment of the interview (rho = -0.44, p = 0.01), the use of steroids (rho = -0.20, p = 0.02) and recurrent CD as indication for surgery (rho = 0.19, p = 0.05). At multivariate analysis, only minimally invasive surgery was associated with significantly less CRD and less severe disease of these patients (less recurrent Cd as indication for surgery or simpler surgery). Quality of life is essentially predicted by current disease activity and minimally invasive surgery. Finally, minimally invasive surgery tended to be associated to a less frequent CD recurrence (p = 0.08)

Disclosure of Interest: All authors have declared no conflicts of interest.
OP178 LONG-TERM FOLLOW-UP AFTER ILEORECTAL ANASTOMOSIS IN ULCERATIVE COLITIS (UC): A GETAID RETROSPECTIVE COHORT STUDY OF 343 PATIENTS

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Introduction:

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Aims & Methods:

point. Improvement in IBDQ was defined as an increase of ≥ 20 points. Failure was defined as when patients underwent colectomy or prescribed trial medication (eg. Vedolizumab, Enteralizumab).

Results: In total, 30 patients (57% female) with a median age of 40 (IQR, 33–47) underwent appendectomy with a mean preoperative total Mayo score of 9 (SD 3). Among patients baseline IBDQ was 125 (SD 34). After 3 months, clinical response was seen in 16 (53%) patients of whom 7 (30%) were in remission (7 patients refused endoscopy at this time point). Improvement in IBDQ was seen in 14 (47%) patients with a mean of 120 (SD 29) that increased to 168 (SD 29). After 12 months, 11 patients failed (7 colectomy, 4 trial medication) and 5 did not yet reach the endpoint. In the remaining 14 patients, 9 (36%) had last clinical response of whom 5 (23%) were in remission (3 patients refused endoscopy).

Conclusion: Appendectomy was effective in at least 30% of therapy-refractory UC patients. These early results suggests 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.

Disclosure of Interest:

TUESDAY, OCTOBER 18, 2016 08:30–10:00

GI INFECTIONS FROM MECHANISMS TO TREATMENT – ROOM L8_____________________

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

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

Aims & Methods: The aim of this study was to determine the risk of Clostridium difficile infection in patients with pernicious anaemia. We conducted a population based cohort study using English linked primary 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 infection1. 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 the effect should be manifested in patients with achlorhydria (no acid production), a condition associated with pernicious anaemia. Elucidating this association would provide a clear understanding of the acid-suppression hypothesis underlying the increased risk of infection in patients who have received gastric acid suppressive therapy.

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microbiota-based drug candidate targeted at recurrent CDI, is sourced from human-derived mice feces from extensively donor-derived donors and manufactured using standardised, quality controlled processes.

Aims & Methods: To compare the bacterial abundance in the source material for RBX2660 (DS) with the bacterial abundance in the finished drug product (DP) used in the Phase 2B PUNCH CD 2 study. A total of 70 DS samples sourced from 17 unrelated donors (mean age 27; range 18 to 57 years; 94% male) from August 2014 to February 2016 were compared with 70 matched DP samples using the Ga-map Dysbiosis Test (GA-test), Genetic Analysis AS, Oslo, Norway. The GA-test uses 54 probes targeting V3 to V7 of the bacterial 16S rRNA gene to characterise and identify bacteria present. Approximately 300-400 bacteria at different taxonomic levels are covered, providing for an assessment of the microbial community using multiple variable regions. The GA-test enables serial assessment of the faecal bacterial abundance profile as well as potentially clinically relevant alterations in the microbiome over time. These capabilities of the GA-test were used to assess the production processes for RBX2660. The differences in bacterial abundance between the DP and DS were calculated from log-addition of cycle counts (DP-DS); averaging the differences.

Results: The GA-test found that the bacterial abundance in the RBX2660 DP was lower than in the DS of 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 showed increased signal strength in the DP compared with the DS, while Proteobacteria demonstrated equal signal strength in both samples. The comparative abundance in the DP vs. the DS is shown in Table 1. Accuracy was as high as 83.4% at cross-validation. Principal component analysis found that the bacterial profiles in the RBX2660 DP, though lower than in the donor source material, were largely kept intact during the production process for all 17 donors.

Table 1: Comparative Signal Strength of Bacteria

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Signal Strength in DP vs. DS</th>
<th>Mean Difference (95% CIM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteroides</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>Increased</td>
<td>0.07 (0.03, 0.11)</td>
</tr>
<tr>
<td>Parabacteroides</td>
<td>Increased</td>
<td>0.12 (0.07, 0.17)</td>
</tr>
<tr>
<td>Alitiges</td>
<td>Increased</td>
<td>0.17 (0.11, 0.23)</td>
</tr>
<tr>
<td>Firmicutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lachnospiraceae</td>
<td>Decreased</td>
<td>-0.13 (-0.15, -0.11)</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Decreased</td>
<td>-0.16 (-0.20, -0.13)</td>
</tr>
<tr>
<td>Negativicutes</td>
<td>Increased</td>
<td>0.03 (0.01, 0.06)</td>
</tr>
<tr>
<td>Clostridia</td>
<td>Decreased</td>
<td>-0.18 (-0.20, -0.16)</td>
</tr>
<tr>
<td>Actinobacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bifidobacterium</td>
<td>Decreased</td>
<td>-0.33 (-0.38, -0.28)</td>
</tr>
<tr>
<td>DP = drug product</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DS = drug source</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIM = confidence interval of mean</td>
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</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 COLONIC EPITHELIAL CELLS IN MICE

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Introduction: Adhesive-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 pil and abnormally expressed CEACAM6 protein on host cells. We previously reported an original mechanism of CEACAM6 regulation depending on DNA methylation/transcription factor 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 CEACAM6 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 microbiota composition, on DNA methylation and on genes expression on microbiota composition.

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. Several different parameters such as the ratio of 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 an important effect on gut inflammation. No significant modifications were observed on histological sections following HMD. Microbiota analysis revealed a 1000-fold decrease in E. coli population in fed HMD compared to mice receiving a conventional diet. As expected, global DNA methylation analysis revealed a global increase in cytosine methylation in mice fed a HMD compared to 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 genes expression such as a decrease in CEACAM6 and modify microbiota composition leading to eradication of the E. coli population in the intestine. A diet-based strategy could help decreasing AIEC colonization in CD patients by modulating CEACAM6 expression.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP184 ENTEROHEMORRHAGIC ESCHERICHIA COLI TROPISM TO Peyer’s PATCHES: ROLE OF LONG POLAR FIMBRIAE AND INHIBITION BY A PROBIOTIC YEAST

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Introduction: Enterohemorrhagic Escherichia coli (EHEC) are food-borne pathogens associated with diarrhea, hemorrhagic colitis and life-threatening complications such as hemolytic-uremic syndrome. EHEC interact with the Ficollicule-Associated Ephithelium (FAE) of Peyer’s patches of the distal ileum in humans and translocate across the intestinal epithelium via M cells. Molecular mechanisms are still unknown but Long Polar Fimbriae (Lpf), which contribute to interactions with the ileal biopsies, play a role in EHEC infections and use of antibiotics remains controversial. Probiotic could be an alternative strategy.

Aims & Methods: The objectives of the study were to investigate the role of Lpf in EHEC tropism to Peyer’s patches, and to explore the influence of probiotic yeasts on EHEC interactions with intestinal mucosa. The expression of lpf genes (encoded by two lpf operons) of EHEC O157:H7 strain EDL933 was analyzed using in vitro models of the human ileum, gestational tract and large intestine. To investigate the involvement of Lpf in the ability of EDL933 to target Peyer’s patches, we generated the ΔlfpA1, ΔlfpA2, ΔlfpA1-ΔlfpA2 isogenic mutants and trans-complemented them with lpf genes. Lpf interaction with M cells was measured using an in vitro model of specialized M cells. M-like 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 robotic yeasts, mice were given the probiotic for 7 days before ileal loop assays were conducted with O157:H7 wild type.

Results: Lpf isogenic mutants (i) were not able to interact with ileal biopsies compared to 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. We are investigating that expression of 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 antibiotics significantly inhibited O157:H7 interactions with Peyer’s patches and reduced the number of hemorrhagic Peyer’s patches in murine ileal loops. Since yeast cell surface is rich in mannose, the role of carbohydrates in EHEC interactions with Peyer’s patches was investigated. Among the carbohydrates tested, only mannose specifically limited the interactions of EHEC with Peyer’s Patches.

Conclusion: We conclude that Lpf are involved in the interactions of EHEC with ileal M cells and that this interaction is significantly lower in the presence of mannose.

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 1.86

OP186 SELF-EXPANDABLE METALLIC STENT AS BRIDGE TO SURGERY IS MORE SUPERIOR THAN TRANSDURAL DRAINAGE TUBE AT QUALITY OF LIFE FOR THE PATIENTS WITH PRIMARY MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: Self-expandable metallic stent (SEMS) or transmural 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 TDT group (27.1±18.0 vs 12.1±7.9 days, p=0.04), because the rate of temporary discharge was significantly higher in SEMS group (41.7% vs 0.0%, p<0.001). No significant difference was shown about the hospitalization in both group (36.1±23.5 days vs 46.4±36.0 days, p=0.36). The oral intake (at least soft solids) was significantly higher in SEMS group (88.9% vs 25.0%, p<0.001). The Colonic Stent Safe Procedure Research Group ColorRectal Obstruction Scoring System (CROSS) score before decompression was significantly different in both group (1.0±0.9 vs 1.2±0.7, p=0.49), but CROSS score after decompression was significantly improved in SEMS group (3.7±0.8 vs 2.3±0.5, p<0.001). The complications after procedure, such as perforation, migration, obstruction, had no significant difference in both group.

Table: Patients characteristics and results

<table>
<thead>
<tr>
<th></th>
<th>SEMS (n=27)</th>
<th>TDT (n=42)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, years)</td>
<td>73±17.0</td>
<td>65±15.2</td>
<td>N.S.</td>
</tr>
<tr>
<td>-Age ≥ 85 years</td>
<td>9 (33.3%)</td>
<td>7 (17.1%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Obstructed location (left side)</td>
<td>23 (85.2%)</td>
<td>38 (90.5%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Primary colorectal cancer</td>
<td>21 (77.8%)</td>
<td>28 (70.0%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>-BTS</td>
<td>12 (44.4%)</td>
<td>24 (57.1%)</td>
<td>0.02</td>
</tr>
<tr>
<td>-Bridge to SEMS insertion</td>
<td>2</td>
<td>2</td>
<td>N.S.</td>
</tr>
<tr>
<td>-Palliation</td>
<td>7</td>
<td>1</td>
<td>N.S.</td>
</tr>
<tr>
<td>-Emergent surgery</td>
<td>2</td>
<td>1</td>
<td>N.S.</td>
</tr>
<tr>
<td>Metastatic colorectal cancer</td>
<td>6 (22.2%)</td>
<td>12 (30.0%)</td>
<td>0.32</td>
</tr>
<tr>
<td>-BTS</td>
<td>0</td>
<td>5</td>
<td>N.S.</td>
</tr>
<tr>
<td>-Bridge to SEMS insertion</td>
<td>2</td>
<td>2</td>
<td>N.S.</td>
</tr>
<tr>
<td>-Palliation</td>
<td>5</td>
<td>7</td>
<td>N.S.</td>
</tr>
<tr>
<td>-Emergent surgery</td>
<td>1</td>
<td>1</td>
<td>N.S.</td>
</tr>
<tr>
<td>-Technical Success</td>
<td>27 (100%)</td>
<td>40 (95.2%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Perforation</td>
<td>2 (7.4%)</td>
<td>6 (14.3%)</td>
<td>N.S.</td>
</tr>
</tbody>
</table>
Aims & Methods: This study aimed to clarify the clinical factors associated with the technical difficulty of SEMS placement for malignant colorectal obstruction. This study represents the largest material from a single centre ever published.

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 colorectal obstruction in 396 patients, including 158 as bridge to surgery (BTS), 237 as palliation, three with malignant anastomotic stricture and 20 patients with obstruction due to external tumor compression. The benign indications in 37 patients were respectively diverticulitis stricture in 15, diverticulitis fistula in two and benign anastomotic stricture in 20. Two hundred and seventy-seven patients had manifested total colonic obstruction and 121 had small bowel dilatation at the time of the procedure. The placement of the SEMS was 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. Mean 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 of 87.7%. Stent procedure related complications were 4.2%, mainly guidewire perforations, and none of these patients died within 30 days after procedure. The second stent intervention was performed in 5.9% 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 2.5% in the palliative group.

Conclusions: Our data show 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


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 colorectal obstruction in 396 patients, including 158 as bridge to surgery (BTS), 237 as palliation, three with malignant anastomotic stricture and 20 patients with obstruction due to external tumor compression. The benign indications in 37 patients were respectively diverticulitis stricture in 15, diverticulitis fistula in two and benign anastomotic stricture in 20. Two hundred and seventy-seven patients had manifested total colonic obstruction and 121 had small bowel dilatation at the time of the procedure. The placement of the SEMS was 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. Mean 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 of 87.7%. Stent procedure related complications were 4.2%, mainly guidewire perforations, and none of these patients died within 30 days after procedure. The second stent intervention was performed in 5.9% 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 2.5% in the palliative group.

Conclusions: Our data show 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 treatment of obstructive colorectal cancer. Although endoscopic stenting is widely accepted in a palliative setting, disagreement exists about its role in a curative resection. It offers the opportunity for an intraoperative characterization of the surgical resection. 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 group, treated with a stent as a bridge to surgery (BTS) for colon cancer. Ninety-seven patients, who presented in a Belgian secondary hospital between June 1998 and November 2013 with a large bowel obstruction due to colon cancer, were included. All patients underwent endoscopic stenting as a BTS in a potentially curable disease. Procedure-related complications and long-term follow-up survival data were collected and compared with the colon cancer mortality in Belgium in the same era (3).
Results: Overall survival in this observational cohort did not differ significantly from that of the colon cancer patients in the same period (p = 0.14). One- five- and ten-year survival was not statistically different in both groups (95.9% vs 79.0%; 54.7% vs 51.2%; 41.0% vs 35.6% respectively). Additionally, for tumour stage II, III and IV no statistical differences between both cohorts were found (p = 0.21, p = 0.58, p = 0.10 respectively). Technical success rate was 94.8%. Seventy patients did not experience any complication. Stent migration occurred in 9 patients, whereas stent-related micro- and macro perforations were observed in 14 patients, without influencing survival. Incidence rates of peritoneal leaks when stents did not differ significantly between patients with and without any type of perforation (22.2% vs 15.2% respectively, p = 0.47). On average, surgery took place 16.6 days after colonic stenting, ranging from an operation on the same day as the endoscopic procedure, to an interval of maximal 124 days. In 82.5% of the cases a laparoscopic resection of the tumor was performed. Five point two percent of the patients got directly open surgery. In 5.2% of the patients a laparoscopic procedure was converted to laparotomy, because of adhesions or peritonitis. Stoma rates were low (5.2%).

Conclusion: The results indicate that stenting before surgery is effective and safe in the treatment with curative intent of patients with obstructive colon cancer and reinforce the debate on stenting as a BTS.

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

References:

OP190 IMPACT OF MORTALITY FROM SURGICAL ADENOMA REMOVAL ON THE EFFECTIVENESS OF COLORECTAL CANCER SCREENING

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Introduction: Implementation of colorectal cancer (CRC) screening programs results in an increase in the number of adenoma diagnoses. Some of the advanced adenomas (AADs) cannot be endoscopically removed and patients may then be referred for surgery. However these surgical resections have an associated mortality. We simulated a scenario with and without perioperative mortality in relation to AAD removal on the effectiveness of CRC screening.

Aims & Methods: We used the MISCAN-Colon simulation micromodel 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 nm) during diagnostic colonoscopy need to be surgically removed, based on findings during diagnostic colonoscopy need to be surgically removed. 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.

Results: During the roll-out of the Dutch screening program between 2014 and 2020, perioperative mortality caused up to 18 deaths every year. After 2020 the number of AAD screen detected decreased and thus perioperative mortality decreased gradually through approximately 11 per year in 2033. Between 2014 and 2020 there was a total of 253 individuals died from perioperative complications. This corresponded with a decrease in prevented CRC deaths of 1.5% (22135 without operation mortality vs 21928 with), a decrease in LYG from screening of 2.5% and in QALY’s of 1.0%. The impact on costs of the screening program was negligible. With higher and lower perioperative mortality assumptions, the outcomes altered proportionally.

Conclusion: Mortality due to surgical AAD resection has a negative impact on the effectiveness of CRC screening, although the impact is modest. Benefits of CRC screening as a whole are maintained. However, deaths due to surgical AAD resection are an order of magnitude larger than deaths due to complications of colonoscopy. Future studies into the effectiveness of CRC screening should therefore incorporate the harms of surgical AAD removal.

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

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

COMPICATIONS IN IBD – ROOM F2

OP192 THE OCCURENCE OF ANAEMIA AND ANAEMIA SUBTYPES DURING THE FIRST YEAR OF DISEASE IN AN EAST-WEST EUROPEAN INCEPTION COHORT – AN ECCO-EPICOM COHORT STUDY

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Introduction: The incidence of anaemia in inflammatory bowel disease (IBD) is about 15% during the first year of diagnosis. The association of anaemia with specific subtypes of IBD and their clinical characteristics is not clear.

Aims & Methods: Cross-sectional study of patients with IBD participating in the ECCO-EPICOM cohort study. Data were collected prospectively. The primary endpoints were the prevalence of anaemias and their subtypes at diagnosis and at 12 months. We also compared demographics, disease characteristics, disease activity, and therapeutic regimens at diagnosis and at 12 months in IBD patients with and without anaemia.

Results: Of 4,752 patients, 3,677 (77%) were included in this study. The incidence of anaemia during the first year of disease was 19%. The most common anaemia subtype at diagnosis was iron deficiency anaemia (63%), followed by normochromic normocytic anaemia (18%), microcytic hypochromic anaemia (13%), and other anaemia subtypes (6%). At 12 months, the incidence of anaemia was 26%, with iron deficiency anaemia (72%), normochromic normocytic anaemia (17%), microcytic hypochromic anaemia (9%), and other anaemia subtypes (2%). In a logistic regression analysis, factors associated with anaemia at diagnosis included disease duration and delays in diagnosis, whereas smoking was a protective factor. At 12 months, factors associated with anaemia included treatment with corticosteroids or immunomodulators, whereas smoking was protective.

Conclusion: The incidence of anaemia during the first year of disease was high, with iron deficiency anaemia being the most common subtype. Factors associated with anaemia at diagnosis included disease duration and delays in diagnosis, whereas smoking was a protective factor. At 12 months, factors associated with anaemia included treatment with corticosteroids or immunomodulators, whereas smoking was protective.

Disclosure of Interest: All authors have declared no conflicts of interest.
Anaemia - overall 43% 26% 29% 13% 58% 25% 45% 12%

Table 1:

Prevalence of anemia at diagnosis and at 1-year follow up.

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Introduction: The EpiCom-cohort is a European prospective population-based cohort of unselected patients uniformly diagnosed with inflammatory bowel disease (IBD) in 2010 in 31 Western and Eastern European centres. Previously, this cohort has demonstrated differences in the treatment strategy of IBD patients between Eastern and Western European centre including that significantly more patients in Eastern 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 an 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 who were diagnosed at diagnosis remained anaemic (23% UC, 24% 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.

Conclusion: In this unselected, population-based inception cohort the frequency of anaemia was high at the time of diagnosis, especially for CD, but decreased during the first year of follow-up. More Eastern than Western European patients remained anaemic after 1 year of follow-up. These geographic differences could be caused by differences in awareness of anaemia or they might reflect differences in global care and inflammation control of IBD patients in Europe. Geographic variations in the use of biological therapy might contribute to the observed differences in anaemia frequency.

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

References

OP193 INCIDENCE AND RISK FACTORS OF SERIOUS VIRAL INFECTIONS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Use of immunosuppressants in IBD is associated with an increased risk of serious infections that varies considerably according to infection and immunosuppressant subtypes. This study aimed to determine the incidence rate and risk factors for serious viral infection (SVI) according to drug exposure and IBD activity in patients with IBD.

Aims & Methods: Using MICISTA registry, a prospective observational cohort of IBD patients treated at our tertiary care hospital, we identified between Jan 2005 and Dec 2014 patients who developed SVI as defined by need for hospitalization, definite organ damage or disabling sequelae. Cases of CMV colitis without systemic manifestations were excluded. We first estimated incidence rates of SVI, overall and according to maximal yearly treatment. Additionally, we performed a case-control study (4 controls for 1 case matched for age, gender, IBD subtype and duration) assessing risk of SVI according to IBD drug use and IBD clinical activity in the 3 months preceding the SVI (data extracted from individual health records).

Results: We identified 31 patients with SVI among 2645 patients, followed for a median period of 6.2 years and a total observational time of 16922 patient-years. We identified 13 cases of CMV systemic infection (primary infection (n = 6), reactivation (n = 7)), 10 cases of EBV infection (primary infection (n = 6) including 2 haemophagocytic syndromes, reactivation (n = 4)), 3 cases of VZV infection (varicella (n = 3), shingles (n = 2) and 3 cases of HSV infection (severe esophagitis, facial nerve paralysis, severe refractory cutaneous manifestation). Most patients required hospitalization (94%) and received IV anti-viral therapy (95%). The incidence rate of SVI in patients with IBD was 1.83 per 1000 patient-years. Table 1 shows the incidence rate of SVI according to the maximal treatment received during the year. In the case control study, risk of SVI was associated with exposure to thiopurine (adjusted odds-ratio (aOR) 5.1: 95% CI 1.9–13.4; p = 0.001) and methotrexate (aOR 4.1: 95% CI 1.0–16.8; p = 0.05), and active clinical pathology (aOR 3.2: 95% CI 1.3–8.1; p = 0.02). Odds-ratios for corticosteroids and anti-TNF did not reach statistical significance (1.1 and 1.2, respectively).

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

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

OP194 COLORECTAL CANCER RISK IN A NATIONWIDE INFLAMMATORY BOWEL DISEASE COHORT WITH LOW GRADE DYSPLASIA

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Introduction: Patients with long-standing colonic inflammatory bowel disease (IBD) bear an increased colorectal cancer (CRC) risk. Endoscopic surveillance allows early detection and removal of preneoplastic lesions such as low-grade dysplasia (LGD), and may subsequently prevent CRC. However, the long-term risk of developing CRC in a patient with LGD is uncertain.
since most available studies are small and cover a relatively short follow-up period, we published a systematic review of the literature, documenting 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 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 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 years per patient after LGD diagnosis (total follow-up time: 11741 patient years). 825 (70.1%) patients had ulcerative colitis, 328 (28.1%) patients had Crohn’s disease and 16 (1.4%) patients had indeterminate colitis. Hundred nine out of 1177 (9.3%) patients underwent colectomy. CRC developed in 56 out of 1177 patients resulting in a cumulative incidence of 2.9%, 5.8%, 11.1% and 18.7% respectively up to 5, 10, 15 and 20 years. Patients with an IBD duration of more than 5 years before LGD development had a significantly higher cumulative CRC incidence (14.7% after 15 years) compared to those with a shorter IBD duration (9.4% after 15 years; log rank p < 0.001). 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 (HR) 2.59, 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 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 tissue. 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 pattern, pre-stenotic dilation, presence of oedema and/or comb-sign, presence of fistulas and primary T2 sequences. Furthermore, all patients with and without by DWI sequences defining: visual analysis of intensity and analysis of Apparent Diffusion Coefficient (ADC) maps. Statistical analysis was performed dividing all patients in 2 groups (operated vs not operated) using T-student and X-square test when indicated. To identify the variables associated to surgical risk we performed a logistic multiple regression expressing the risk in terms of Odd Ratio.

**Results:** 210 patients were enrolled and 127 bowel segments resulted pathologic at MRI. We performed a logistic multiple regression expressing the risk in terms of Odd Ratio. Finally, the diagnostic accuracy was tested by a ROC curve.

**Conclusion:** Among 404 patients who underwent 1236 colonoscopies, 38 patients who developed CRC in inflamed mucosa and 92 matched controls were included in a nested case-control study. Independent factors significantly associated with CRC were primary sclerosing cholangitis (PSC) (Odds ratio (OR), 6.26; CI 95% 1.07–37.51, p = 0.04), 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 = 0.001) and 5-aminosalicylates (OR, 0.27; CI 95% 0.084–0.876, p = 0.03) at the time of neoplasia or last colectomy. 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 CRC was 100% in patients with colonoscopies performed 1 and 3 years after the first surveillance colonoscopy.

**Conclusion of Interest:** In IBD patients undergoing endoscopic surveillance, the risk of first CRC is increased in case of PSC, persistence of histological acute inflammation and persistent 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. Bourier: Anne Bouvier has received lecture fees from UCB
H. Sokol: Harry Sokol received consulting fees from Enterome, Astellas, Roche, Merck, Maai and Danone.
P. Seksis: Philippe Seksis 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, Abbvie, MSD, Ferring Pharmaceuticals, Janssen, and research support from Abbvie, Biocodex and Ferring Pharmaceuticals.
All other authors have declared no conflicts of interest.
Table 1: Time-dependent cox-regression analysis of baseline FIT of advanced neoplasia.

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male) 1.7</td>
<td>1.3-2.3</td>
</tr>
<tr>
<td>Age (years) 1.1</td>
<td>1.0-1.1</td>
</tr>
<tr>
<td>Baseline fHb conc. 0 µg Hb/g</td>
<td>Ref.</td>
</tr>
</tbody>
</table>
| >0.5-5 µg Hb/g | 1.8 | 1.3-2.4 | 1.7 
| >5-10 µg Hb/g | 7.0 | 4.6-10.5 | 6.0 |
| Socioeconomic status High | Ref. | 0.08 |
| Average | 1.5 | 0.7-1.3 |
| Low | 2.6 | 0.6-1.4 |

Conclusion: Among FIT negative screenes, baseline fHb concentration is an independent predictor for the risk of future AN. Moreover, fHb concentrations of more than 5 µg Hb/g had a 23% higher cumulative incidence of AN than those with a baseline fHb of 0 µg Hb/g (p < 0.001). In multivariate Cox regression analysis HRs increased with fHb concentration, up to a 14-fold risk increase for two consecutive FITs with both a fHb concentration of 8 µg Hb/g.

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

References
**Table (OP202)**

<table>
<thead>
<tr>
<th>Screen-detected cancer</th>
<th>FIT interval cancer</th>
<th>Colonoscopy interval cancer</th>
<th>CRC in non-participants</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CRCs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age diagnosis (%(n))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>24.1 (28)</td>
<td>22.2 (60.7)</td>
<td>7.7 (1)</td>
<td>19.3 (21)</td>
</tr>
<tr>
<td>-60–69</td>
<td>50.3 (50)</td>
<td>71.4 (77.8)</td>
<td>10.3 (14.4)</td>
<td>34.9 (38)</td>
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<tr>
<td>70–</td>
<td>62.9 (73)</td>
<td>53.8 (7)</td>
<td>63.3 (69)</td>
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</tr>
<tr>
<td>0.55 to /C0</td>
<td>11.2 (13.7)</td>
<td>15.4 (2)</td>
<td>0.814</td>
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</tr>
<tr>
<td>Sex (male;%(n))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>62.9 (73)</td>
<td>59.3 (16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES (n)–Low–Average–High</td>
<td>7.4 (22.7)</td>
<td>77.8 (14.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal–Distal–Unknown</td>
<td>29.3 (34.7)</td>
<td>37.0 (63.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage–I–II–III–IV-Missing</td>
<td>51.7 (60.1)</td>
<td>29.6 (62.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival (%(n))</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>88 (102)</td>
<td>81.5 (22)</td>
<td></td>
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</table>

**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) on smoking, body weight, physical activity, alcohol intake and selected dietary items at baseline and at one-year follow-up. Participants were randomly assigned to five biennial rounds of fecal immunochemical test (FIT), one round flexible sigmoidoscopy (FS) or no screening (controls). In total, 1809 and 1327 participants with a negative screening test result in the FIT and FS group, respectively, completed the LSQ, as did 1029 controls. ANCOVA and logistic regression were used to calculate differences in changes of health behavior (and 95% confidence intervals (CI)) between the arms at follow-up.

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

**Conclusion:** The present study does not suggest unfavorable short-term consequences in health behavior after getting a negative CRC screening test result whether this is from once only FS or first round of FIT screening.

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

**OP202 SCREEN-DETECTED AND NON-Screen-DETECTED COLORECTAL CANCERS AFTER FOUR ROUNDS OF FECAL IMMUNOCHEMICAL TEST-BASED COLORECTAL CANCER SCREENING**

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**Introduction:** Fecal immunochemical test (FIT)-based colorectal cancer (CRC) screening aims to detect CRC in an early stage, thereby reducing morbidity and mortality from this disease. Whereas data on survival and costs per individual in the lifetime of 20,000,000 individuals.

**Results:** A total of 27,340 people were invited for FIT-screening, of whom 18,752 (68.6%) participated at least once. Median follow-up time was 46 months (IQR: 18.5–72.4). Among participants, 3,009 (16%) had a positive FIT in one of the 4 screening rounds. In total, 265 patients were diagnosed with CRC: 116 were SD-CRCs, 27 FIT interval CRCs, 13 colonoscopy interval cancers and 109 CRCs 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 most 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 CRCs.

**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 to 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, life-years lived and costs per individual in the lifetime of 20,000,000 individuals.
Result: FIT screening without a surveillance programme reduced CRC incidence and deaths respectively by 25.4% and 25.5% compared to FIT screening without any surveillance or no surveillance strategy. CRC incidence and mortality reductions increased to 28.1% and 40.8% when surveillance based on the Dutch guideline was added to FIT screening. Prolonging surveillance intervals slightly reduced surveillance effectiveness with portal hypertension (HVPG >10 mmHg) translated into a clinically meaningful benefit, it is an acceptable surrogate of liver disease.

Conclusion: Adding surveillance to FIT screening reduces CRC burden and is cost-effective compared to screening without surveillance. However, the colono-scopy burden to mark advanced chronic liver disease. Since a decrease in HVPG translates into a clinically meaningful benefit, it is an acceptable surrogate endpoint.

Aims & Methods: We aimed to investigate the impact of sustained virological response (SVR) to interferon (IFN)-free therapies on portal hypertension in patients with paired HVPG measurements. One hundred and four patients with portal hypertension (HVPG ≥ 6 mmHg) who underwent HVPG and transient elastography (TE) before IFN-free therapy (baseline [BL]) were retrospectively studied. The effect of SVR on portal pressure was investigated in patients with SVR who also underwent follow-up (FU)-HVPG and TE after IFN-free therapy (group A; n = 40), comprising all patients who achieved SVR to IFN-free therapy (n = 43), and the subgroups of patients with paired HVPG of 6–9 mmHg and ≥ 10 mmHg, respectively. Multivariate-adjusted analyses revealed that 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 of liver disease were set at 25.4% and 35.7% for ruling-in and ruling-out of liver disease. The liver stiffness values at FU for ruling-in and ruling-out of liver disease were set at 25.4% and 35.7% for ruling-in and ruling-out of liver disease. The liver stiffness values at FU for ruling-in and ruling-out of liver disease were set at 25.4% and 35.7% for ruling-in and ruling-out of liver disease.
Aims & Methods: In total, 153 consecutive patients with HCV genotype 1b initiating DCV/ASV therapy, 45% of whom had cirrhosis, were enrolled. The cohort comprised 52 patients with compensated cirrhosis and 101 patients without cirrhosis (67 males and 86 females; median age, 71 years; 9 patients were >80 years old). NSSA resistance-associated variants (RAVs) were examined using direct sequencing. The patients were treated with 80 mg of DCV daily and 100 mg of ASV twice per day for 24 weeks. Clinical, biological, and virological data, including adverse effects, were recorded at baseline and during follow-up.

Result: Only 10 (6.5%) patients had L31M or Y93H RAVs. There was no statistically significant difference in age, sex, IL28B genotype, HCV viral load at baseline, ALT level, creatinine level, or NSSA RAVs between patients with and without cirrhosis. On the other hand, those with cirrhosis showed significantly lower levels of platelets, white blood cells, and hemoglobin and higher levels of liver enzymes compared to those without cirrhosis. The rate of SVR12 was 94% (49/52) in patients with cirrhosis and 97% (96/99) in patients without cirrhosis. Grade 3/4 complications frequently occurred in patients with cirrhosis (p = 0.04), of whom two had anemia, four had elevated liver enzymes, and one had acute liver failure. All patients responded to decompensated cirrhosis with a sustained virological response. One patient, who had been diagnosed with primary biliary cirrhosis, developed decompensation and portal hypertension. The patients were given sofosbuvir 200 mg, ribavirin 200 mg, and asunaprevir (ASV; second-generation HCV NS3/NS4A protease inhibitor) was approved for patients with HCV genotype 1 in Japan since September 2014. Now, elderly patients and those with advanced hepatic fibrosis including chronic liver disease, are offered IFN-free therapy. The primary objective was to assess the efficacy and tolerability of DCV/ASV combination therapy in patients with hepatic cirrhosis.

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

References

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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 (LS) in response to IFN-free DAA therapy and evaluated liver histology after successful interferon (IFN)-free DAA therapy.

Aims & Methods: HIV/HCV patients undergoing IFN-free DAA treatment and who had paired hepatic venous pressure gradient (HVPG) and liver stiffness (LS) measurements at baseline and weeks 12 and 24 were included. LS and HVPG were measured in a fasted, non-seated state. Comcomitant beta-blocker treatment was stopped for all measurements. Post-treatment liver biopsies were assessed by METAVIR score.

Result: Of 19 patients (56% male, age: 53.4±6.7 years, 95% comitant 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: GT-1a: 12, GT-1b: 2 and GT-3a: 5. All patients had portal hypertension (HVPG >5 mmHg) and 14 patients (74%) presented with liver cirrhosis (LS >12 kPa). DAA treatment resulted in 100% SVR12. LS decreased significantly from 23.0±16.5 to 16.9±16.1 kPa (mean change (Δ): -6.1±5.2 kPa; p < 0.001). Also, HVPG decreased from 10.4±4.0 to 7.6±4.3 mmHg (Δ: -2.8±4.2 mmHg; p < 0.001). In patients with clinically significant portal hypertension (HVPG ≥10 mmHg, n = 9), HVPG decreased from 13.8±3.0 to 10.9±3.8 mmHg (Δ: -2.9±2.8 mmHg; p = 0.015) – resulting in a hemodynamic improvement of ≥10% 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±1.2 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 and showed a significant reduction in necroinflammatory activity (METAVIR A0). 8 of 14 (57%) patients with cirrhosis at baseline, presented a post-treatment histological METAVIR ≥F3. Serum transaminases were normalized after therapy (AST: 66±34 vs. 33±20, p < 0.001; ALT: 15±8 vs. 8±5, p < 0.001; AST/ALT ratio 3.4±1.5, p < 0.001), 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 necroinflammatory 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. Schwalb: received payments for lectures from Roche and Böhringer Ingelheim, and travel support from AbbVie, Gilead, Janssen, and Roche
M. Mandorfer: received honoraria for consulting from Janssen, payments for lectures from Bristol-Myers Squibb, Janssen, and Roche, as well as travel support from AbbVie, Gilead, MSD, and Roche.

B. Schemer: received travel support from Gilead.

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

K. Grabner-Pfisternhammer: received honoraria for consulting from Gilead, payments for lectures from Bristol-Myers Squibb and ViV, as well as travel support from Bristol-Myers Squibb, Gilead, and GlaxoSmithKline.

A. Fertlisch: received travel support from Gilead and Gilead.

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

M. Peck: received travel grants from Gilead, MSD, and Roche, honoraria from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, and MSD, and payments for lectures from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, and Roche.

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

All other authors have declared no conflicts of interest.

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

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Introduction: The benefits of narrow band imaging (NBI) for improving the detection of colorectal polyps remain questionable. The newly available second generation of NBI using 290 system (290-NBI) provides an additional two folds brighter image compared with the previous version. Aims & Methods: The aim of this study was to compare polyp miss rates between 290-NBI and high-resolution white light endoscopy (HR-WLE). Methods: From June 2015 to September 2015, 102 patients were randomized to undergo either HD-WLE or 290-NBI colonoscopy. In HD-WLE group, we performed colonoscopic examination as first inspection with HR-WLE followed by a second inspection with NBI. In 290-NBI group, colonoscopic examination were performed first inspection with NBI followed by a second inspection with HR-WLE. The primary outcomes were polyp miss rates. Result: A total of 127 polyps of 102 patients were detected. In HD-WLE group, 39 polyps were detected during the first inspection. A second inspection with NBI added 20 polyps, resulting in polyp miss rate of 33.9% with HR-WLE. In the NBI group, 54 polyps were detected during the first inspection. Subsequent inspection with NBI added 14 polyps resulting in polyp miss rate of NBI of 20.6% (33.9% vs 20.6%, p = 0.008). In subgroup analysis, the polyp miss rates of flat type of HR-WLE and NBI showed significant difference (18.6% vs. 5.9%, p = 0.029). 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 MICSROSATELLITE INSTABILITY PATHWAYS WITH POSTCOLONOCOPY COLORECTAL CANCer IN A RETROSPECTIVE COHORT STUDY


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Introduction: Over 50% of the postcolonoscopic colorectal cancers (PCCCRs) (i.e. CRC diagnosed after a colonoscopy that excluded cancer) originate from missed precursor lesions, in particular the subtle appearing non-polypoid (flat and depressed) adenomas and sessile serrated lesions. The biologic pathway of PCCCRs and precursor lesions is unclear. We hypothesized that PCCCRs and subtle appearing precursor lesions 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 PCCCRs diagnosed from 2001 to 2010 in a large gastroenterology practice from the Netherlands (le Clerc et al, Gut 2014). PCCCRs 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 PCCCR (incomplete colonoscopy) insufficient bowel preparation, missed lesion, incompletely resected lesion or new cancer. PCCCR's were assigned to 5 groups: (1) missed lesion (inadequate bowel preparation) (2) incomplete resection (3) new cancer (4) insufficient bowel preparation (5) 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. SMI and CIMP status were examined using the pentaplex marker panel from Promega and the Weisberger CIMP panel using methylation-specific PCR, respectively.

Result: In total, 120 PCCRCs and 10 prevalent CRCs were examined. Regarding clinicopathological features, PCCRCs are more often located proximally in the colon (p < 0.001), non-polypoid appearing (p < 0.001), early stage tumors (p = 0.008), and poorly differentiated (p = 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, 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 adenomas and sessile serrated lesions are in the origin of PCCRC.

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

Reference

OP213 MOTORIZED SPIRAL ENTEROSCOPY: A NEW TECHNIQUE FOR ONE-STAGE COMPLETE ENTEROSCOPY

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Introduction: Three different platforms have been developed to perform deep enteroscopy; namely, single balloon, double balloon, and spiral enteroscopy. None of these devices permits routine evaluation of the entire small intestine, even with a combination of antegrade and retrograde enteroscopy. We report our early clinical experience with a motorized spiral enteroscope, which may provide a modality for one-stage complete enteroscopy.

Aims & Methods: We report early experience with a prospective multi-center efficacy and safety trial. The study was approved by the institutional review boards of each of the participating centers. Patients referred for evaluation of small bowel disease at one of the three participating centers requiring antegrade enteroscopy were offered participation in the study, and then screened for exclusion criteria. If enrolled, informed consent was obtained.

endotracheal anesthesia, the motorized spiral enteroscope (SIF-Y0019, Olympus, Japan) is inserted through the mouth. The rotational advancement and withdrawal is controlled by the endoscopist using a foot pedal. The primary outcome of the study was the depth of insertion of the enteroscope.

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

Conclusion: We present our initial experience of a safety and efficacy data trial for the motorized spiral enteroscope. We were able to safely accomplish full enteroscopy in 71% of cases with a single antegrade deep enteroscopy using the motorized spiral enteroscope. This percent achievement of complete enteroscopy in a time typically reported for unidirectional deep enteroscopy suggests that this device is a significant development in design of small bowel enteroscopes. One patient experienced bleeding requiring hospitalization within 7 days of the procedure. This was a significant adverse event (SAE) by protocol. However on a further review it was determined that the patient bled from a Meckel’s diverticulum, identified during deep enteroscopy. Subsequent surgery was curative.

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

Table 1. (OP213)

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

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

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Introduction: The Aer-O-Scope Colonoscope System (GI View Ltd., Ramat Gan, Israel) is a self-propelled, joystick controllable, 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 pre-defined target of interest, a pseudo-polyp, within an ex vivo swine colon and deliver "simulated" endoscopic therapy including: polypectomy with snare or biopsy forceps, submucosal injection, or thermal coagulation using argon plasma coagulation (APC). This was a prospective cohort study (n = 12 ex vivo swine colons housed in four different models that simulated variants of a human colon). Varying sized pseudo-polyps (n = 8 in each ex vivo swine colon) were created using colored thread and were randomly distributed throughout each ex vivo swine colon. Thus, n = 96 pseudo-polyps in total were created: 1 mm–5 mm (n = 30); 6 mm–9 mm (n = 13, 14%); ≥10 mm (n = 6, 6%). Following one day of Aer-O-Scope training for joystick utilization and endoscopic therapeutic access, two endoscopists (IMG and SB) performed all the colonoscopies (n = 12 colonoscopies per each endoscopist) on three separate procedure dates, in random order, and blinded to the type of colon model. The study’s primary endpoint was a success rate of at least 90% in providing simulated endoscopic therapy and the study’s secondary endpoint was endoscopist-perceived usability of the Aer-O-Scope for endoscopic therapy. We planned on performing a total of 240 simulated endoscopic therapies (n = 192 biopsy forceps, snare polypectomy, or combination injection/snare polypectomy and n = 48 APC applications). This sample size allowed up to a 10% pseudo-polyp miss rate with a two-sided
OP215 OUTCOME OF ENDOCYTIC MUCOSAL RESECTION OF 424 LARGE SESSILE COLONIC POLYPS (≥20MM) OVER A 9 YEAR PERIOD: A SINGLE CENTRE EXPERIENCE AND ANALYSIS OF CHANGE WITH TIME

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Introduction: Endoscopic mucosal resection (EMR) has become the standard technique for resection of large sessile and flat colonic polyps. We aimed to assess the clinical outcome of colonic EMR of polyps 2 cm and greater in size at the 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 ≥20 mm removed by EMR between 2006 and 2014 by 3 endoscopists (PW, GLW, OP). 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: 154 patients were assessed for EMR, among which there were 424 completed EMRs (85% complete). SC1 was performed in 140/154 (91.4%) and SC2 in 211/234 (90.2%). Complete resection at SC1 (polyp eradication at 2nd surveillance after at least 1 year) was achieved in 138/140 (98.6%) and 95/99 (95.9%) at SC2. Complication rates were very low (9.5% at SC1 and 15.7% at SC2), with delayed bleeding in 1/424 (0.2%) and perforation in 0/424 (0%). There were no deaths or systemic complications. All patients were referred for surgical resection (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%). Piecemeal EMR was done in 381 (90%), and “en bloc” in 43 (10%). Of those who have undergone surveillance so far, recurrence was found in 56/284 (19.7%) at initial SC1 (mean 7 month; range 2–36) and was endoscopically treated in 53/56 (94.6%); 5/56 (4%) for surgical resection (2 cancer, 1 non lifting). Complete eradication after one year (SC2) was achieved in 165/165 (100%). In 65 EMR was not attempted and patients were referred for surgical resection (cancer 31, technical difficulty 34). In a further 32, EMR was attempted but abandoned; all were referred for surgery (cancer 18, benign polyp 14).

Conclusion: 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%, 64.0%, 97.5% and 72.5% respectively.

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

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 neoplastic areas allowing for earlier treatment. Although the technique of AAC is very simple, lesion recognition with acetic acid (AA) remains a challenge and therefore hampering its widespread usage.

Aims & Methods: We aim to develop a simple and easy to use classification system for AAC to allow for the 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 whitening - 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 in Table 1.

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

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%, 64.0%, 97.5% and 72.5% respectively.

Conclusion: We have developed and established the validity of a simple classification system to identify Barrett’s neoplasia using AAC. When non-AAC trained endoscopists apply these criteria, the sensitivity and NPV meet the recommended PIVI threshold.

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

OP217 STEPWISE DEVELOPMENT OF A VOLUMETRIC LASER ENDOMICSOCOPY PREDICTION SCORE FOR BARRETT’S NEOPLASIA: A USING MATCHED ANATOMIC IMAGES OF ENDOCYTIC RESECTION SPECIMENS

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

Aims & Methods: Aims of this study were to determine (additional) VLE features of neoplasia, based on precise VLE-histology correlations ex vivo, and to develop and validate a VLE prediction score for early BE neoplasia.

A unique database of VLE images from endoscopic resection specimens and histological slides of BE patients +/- neoplasia was used. Precise

Table 1: Validation results of the classification criteria

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of aceto whitening</td>
<td>96.2%</td>
<td>91.8%</td>
<td>90.9%</td>
<td>97.5%</td>
</tr>
<tr>
<td>Surface pattern</td>
<td>77.0%</td>
<td>99.0%</td>
<td>91.4%</td>
<td>96.9%</td>
</tr>
<tr>
<td>Normal</td>
<td>(69.7–83.3%)</td>
<td>(97.5–99.9%)</td>
<td>(88.4–93.9%)</td>
<td>(92.2–99.1%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>99%</td>
<td>99%</td>
<td>99%</td>
<td>99%</td>
</tr>
</tbody>
</table>

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A unique database of VLE images from endoscopic resection specimens and histological slides of BE patients +/- neoplasia was used. Precise
Aims & Methods: The blue/green range is limited by high levels of tissue autofluorescence. This mucosa (1). However in an endoscopy setting, the detection of fluorescence in

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IMAGING: AN EX-VIVO STUDY ON HUMAN TISSUE USING LECTIN-BASED NEAR INFRA-RED MOLECULAR

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

References


OP218 RESULTS OF A PROSPECTIVE MULTICENTER REGISTRY OF RADIOFREQUENCY ABLATION FOR BARRETT’S ESOPHAGUS

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2Physics, University of Cambridge, Cambridge/United Kingdom
3Histopathology, Cambridge University Hospitals, Cambridge/United Kingdom
4Physics, University of Cambridge, Cambridge/United Kingdom

Conclusion: WGA-based NIR imaging is an effective method for differentiating dysplastic from non-dysplastic Barrett’s mucosa ex vivo, which reduces the effects of tissue autofluorescence. In-vivo studies are now required to test the efficacy and potential clinical utility of this approach.

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

Reference

OP219 RESULTS OF A PROSPECTIVE MULTICENTER REGISTRY OF RADIOFREQUENCY ABLATION FOR BARRETT’S ESOPHAGUS

J. Vliebergh, P. H. Deprez2, H. Willekens1, D. De Loove3, H. Orlent4, E. Mucken5, P. Christiansen6, F. Mana7, G. De Hertogh8, R. Bischoops9
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Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

Disclosure of Interest: All authors have declared no conflicts of interest.
OP220 LONG-TERM FOLLOW-UP RESULTS OF STEPWISE RADICAL ENDOSCOPIC RESECTION FOR BARRETT’S ESOPHAGUS WITH EARLY NEOPLASIA

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Introduction: Stepwise radical endoscopic resection (SRR) allows for complete eradication of Barrett’s esophagus (BE) with early neoplasia. This approach has been shown very effective in reaching complete eradication of high-grade dysplasia (HGD) or early cancer (EC) (CE-neo) in 98% and all intestinal metaplasia (CE-IM) in 85% of patients.

Aims & Methods: The aim of this study was to report the long-term follow-up (FU) results after successful SRR for BE with early neoplasia. We screened all patients treated with SRR in two centers between 2001–2014, for BE ≤5 cm with HGD/EC, without signs of invasion. In total, 487 patients were included. Digitalized FU endoscopies and histological outcomes were collected and entered in a dedicated database. Duration of FU was calculated from last treatment till last FU endoscopy. Primary outcomes: recurrence of HGD/EC and recurrence of CE. Secondary outcomes: complications mainly strictly related to the procedure and or overtreatment.

Result: Seventy-three patients were included (64 men, mean age 66 yrs, median BE 2C2M1). Worst baseline pathology: HGD, n = 50; EC, n = 23. Median FU was 51 months; range 24–104 (IQ: 4–8) years. Recurrence of HGD/EC was observed in 1 patient (1.4%) after 129 months FU (T1N0M0 treated with curative surgery). Recurrence of CE 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 recurrence was limited to small (<1 cm) islands or tongues. Histological recurrence without visible BE was found in 25 patients: 3 patients had BB in neosquamous biopsies (4% overall, 0.7% per patient year); 24 patients (33%) showed IM in biopsies just distal to visible islands or tongues. Secondary outcomes included recurrent BE with high levels of BMP4 expression at the distal neo-z-line.

Conclusion: This study presents the longest published follow-up data on SRR to date. The long-term outcomes show that after successful SRR of BE ≤5 cm recurrence of HGD/EC is rare (1.4% overall, 0.7% per patient year). Recent developments in SRR focused on treatments specifically directed against the neo-z-line. Endoscopy (after additional treatment) was seen in 100% and 96% respectively.

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

References
5. Fennell CM, Liu D, Duong CP, et al. New anti-BMP4 antibody can induce apoptosis in tumour equilibrant xenograft model of a SMAD4 negative esophageal cancer cell line.

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

TUESDAY, OCTOBER 18, 2016 10:30–12:00
ACCURACY IN UPPER GI ENDOSCOPY – ROOM L6

OP222 PREMEDICATION WITH SINITHEMICHONE AND N-ACTYL-CYSTEINE IN DUODENUM: COMPARISON DURING UPPER ENDOSCOPY – A PROSPECTIVE DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

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Introduction: Upper endoscopy is the most common method for the diagnosis of upper gastrointestinal tract diseases. Our aim was to determine if pre-medication with simethicone or N-Acetylcysteine improves mucosal visualization during upper endoscopy.

Aims & Methods: Randomized double-blinded, placebo controlled trial of 297 patients scheduled for upper endoscopy. Pre-medication with 15–30 minutes before: A: 100-mL W of placebo; B: Water plus 100 mg simethicone; C: Water plus simethicone plus 600 mg N-acetylcysteine. Primary outcome was the quality of mucosal visualization (score: 1-excellent; 2-adequate; 3-inadequate). Percentages were compared with http://clinicaltrials.gov (NCT02357303). Statistical analysis with X2 and one-way ANOVA with Tukey’s correction.

Result: Visualization scores between groups B and C (versus A) were significantly better in the oesophagus 1.09 and 1.15 vs. 1.31 (p < 0.05) and stomach 1.26 and 1.30 vs. 1.67 (p = 0.01) and better without significance in the duodenum 1.07 and 1.09 vs. 1.20 (p = NS). “Excellent” scores versus others provided similar results (B and C vs. A): oesophagus 91% and 87% vs. 71% (p < 0.001), stomach 76% and 75% vs. 39% (p < 0.001) and duodenum 85% and 82% vs. 73% (p = NS). There was no significant effect in scores between groups B and C or C versus A: 1.45 vs. 1.68 and 1.86 (p = NS). The rate of reported lesions was higher in group B (without statistical significance).

Conclusion: Pre-medication with simethicone leads to better mucosal visualization, might improve diagnostic yield and should be considered standard practice. Addition of N-acetylcysteine had no benefit over simethicone alone.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP224 FEASIBILITY OF A COMPUTER ALGORITHM FOR DETECTION OF EARLY BARRETT’S NEOPLASIA USING VOLUMETRIC LASER ENDOMICROSCOPY

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6Dept. Of Molecular-targeting Cancer Prevention, Kyoto Prefectural University of Medicine, Kyoto/Japan

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Introduction: Accurate diagnosis of lateral extent of early gastric cancer (EGC) is important in terms of deciding treatment indication and achieving complete resection by endoscopy or surgery. Magnifying narrow band imaging (M-NBI) has been reported to increase yield of endoscopic diagnosis for determining extent of EGC.

Aims & Methods: To compare diagnostic ability of M-NBI for determining lateral extent of EGC with that of chromoendoscopy (CE). This study was conducted as a multicenter prospective randomized controlled trial including one university hospital, one cancer referral center and three general hospitals. Inclusion criteria were patients with EGC sized 1 cm or over who underwent endoscopic or surgical treatment. Exclusion criteria were history of gastric resection and high risk of bleeding for biopsy. After stratification by institution, tumor location, and histological type, patients were randomly assigned to M-NBI or CE groups. In each group, tumor extent was firstly evaluated by white light endoscopy according to difference of mucosal height and color, then the margin of the tumor was determined by the assigned method. Diagnostic criteria of M-NBI were 1) demarcation line and 2) irregular microvesse микрообластей pattern; 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.” The primary endpoint was difference of 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.

Result: A total of 382 patients were enrolled and were assigned to the M-NBI group (n = 191) and the CE group (n = 191). Eight patients in the M-NBI group and 12 in the CE group were excluded remaining 183 in the M-NBI and 179 in the CE group for analysis. Successful delineation rates (95% CI) in the M-NBI and CE groups were 86% (81–91%) and 84% (78–89%), respectively (p = 0.498).

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

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

Reference

OP225 OPTICAL ENHANCEMENT SYSTEM™ PLUS OPTICAL MAGNIFICATION UTILITY IN THE IDENTIFICATION OF NORMAL GASTRIC MUCOSA, HELICOBACTER PYLORI ASSOCIATED GASTRITIS, AND GASTRIC ATROPHY


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Introduction: It has been proposed that high-resolution zoom endoscopes (optical zoom up to 115 times) could predict gastric pit pattern for gastric pathology. Recently an image-enhanced endoscopic technology called Optical Enhancement system (OE System™) was introduced, improving visualization of microvessels. In addition to this, new high-definition zoom scopes called Magniview™ are available allowing an optical zoom up to 136 times with a better evaluation of the mucosa and superficial vascular aspects.

Aim of the study: The aim of this study was to evaluate the utility OE System™ plus Magniview™ in the diagnosis of normal gastric mucosa, Helicobacter pylori associated gastritis, and gastric atrophy. Methods: Prospective, non-randomized and double blind study. All of the participants enrolled had functional dyspepsia according to the Rome III criteria and were tested for Helicobacter Pylori (HP) using stool antigen test. After this phase two groups were selected, dyspeptic HP (+) and dyspeptic HP (-) patients (control group). Finally an upper endoscopy using OE system™ plus Magniview™ scopes was performed and the gastric body evaluated using a previously described classification of four patterns based on the combination of the parameters subepithelial capillary network (SECN), collecting venules and round pits. Type I pattern predicts normal mucosa. Type II-A) Ability to predict normal mucosa. B) Ability to predict Helicobacter pylori infection. C) Ability to predict mucosa atrophy.

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

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

<table>
<thead>
<tr>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
<th>Accuracy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>90.00 (55.50–99.75)</td>
<td>79.03 (66.82–88.34)</td>
<td>40.91 (20.70–63.65)</td>
<td>90.00 (89.35–99.95)</td>
</tr>
<tr>
<td>Type II-III</td>
<td>91.43 (76.94–98.20)</td>
<td>78.38 (61.79–90.17)</td>
<td>80.00 (64.35–90.95)</td>
<td>90.62 (74.98–98.02)</td>
</tr>
<tr>
<td>Type IV</td>
<td>66.67 (9.43–99.16)</td>
<td>88.41 (78.43–94.86)</td>
<td>20.00 (2.52–55.61)</td>
<td>98.39 (91.34–99.96)</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. (I) It is biologically 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 with the age range of 6 adults. The areas were analyzed and classified according to 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 predicted normal mucosa, type II-III HP infection, and Type IV atrophy with a sensitivity of 90%, 91% and 66.7% respectively and an accuracy of 80.5%, 84.7% and 85.7% respectively. Finally the intra and inter-observer agreement was calculated with a kappa value of 0.91 and 0.89 respectively.

**Conclusion:** endoscopy plus opacification 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 details in x-rays with computer-generated images. It is used in endoscopic procedures for guidance of the procedure. The use of RMF has so far not been evaluated for endoscopic procedures.

**Aims & Methods:** We aimed to evaluate the usefulness of Road Map Fluoroscopy to guide endoscopic interventions in the esophagus. Patients with esophageal strictures were consecutively enrolled in a monocentric observational trial. After identification of the stenosis, a Road Map (Philips Multidigita3, Phillips Healthcare, Netherlands) was performed with a water soluble radiopaque contrast agent (Urografin 370, Gastrografin,piramid). 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). MCDO provides the possibility of permanent radiographic illustration of anatomic 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 fluoroscopic images. With the help of fluoroscopy all relevant dimensions can be measured exactly. The use of RMF has so far not been evaluated for endoscopic procedures.

**Aim & Methods:** We aimed to evaluate the usefulness of Road Map Fluoroscopy to guide endoscopic interventions in the esophagus. Patients with esophageal strictures were consecutively enrolled in a monocentric observational trial. After identification of the stenosis, a Road Map (Philips Multidigita3, Phillips Healthcare, Netherlands) was performed with a water soluble radiopaque contrast agent (Urografin 370, Gastrografin piramid). 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). MCDO provides the possibility of permanent radiographic illustration of anatomic 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 fluoroscopic images. With the help of fluoroscopy all relevant dimensions can be measured exactly. The use of RMF has so far not been evaluated for endoscopic procedures.

**Conclusion:** 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). MCDO provides the possibility of permanent radiographic illustration of anatomic 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 fluoroscopic images. With the help of fluoroscopy all relevant dimensions can be measured exactly. The use of RMF has so far not been evaluated for endoscopic procedures.

**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.
Aims & Methods: Aim of the study: To investigate in detail the gastrointestinal pathology and lymphoid changes in CVID patients living in south India. Patients and Methods: Our study cohort consisted of 105 adult CVID patients followed up between 2007–2015 in Helsinki University Hospital's Adult Immunodeficiency Unit and the previous outpatient clinics of Caire and Eksote. CVID patients were diagnosed according to the German CVID diagnostic criteria and lived within the Helsinki hospital district of southern Finland (1.9 million inhabitants). Adult patients of this cohort were diagnosed from the year 1960 to 2015 when recruitment stopped. We investigated retrospectively their medical records, laboratory results, endoscopy, and histology. Methods and data were collected from an electronic database designed for the study. Of this patient cohort, 12 patients died and 11 were lost to follow up. Result: Upper endoscopy and ileo-colonoscopy were done at least once to 83 (79%) of patients, respectively. Helicobacter pylori was found in 7 patients, was negative in 74 and unknown in 23 patients. Eradication was successful in all Helicobacter-positive patients. Helicobacter-negative chronic gastritis without marked atrophy, but ranging from mild to severe inflammatory activity was found in 11 patients (11%). In 19 patients, atrophic gastritis addition, severe bile acid malabsorption was found in 10 patients (10%). 2. Small bowel: All tested patients were seronegative for coeliac disease. Of patients with increased intra-epithelial lymphocytes and villous atrophy of duodenum, 2 had complete histological and clinical response to gluten-free diet and all 4 others were responsive but had no enteroctye antibodies. 3. The patients with refractory duodenal villous atrophy and inflammation had also inflammatory changes in colon as well. 3. Hepatobiliary: Primary sclerosing cholangitis or CVID-associated cholangitis was diagnosed in 5 patients. 3. Large Bowel: Inflammatory changes of mucosa ranged from specific colitis and microscopic colitis (including lymphocytic colitis and collagen colitis) to crypt-destructive and/or graft-versus-host like severe inflammation. Crypt selective IBD-like features in colitis ulcers were identified in 5 patients (2 colectomies) and one patient had strictureing ileocolonic Crohn's disease. Altogether, inflammation of colon was more common than small bowel enteropathy and it was found in 20 patients (19%). Prior to ileocolonoscopy, bacterial and parasitic infections were ruled out by standard laboratory methods including fecal sample screening. Nodular lymphatic hyperplasia was detected from gastric mucosa to rectum, and ranged from asymptomatic enhanced ileal nodularity to major changes of the gastric and bowel mucosal appearance and function. It was relatively common finding and noted in 36 patients (34%). 4. Mortality and gastrointestinal malignancies: 12 patients died during the follow up and in 3 patients it was directly due to metastatic malignancies of gastrointestinal tract; 2 patients with gastric adenocarcinoma and one patient with rectal adenocarcinoma. One patient with colon polyp and small bowel enteropathy had been found also in other 2 patients that died due to the cardiovascular disease. Meanwhile, one patient with unspescific inflammatory nodularity of colon eventually developed caecal large B-cell lymphoma which was diagnosed, and treated successfully. Conclusion: Gastrointestinal and hepatobiliary manifestations are common among patients with CVID and the risk malignancies are increased. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP229 BILE ACID DIARRHOEA: EVIDENCE FOR LOWER SEHCAT RETENTION IN TYPE 3 PATIENTS FOLLOWING CHOLECYSTECTOMY
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Introduction: Bile Acid Diarrhoea (BAD) is an under-recognised cause of chronic diarrhea. BAD can be assessed by measuring SeHCAT retention. BAD can relate to terminal ileal lesion or desegregation (designated as Type 1), be considered as idiopathic (type 2), or be linked to other underlying conditions (Type 3). Its prevalence is increased following cholecystectomy, but the clinical profile and mechanism of action remains unclear. Methods: A prospective study evaluated SeHCAT usage across the UK (1). 3. 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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Pediatrics, MAMC & Associated LN Hospital, New-Delhi/India
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Introduction: Amino acid citrulline is a non-essential amino acid which does not enter into proteins and small intestine (gut enterocyte) is the main endogenous source of circulating citrulline in blood. Since celiac disease is thought to be a highly heterogeneous spectrum ranging from classic malabsorptive form to atypical potential or latent form. It is envisaged that citrulline could be an important metabolic 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 plasma citrulline levels in each celiac disease group and assess their predictive value and to establish a correlation between histopathological findings and the amino acid levels as a biomarkers for villous atrophy. Methods and Material: The procedure adopted for measuring plasma citrulline was Tenden 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 12.6 SD umol/L whereas the mean citrulline levels in 124 serology negative subjects (first degree relatives) was 24.3umol/L. This difference was statistically highly significant with p value of 0.0001. Correlations between biopsy grades of Subjects with their citrulline levels were established & found to be significant. For Marsh 3c grade lesions, mean citrulline levels were 5.6 ± SD umol/L. For Marsh 3b, mean citrulline levels were 15.0 ± SD 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 level was 12.8 ± SD 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 signature of initial damage of gut enterocytes in celiac disease and also when correlated with Marsh score. Citrulline estimation on dried blood spots using tandem mass spectrometry is a minimally invasive and promising test in near future which could be transferred to the remote place in the country to suggest improvement in gut enterocyte mass. Plasma citrulline estimation assures detection of potential celiac disease and may be use for monitoring of compliance and recovery in CD which is likely to be of immense benefit in the diagnosis of celiac disease and analyzing citrulline on dried blood spot by a highly sensitive test as a marker 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 mice colon.

Aims & Methods: Depletion of intracellular zinc in Caco-2 cells and mouse colon was achieved by the application of a cell permeable zinc chelator 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.

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activity were examined by a mutagenesis technique in the promoter assay and RT-PCR interference technology. The effects of TPEN on occludin and claudin-3 expression in mouse colon were also examined in combination with the calpain inhibitor.

**Result:** Intracellular zinc depletion by TPEN impaired the TJ barrier of intestinal Caco-2 cells. Increased TJ induced TJ disruption is associated with downregulation of 2 TJ proteins, occludin and claudin-3. These changes induced by TPEN were completely restored by supplemental zinc. Biolumination of cell surface proteins revealed that the zinc depletion induced the proteolysis of occludin, but not claudin-3. Occludin proteolysis was sensitive to the inhibition of calpain activity, and increased calpain activity was observed in the zinc-depleted cells. Although qPCR analysis and promoter reporter assay have demonstrated that the zinc depletion-induced claudin-3 mRNA degradation at transcriptional levels, a site-directed mutation in the egfr1 binding site in the claudin-3 promoter sequence induced loss of both the basal promoter activity and the TPEN-induced decreases. Reduced egfr1 expression by a specific siRNA also inhibited the claudin-3 expression and barrier dysfunction. Mouse colon devoid of the claudin-3 main enterin inhibitor restored the TPEN-induced decrease in occludin, but not claudin-3.

**Conclusion:** This study shows that intracellular zinc has an essential role in the maintenance of the intestinal epithelial TJ barrier through regulation of occludin proteolysis and alters barrier function of Caco-2 human intestinal epithelial layers. Dig Dis Sci 2013; 58: 77–87.

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

**References**

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

**References**
1. Finamore A, Massimi M, Conti Devirgiliis L and Mengheri E. Zinc deficien–

ciency induces membrane barrier damage and increases neutrophil transmi-
2. Wang X, Valenzano MC, Mercado JM, Zurbach EP and Mullin JM. Zinc


**Disclosure of Interest:** All authors have declared no conflicts of interest.
the composition of the microbiota, favoring species expressing high level of biota. The mechanisms by which P80 and CMC act are distinct, with P80 altering pro-inflammatory potential, indicating that at least a portion of the effects of microbiota was sufficient to drive low-grade intestinal inflammation and metabolic syndrome.

**Conclusion:** The faecal microbiota of patients with CIPO had a larger caecum size (2.39 ± 0.2 cm3 vs. 1.56 ± 0.22 cm3, p < 0.003) compared to control microbiota colonized mice. Bacterial genes related to bile acid metabolism and deconjugation were differentially expressed in the faeces of patients with CIPO compared to control microbiota colonized mice. GI symptoms, overall health and quality of life were assessed using standardized questionnaires.

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

**Reference**
surgery and of endoscopy (performed at 6 months). Bacterial composition of the ileal mucosa associated microbiota was analyzed at time of surgery using 16S (DAPI staining). The obtained sequences (rarefied 4500 read/sample) were analyzed using the QIIME pipeline to assess composition, alpha and beta diversity. Bacterial taxa associated with clinical parameters were identified using Multivariate association with Linear Models (MaAsLin) taking into account gut phenotype, clinical parameters and treatments.

**Result:** 146 patients were included: 73 (50%) were male, median age at surgery was 32 years (IQR 26–42). Median disease duration was 6 years (IQR 2–12). 44 patients (30%) were active smoker at time of surgery. Thirty patients (21%) had a previous resection, and 35 patients (24%) had perianal lesions. Indication for surgery was stricture disease (n = 95), penetrating disease (n = 53). At time of surgery, 67 patients (46%) had received anti-TNF therapy within the last 3 months. After surgery, 31 patients received thiopurines, and 52 patients received anti-TNF therapy. The microbiota was mainly composed of bacteria from the Firmicutes (Mean 55%, range 0.3–99%), Proteobacteria (Mean 36%, range 0.5–99%), Bacteroidetes (Mean 5%, range 0–52%) and Actinobacteria (Mean 6%, range 0–81%) phyla. As expected, antibiotics treatment within one-month before surgery had a dramatic impact on microbiota composition (Anosim, p < 0.0001) and diversity (mean observed species: 302 ± 17 vs 236 ± 14, p = 0.0005). In multivariate analysis (MaAsLin), antibiotics treatment was notably associated with an increased abundance of Enterococcus sp. (q = 0.001) and with a decrease in Lachnospiraceae family (q = 0.004). Taking into account only the patients who did not received antibiotics within a month before surgery, we then looked for predictive factors of endoscopic recurrence. Patients with endoscopic recurrence, defined by a Rutgeerts score, had a lower bacterial diversity at time of surgery compared to patients in endoscopic remission (n = 65) (mean observed species: 276 ± 14 vs 365 ± 45, p = 0.015).

**Conclusion:** ileal mucosa associated microbiota of CD patients at time of surgery is dominated by bacteria belonging to Firmicutes, Proteobacteria, Bacteroidetes and Actinobacteria phyla. Antibiotics given during the last month prior to surgery induce major perturbations of the microbiota. Reduction in bacterial diversity at time of surgery is predictive of endoscopic recurrence.

**Disclosure of Interest:** H. Sokol: Consulting fee: danone, Roche, Enterome, induce major perturbations of the microbiota. Reduction in bacterial diversity at time of surgery was 32 years (IQR 26–42). Median disease duration was 6 years (IQR 2–12). 44 patients (30%) were active smoker at time of surgery. Thirty patients (21%) had a previous resection, and 35 patients (24%) had perianal lesions. Indication for surgery was stricture disease (n = 95), penetrating disease (n = 53). At time of surgery, 67 patients (46%) had received anti-TNF therapy within the last 3 months. After surgery, 31 patients received thiopurines, and 52 patients received anti-TNF therapy. The microbiota was mainly composed of bacteria from the Firmicutes (Mean 55%, range 0.3–99%), Proteobacteria (Mean 36%, range 0.5–99%), Bacteroidetes (Mean 5%, range 0–52%) and Actinobacteria (Mean 6%, range 0–81%) phyla. As expected, antibiotics treatment within one-month before surgery had a dramatic impact on microbiota composition (Anosim, p < 0.0001) and diversity (mean observed species: 302 ± 17 vs 236 ± 14, p = 0.0005). In multivariate analysis (MaAsLin), antibiotics treatment was notably associated with an increased abundance of Enterococcus sp. (q = 0.001) and with a decrease in Lachnospiraceae family (q = 0.004). Taking into account only the patients who did not received antibiotics within a month before surgery, we then looked for predictive factors of endoscopic recurrence. Patients with endoscopic recurrence, defined by a Rutgeerts score, had a lower bacterial diversity at time of surgery compared to patients in endoscopic remission (n = 65) (mean observed species: 276 ± 14 vs 365 ± 45, p = 0.015).

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**Disclosure of Interest:** H. Sokol: Consulting fee: danone, Roche, Entenerima, Maat, MSD, Astellas

All other authors have declared no conflicts of interest.

**Reference**

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

### Op238 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 etiology of the disease 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), inflammatory cytokines and proteins 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, resulting in PAMP misrecognition, a mechanism for dysbiosis and CCA). 3) Liver biopsy suggestive of PSC, or documentation of diagnosis of PSC due to: 1) constantly elevated or fluctuating 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 ERC and before injecting contrast media a bile aspirate was sampled from extrahepatic bile ducts using balloon catheter, whenever possible. Brush cytology was routinely performed during ERC. ERC findings were scored according to the modified Amsterdam score (mAn 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, microbial diversity decreases in long progression and further more in dysplasia/CCA.

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

**References**


The microbiota is considered important for development of intestinal diseases. In order to create a molecular snapshot of IBD in its early manifestation, one part of the IBD-Character project identified faecal microbiota profiles among the strictly treatment-naive IBD and symptomatic non-IBD patients, and a healthy control group.

**Aims & Methods:** Patients were characterized by international criteria including endoscopy and biopsies. Faecal samples collected during five days prior to diagnosis were stored at -80°C for examination on GA-map® Dysbiosis Test (1) and used for DNA extraction and analysis. The细菌 profiles of IBD, non-IBD and control groups were compared.

**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  [18%]</td>
<td>7  [16%]</td>
<td>11 [18%]</td>
<td>4 [31%]</td>
<td>21 [17%]</td>
<td>27 [56%]</td>
<td>2 [100%]</td>
</tr>
<tr>
<td>Low</td>
<td>96</td>
<td>33 (19-66)</td>
<td>49</td>
<td>33  [28%]</td>
<td>14 [31%]</td>
<td>15 [24%]</td>
<td>4 [31%]</td>
<td>50 [40%]</td>
<td>13 [27%]</td>
<td>0</td>
</tr>
<tr>
<td>High</td>
<td>126</td>
<td>32 (18-69)</td>
<td>80</td>
<td>65  [54%]</td>
<td>24 [53%]</td>
<td>36 [58%]</td>
<td>5 [38%]</td>
<td>53 [43%]</td>
<td>8 [17%]</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>294</td>
<td>172</td>
<td>40</td>
<td>120</td>
<td>4</td>
<td>62</td>
<td>13</td>
<td>124</td>
<td>48</td>
<td>2</td>
</tr>
</tbody>
</table>

**Conclusion:** This study confirms that IBS patients have increased faecal levels of chromogranins in the lumen. Aims & Methods: The aim of the current study was to study microbiota localization in human subjects with metabolic syndrome. Subjects were enrolled at the Veterinary 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 mucus. Dysbiosis status was significantly reduced (p < 0.05) and E1 (n = 22) patients clustered together, while the combined group of E2 (n = 20) and E3 (n = 23) patients were a separate cluster. Among 10 bacteria groups contributing to the clustering we looked into three of the groups in details: Bifidobacterium and Escherichia were significantly reduced (p < 0.01), and Escherichia/Proteobacteria were significantly increased (p < 0.01) in the E2/E3 group as compared to E1. A positive correlation was observed among the healthy individuals was higher than observed in other studies (1).

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


**OP240 METABOLIC SYNDROME CORRELATES WITH MICROBIOTA ENCROACHMENT 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 mucosal encroachment of the epithelium, as a consequence of an innate immune deficiency or ingestion of substances that alter host-microbiota interactions, promotes low-grade inflammation that can drive metabolic disease (1-2).

**Aims & Methods:** The aim of the current study was to study microbiota localization in human subjects with metabolic syndrome. Subjects were enrolled at the Veterinary 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 mucus. Dysbiosis status was significantly reduced (p < 0.05) and E1 (n = 22) patients clustered together, while the combined group of E2 (n = 20) and E3 (n = 23) patients were a separate cluster. Among 10 bacteria groups contributing to the clustering we looked into three of the groups in details: Bifidobacterium and Escherichia were significantly reduced (p < 0.01), and Escherichia/Proteobacteria were significantly increased (p < 0.01) in the E2/E3 group as compared to E1. A positive correlation was observed among the healthy individuals was higher than observed in other studies (1).

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

**References:**

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><strong>Actinobacteria</strong></td>
<td><strong>Collinsella</strong></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><strong>Bacteroidetes</strong></td>
<td><strong>Prevotella_9</strong></td>
<td>72(6, 1813)a</td>
<td>17(1, 9272)</td>
<td>41(6, 5677)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Alistipes</strong></td>
<td></td>
<td>434(131, 1064)b</td>
<td>155(13, 467)a</td>
<td>75(970, 849)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Barnesiella</strong></td>
<td></td>
<td>35(0, 217)b</td>
<td>3(0, 45)</td>
<td>23(0, 142)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Butyriviriosmas</strong></td>
<td></td>
<td>22(4, 80)b</td>
<td>5(0, 15)</td>
<td>90(9, 49)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Parabacteroides</strong></td>
<td></td>
<td>242(152, 683)b</td>
<td>108(45, 245)a</td>
<td>225(145, 538)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Paraproteobacteria</strong></td>
<td></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><strong>Odoribacter</strong></td>
<td></td>
<td>35(1, 88)b</td>
<td>5(0, 47)</td>
<td>33(1, 73)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Firmicutes</strong></td>
<td><strong>Fusobacterium</strong></td>
<td>3387(1778, 6294)b</td>
<td>217(449, 4175)</td>
<td>2860(1290, 4699)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Pseudobutyriovibrio</strong></td>
<td></td>
<td>352(124, 5860)b</td>
<td>124(261, 3630)</td>
<td>191(1163, 3133)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Subdoligranulum</strong></td>
<td></td>
<td>1101(621, 2182)b</td>
<td>544(77, 1660)</td>
<td>124(3136, 1062)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Lachnospiraceae_NKAA136</strong></td>
<td></td>
<td>234(02, 672)b</td>
<td>85(22, 468)a</td>
<td>406(169, 1446)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Eubacterium_coprostanoligenes</strong></td>
<td></td>
<td>19(76, 571)b</td>
<td>90(3, 197)</td>
<td>139(10, 810)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Ruminococcus_1</strong></td>
<td></td>
<td>145(35, 523)b</td>
<td>7(1, 111)a</td>
<td>29(4, 136)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Eubacterium_hallii</strong></td>
<td></td>
<td>313(132, 636)b</td>
<td>118(44, 367)</td>
<td>141(61, 620)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Christensenellaceae-R7</strong></td>
<td></td>
<td>104(4, 209)b</td>
<td>8(1, 81)</td>
<td>616(357)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus</strong></td>
<td></td>
<td>7(3, 13)</td>
<td>11(4, 30)</td>
<td>3(0, 16)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Family_XIII</strong></td>
<td></td>
<td>18(2, 28)b</td>
<td>3(0, 16)</td>
<td>15(3, 41)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Incercet_Sedis</strong></td>
<td></td>
<td>156(54, 426)b</td>
<td>53(10, 267)</td>
<td>77(15, 515)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Lachnospiraceae_NC2004</strong></td>
<td></td>
<td>25(7, 60)a</td>
<td>162(37)</td>
<td>13(2, 28)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Lachnospiraceae</strong></td>
<td></td>
<td>1020(595, 1971)b</td>
<td>598(289, 1131)</td>
<td>863(409, 2223)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Romboutsia</strong></td>
<td></td>
<td>86(15, 201)b</td>
<td>156(46, 478)</td>
<td>127(40, 284)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Ruminococcaceae</strong></td>
<td></td>
<td>96(837, 1803)b</td>
<td>32(85, 903)a</td>
<td>804(266, 1183)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Proteobacteria</strong></td>
<td><strong>Escherichia_Shigella</strong></td>
<td>49(31, 471)b</td>
<td>336(65, 1458a)</td>
<td>270(21, 216)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Kleibiosa</strong></td>
<td></td>
<td>43(4, 130)b</td>
<td>106(11, 494)</td>
<td>401(173)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Raoultella</strong></td>
<td></td>
<td>7(3, 11a)</td>
<td>11(4, 30)</td>
<td>20(9)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Sutterella</strong></td>
<td></td>
<td>7(1, 136)</td>
<td>20(5, 7)</td>
<td>50(4, 163)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Indication: IBS-P, IBS with SIBO; IBS-N, IBS without SIBO; HC, healthy controls; NS, no significance; a, compared with HC, p < 0.05; b, compared with IBS-N, p < 0.05

OP241 CLINICAL FEATURES AND FECAL MICROBIOTA PROFILE IN IRITRIBILE BOWEL SYNDROME PATIENTS WITH SMALL INTESTINAL BACTERIAL OVERGROWTH

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Introduction: Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder, but the relationship between diarrhea-predominant IBS (IBS-D) and small intestinal bacterial overgrowth (SIBO) is unclear.

Aims & Methods: We aimed to investigate the clinical features and fecal microbiota profiles of IBS-D patients with SIBO by hydrogen and methane 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 in 6-hour urine], systematic inflammation severity (IL-10, IL-12 and IL-10/IL-12) and psychological parameters and fecal microbiota profile, so IBS-P may be just SIBO which should be screened before diagnosis of IBS-D according to Rome II criteria.

Conclusion: (1) According to Rome II criteria, approximately 41.67% IBS-D patients present SIBO, which can be better screened by hydrogen and methane LB. (2) SIBO can cause malnutrition and worsen nutritional status. (3) The intestinal permeability, systemic 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-D 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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2 Microbiology, Agostino Gemelli Hospital Dept of Microbiology, Rome/Italy
3 Public Health, Academic Medical Centre, University of Amsterdam, Amsterdam/Netherlands
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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.

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United European Gastroenterology Journal 4(5S)
To perform the study, we identified a 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 rCDI in our Centre. Demographic, clinical, endoscopic, and follow-up data were collected. Repeat fecal infusions were administered if the partial or full resolution of disease did not occur after first infusion. Gender, age, patient 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 all candidate predictors of faeces were analysed as potential impact factors. Multivariate associations were investigated using logistic regression analysis. P-values of <0.05 were considered statistically significant.

**Result:** A total of 54 patients with rCDI (Males = 24; mean age = 71 years old, range = 29-94) received FMT from healthy donors by colonoscopy. Fifteen patients received triple infusions, for a total of 84 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 repeated infusion was more common among patient who experienced a number or CDI recurrences higher than 3 than among those who did not, although without reaching statistical significance (OR = 26.80; 95% CI: 1.69–1000; p = 0.054). The large confidence interval observed for most predictors could be explained presumably by the relatively low number of cases in our sample. Finally, the infusion of frozen material was significantly associated with lower need of multiple FMT (OR = 0.01; 95% CI: 0.0–0.19; 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 repeated fecal infusions. Additionally, freezing FMT appears to be significantly associated with a decreased need of multiple FMT. As the small sample size represents a limitation of our analysis, our findings, although promising, should be confirmed by further, larger studies.

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

**References**


**TUESDAY, OCTOBER 18, 2016 14:00–15:30 ENDOSCOPIC TREATMENT OF COMPLICATIONS AFTER UPPER GI SURGERY – ROOM E2**

**OP243 ENDOSCOPIC BALLOON DILATION FOLLOWED BY STEROID INJECTION IN ANASTOMOTIC STRICTURES AFTER ESOPHAGECTOMY: A MULTICENTER RANDOMIZED, DOUBLE-BLIND CONTROLLED TRIAL**

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

**Aims & Methods:** We conducted a multicenter randomized controlled trial to evaluate the usefulness of administration of local steroid injections to prevent the recurrence of anastomotic stricture. Patients were randomized to receive either triamcinolone or placebo immediately after EBD. The primary endpoint was the number of 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 or death from any cause. Patients with a dysphagia symptom score of two or more after esophagectomy with anastomotic stricture confirmed by endoscopy were included. Patients and investigators were blinded to the type of agent injected. The syringe containing triamcinolone or placebo was prepared by nursing staff unconnected to the trial. Patients underwent EBD with a standard through-the-scope balloon dilator. The balloon was inflated with water, aiming for a luminal diameter of maximum 15 mm for 3 min. After EBD, a second endoscopist who was not involved in the follow-up evaluation of the patient performed the injections into the basilar laceration. A total of 30 mg of triamcinolone acetate (50 mg/5 mL; Bristol-Myers Squibb) or an identical volume of normal saline solution as a placebo was injected per single site using a 25-gauge needle. Neither the patient nor the treating physician knew which treatment was given.

**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 (range, 1–29) 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 authors have declared no conflicts of interest.

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

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

**Aims & Methods:** From January 2014 to April 2016 we performed a prospective bi-centre case series of consecutive "tunnel + clip" oesophageal ESDs. Four young operators (fewer than 50 ESDs and fewer than 5 oesophageal ESDs) performed consecutively the ESD using the tunnel + clip method: generation of a classic tunnel beneath the lesion followed by constant counter-traction thanks to a clip with line dropped at the oral side of the tunnel.

**Results:** Thirty-three lesions (14 SCC and 19 AD/HGD complicating Barrett’s oesophagus) were resected consecutively. En bloc, R0 and curative resection rates were 100% (33/33), 87.8% (29/33) and 75.8% (25/33), respectively. No perforation occurred. The mean speed of ESD was 22.3 mm²/min for a mean lesion size of 61.6 mm. The clip provided considerable assistance in performing the procedure. No pathological damage caused by the clipping was reported.

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

**References**


Aims & Methods: The present study was aimed to validate the efficacy of the latest CAD model for endoscopy (380-fold ultra-magnifying endoscopy) in management of diminutive, rectosigmoid polyps.

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

References
measured the result is instantly sent to a webserver (IBDoc® Portal) allowing the travellers 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 (BÜHMANN [CAL® ELISA]) IBDoc® correlated very well with both methods with a mean bias below 0% in both regard to repeatability and precision 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/g mean bias at cut-off, –7.0 to 5.4%) Moderate/amber (100–300 µg/g) and as High/red (above 300 µg/g, mean bias at cut-off, 1.1–6.5%). No false positive or false negative results (Normal/green instead of High/red and vice versa) were observed when lay-users performing the test were compared to professional users, a 97% 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 health care providers and continues well to existing calprotectin point-of-care and laboratory based methods and has proven to be a supportive tool in daily clinical routine.

Disclosure of Interest: Reinhard: Christian Reinhard is an employee of BÜHMANN Laboratories AG

A. Ritz: Alice Ritz is an employee of BÜHMANN Laboratories AG

M. Überschlag: Marie-Eve Überschlag is an employee of BÜHMANN Laboratories AG

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

All other authors have declared no conflicts of interest.

References
1. Beyer et al., Usability Study of a Smartphone-Based Calprotectin Home Test, UEGW 2015.

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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Introduction: Telendoscopy 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 Monitor IBD At Home questionnaire (MIAH) (1). The score does not include validated against endoscopy. For this reason we previously developed the MIAH+ (1) and evaluated its’ prognostic value (2). The objective of this study was to (a) prospectively compare the MIAH and MIAH+ with existing standard-of-care methods, (b) to determine the percentage of patients with 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 health care providers and continues well to existing calprotectin point-of-care and laboratory based methods and has proven to be a supportive tool in daily clinical routine.

Disclosure of Interest: Reinhard: Christian Reinhard is an employee of BÜHMANN Laboratories AG

A. Ritz: Alice Ritz is an employee of BÜHMANN Laboratories AG

M. Überschlag: Marie-Eve Überschlag is an employee of BÜHMANN Laboratories AG

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

All other authors have declared no conflicts of interest.

References
1. Beyer et al., Usability Study of a Smartphone-Based Calprotectin Home Test, UEGW 2015.
serological markers with the biochemical markers C-reactive protein (CRP), eleetrochemical salivation 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 (Protermus 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 treatment. 

Result: Among the UC patients, 13 (72%) were perianal arthritis- neutrophil cytoplasmic antibody (pANCA) positive, versus 13 (35%) of the CD patients. None of the UC patients harbored anti-Saccharomyces cerevisiae (ASCA) antibodies, whereas 17 (32%) of CD patients were ASCA IgA or IgG positive (p < 0.0001). 18 (49%) were positive for ASCA IgA, 14 (38%) for ASCA IgG, and 12 (33%) for both. There were statistically significant differences between CD and UC patients in the prevalence of antibodies against *Pseudomonas fluorescens* associated with Crohn’s disease (33%), *Escherichia coli* (OmpC) (8% vs. 6%) or flagellin expressed by *Clostridial phyrum* (22% vs. 0%, respectively). The 18 (49%) CD patients who received aggressive therapy with TNF blockers had higher presence of antibodies against ASCA IgA (p = 0.005) and ASCA IgG (p = 0.045) as well as higher titers of ASCA IgG (p = 0.046) compared to the 19 (51%) CD patients who received conventional treatment. If ASCA antibodies were present at baseline the probability of receiving infliximab treatment in 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 5.8 (1.3-25.0) CD patients with UC having 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) 1506 vs. 501 (p = 0.01), CRP (mg/l) 28 vs. 7.5 (p = 0.02) and ESR (mm/h) of 32 vs. 18 (p = 0.01) respectively. Being pANCA negative and/or ASCA IgA positive was associated with the need for TNF blocker therapy, even after adjustment for CRP, ESR and calprotectin levels. After treatment there was no difference in antibody prevalence for ASCA IgA, ASCA IgG, 12, QuantiFecal and UC patients who switched from treatment of less aggressive therapy to more aggressive therapy. Fewer UC patients, 9 (64%), tested positive for pANCA after treatment, compared to baseline, 13 (72%), p = 0.013. Only one of the 18 UC patients received TNF blocker treatment.

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

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

References:

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

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Introduction: Fecal calprotectin (fcalpro) for Inflammatory Bowel Disease (IBD) could be 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 shown to be of independent prognostic value in IBD patients. The aim 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/remission, 42/32 vs. 18 (p = 0.0001). The presence of ASCA antibodies was less frequent at diagnosis in fewer UC patients, 9 (64%), tested positive for pANCA after treatment, compared to baseline, 13 (72%), p = 0.013. Only one of the 18 UC patients received TNF blocker treatment.

Conclusion: ASCA and pANCA status was associated with the need for early aggressive therapy with TNF blockers in our CD patients. We found that being pANCA negative and/or ASCA IgA or ASCA IgG positive were more predictive of needing aggressive treatment than CRP, ESP or fecal calprotectin levels. As calprotectin is a valuable, regardless of treatment modality, and might be a prognostic tool at any time in the disease course. 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, 42/32 vs. 18 (p = 0.0001). The presence of ASCA antibodies was less frequent at diagnosis in fewer UC patients, 9 (64%), tested positive for pANCA after treatment, compared to baseline, 13 (72%), p = 0.013. Only one of the 18 UC patients received TNF blocker treatment.

Conclusion: The QuantOnCal system produces a quantitative test result between 25-2000 mg/g fcalpro of stool, covering the clinically relevant range of this biomarker, in 15 minutes. 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 Inmunnodiagnostik AG, Bensheim, Germany. J. Stein: Jürgen Stein has received payment for lectures and consultancy from Inmunnodiagnostik AG, Bensheim, Germany.
TUESDAY, OCTOBER 18, 2016 14:00–15:30

OP253 RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF BIOFEEDBACK FOR THE TREATMENT OF ABDOMINAL DISTENTION

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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 previous 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 abdomino-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 a referral center (Clinical Trials Gov Registration Number 01250150). Forty-one patients complaining of episodes of visible abdominal distension who fulfilled the Rome III criteria for functional intestinal disorders (47 women, 1 men; 21–74 yr 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. Improvement of abdomino-thoracic activity was quantified by electromyography. 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 increase anterior wall muscle activity (by 101 ±%10 vs −4 ±%2). Biofeedback treatment resulted in a 56% ±%1 reduction of abdominal distension (from 4.6 ±%2 to 2.0 ±%2 score after intervention) vs 13 ±%8 on placebo; p < 0.001 (from 4.7 ±%1 to 4.1 ±%4 score after intervention).

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

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

Result: IBS symptoms consistently and significantly improved after 3 weeks of LFD, with a mean overall reduction of 16.8± points (p < 0.001). On average, 4 of 5 symptoms were significantly worsened in response to FOS compared with placebo, with an overall difference of 65.1± points (p = 0.014). Serum levels of IL-6 and IL-8, but not TNF-α, significantly decreased on the LFD (p = 0.01 and p < 0.001, respectively). The microbial composition applied to luminal microbiota (Bacteroides, Bifidobacterium) decreased (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 normalised 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 expand the link between FODMAPs, gut microbiota and immune activation.

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

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

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Introduction: The reduction of potentially fermentable carbohydrates collectively termed FODMAPs (fermentable oligo-, di-, mono-saccharides 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 and require further research.

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

Results: Adequate symptom relief was achieved in 81% of the 580 FGID patients, with a response rate of 80% in patients presenting with IBS-D (95% CI; 2.96 (1.83–4.79) and 2.50 (1.74–4.22), 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 diarrhea (positive predictor: 2.74 (1.32–4.94, p = 0.001)) and nausea (negative predictor: 0.35 (0.16–0.75), p = 0.02). 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 diarrhea during breath testing (univariate 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 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.

OP256 A RANDOMIZED Triple Blind Controlled Trial Assessing the Effects of Doxepin and Nortriptyline on Diarrhea-Predominant Irritable Bowel Syndrome

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Introduction: Tricyclic antidepressants tend to be constipating and, therefore, may be of most benefit in diarrhea-predominant IBS (IBS-D). The aim of this study was to compare the effects of low doses of doxepin and nortriptyline on IBS-D.

Aims & Methods: Seventy-five patients with IBS according to Rome III criteria were treated for two months. All possible organic diseases responsible for bowel symptoms were excluded. The patients were randomly assigned to one of three groups treated with doxepin (10mg), nortriptyline (10mg) or placebo. Subjects were assessed clinically weekly. The symptoms and adverse effects of the drugs were recorded in the questionnaire. The primary outcome was the responder rate for treatment at the end of treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.
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 therapy, 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 maintain adequate clinical response over 6 months. 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>Treatments</th>
<th>n (%)</th>
<th>Placebo (n = 809)</th>
<th>ELX 75 mg BID (n = 808)</th>
<th>ELX 100 mg BID (n = 806)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate relief: Weeks 1–4</td>
<td>101 (12.5)</td>
<td>708 (87.5)</td>
<td>814 (22.8)</td>
<td>198 (24.6)</td>
</tr>
<tr>
<td>Adequate relief: Weeks 1–12*</td>
<td>78 (77.2)</td>
<td>23 (22.8)</td>
<td>150 (81.5)</td>
<td>34 (18.5)</td>
</tr>
<tr>
<td>Adequate relief: Weeks 1–26*</td>
<td>67 (66.3)</td>
<td>34 (33.7)</td>
<td>136 (73.9)</td>
<td>48 (26.1)</td>
</tr>
<tr>
<td>Adequate relief: Weeks 1–4</td>
<td>399 (49.3)</td>
<td>410 (50.7)</td>
<td>484 (59.9)</td>
<td>324 (40.1)</td>
</tr>
<tr>
<td>Adequate relief: Weeks 1–12*</td>
<td>329 (82.5)</td>
<td>70 (17.5)</td>
<td>405 (83.7)</td>
<td>79 (16.3)</td>
</tr>
<tr>
<td>Adequate relief: Weeks 1–26*</td>
<td>278 (69.7)</td>
<td>121 (30.3)</td>
<td>341 (70.5)</td>
<td>143 (29.5)</td>
</tr>
</tbody>
</table>

BID, twice daily; ELX, eluxadoline

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

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

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Introduction: Eluxadoline (ELX), a mixed μ-opioid receptor (OR) and δ-OR antagonist that is locally active in the gastrointestinal tract, is approved for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults. In two Phase 3 studies, ELX significantly improved symptoms of IBS-D based on a composite endpoint, defined by simultaneous improvement in stool consistency 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 trials. 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), stool consistency (Bristol Stool Scale [BSS]), and quality of daily life on a 0–10 scale. The primary efficacy endpoint was composite response, based on simultaneous daily improvement of ≥30% in WAP score versus baseline and BSS score <5, with ≥50% of days demonstrating a response, evaluated over 12 and 26 weeks. Composite response rates over Weeks 1–12 and 1–26 were calculated for patients who were responders and non-responders over Month 1 (Weeks 1–4) using a pooled analysis of the intent-to-treat (ITT) population. Comparable analyses for adequate relief were conducted, for which a responder was defined as reporting a “yes” response to the question “Over the past week have you had adequate relief of your IBS symptoms?” for ≥50% of weeks in the treatment interval.

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

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

OP259 HUMAN PLURIPOTENT STEM CELL-DERIVED EXOCRINE/DUCTAL ORGANOGENS 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.

References


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

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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 (PanN), (ii) mucinous cystic neoplas (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 controls from a cohort of Fukuoka-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.

References

INTESTINAL FAILURE: FROM PATHWAYS TO TREATMENT – ROOM LT

OP262 NOVEL GENE MUTATIONS IN NEUROGENIC CHRONIC INTESTINAL OBSTRUCTION

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Introduction: Chronic intestinal pseudo-obstruction (CIO) 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 CIO. 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 CIO patients associated with peripheral small fiber neuropathy (SFN), a condition affecting peripheral neurons including those of the autonomic system. Whole exome sequencing (WES) was performed on genomic DNA of n=6 patients (3 trios and 3 sporadic cases) with clinical, radiological and manometry abnormalities associated with peripheral small fiber neuropathy. A neurological work-up established SFN in 3 of them. Libraries were enriched with the Nimblegen SeqCap EZ v3.0 and mined. Thus, the objective of our study was to decipher the PAR pharmacology in human sensory neurons. In contrast to PAR2 and PAR4, PAR1 activation causes calcium mobilization. Thrombin (PAR1 and PAR4 agonist) but not trypsin (PAR3 and PAR2 agonist) increased calcium flux in human sensory neurons. PAR2-AP, PAR4-AP and PAR-IP did not cause calcium mobilization. Thrombin (PAR1 and PAR4 agonist) increased calcium flux in human sensory neurons. PAR-IP-induced calcium mobilization was significantly reduced by pre-incubation with PAR4-AP, but not with PAR3-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 PAR2 and PAR4, PAR1 activation increased calcium increase in human sensory neurons. PAR2 activation reduced calcium mobilization. Thus, in human sensory neurons PAR1 play an important role in neuronal activation and may be relevant in IBS research.

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

Reference

OP263 PROTEASE SIGNALING IN HUMAN SENSORY NEURONS

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Introduction: IBS is a functional bowel disorder characterized by abdominal pain, alteration of bowel habit and/or diarrhea. Among the mediators studied in IBS, increased colonic proteolytic activity appears as a common feature in all IBS sub-groups. Through Protease-Activated Receptors (PARs) activation, proteases can activate primary afferents and act on visceral pain pathways in rodents, but the relevance of PAR activation in human sensory neurons still has to be determined. Thus, the objective of our study was to decipher the PAR pharmacology in human sensory neurons.

Aims & Methods: Cryo-protected or fresh human thoracic dorsal root ganglia (DRG) were obtained from the national disease resource interchange (NDRI). Expression of PAR1, PAR2 and PAR4 was studied on slices of DRG (DRG T12, n=3) by co-staining immunochemistry with a pan-neuronal marker (ppp9.5) and PAR antibodies. Calcium signaling responses to PAR1-AP (100 pM), PAR2-AP (100 nM) and PAR4-AP (100 pM) in DRG neurons were measured using the confocal laser scanning microscope. Significant differences were compared using ANOVA test.

Conclusion: The study shows that PAR signaling is involved in pathological conditions of sensory neurons, such as IBS. Indeed, PAR1-AP evoked calcium increases in DRG T12, which suggests that PAR1 activation may be important in IBS mechanisms.

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

Reference

OP264 DIFFERENTIAL BASAL CHARACTERISTICS IN SHORT BOWEL SYNDROME DUE TO VASCULAR CATASTROPHES ARE ASSOCIATED WITH VARYING RESPONSE TO TEGDULITIDE TREATMENT: POST HOC ANALYSIS

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Introduction: Vascular catastrophes are an underlying condition for massive intestinal resection and failure associated with short bowel syndrome (SBS-IF). This post hoc analysis of data reported in patient e-case forms compared baseline characteristics of patients with SBS-IF due to vascular catastrophes (SBS- Vasc) vs patients with nonvascular causes of SBS-IF (SBS-non-Vasc), including the clinical response to tegdulitide (TED). STEPS (NCT00789967; EudraCT2008-006193-15) was a 24-week, placebo (PBO)-controlled study of TED 0.05 mg/kg/day in patients with SBS-IF. Response was defined as ≥20% reduction from baseline in weekly parenteral support (PS) volume at Week 20 that was maintained at Week 24. Vascular catastrophes were intestinal ischaemia or mesenteric vessel thrombosis or embolism.

Methods: Summary statistics are presented with standard deviations (SD) or 95% confidence intervals (CI); this post hoc analysis was not powered for statistical significance.

Results: The patient characteristics for the SBS-Vasc (n=32) and SBS-non-Vasc (n=35) groups were detailed in the Table. The reason for the majority of the intestinal resections was Crohn’s disease (SBS-non-Vasc) or mesenteric vessel thrombosis or emboli (SBS-Vasc). At baseline, more SBS-Vasc patients were older (55 vs 48 years) and male (53% vs 41%) than SBS-non-Vasc patients. SBS-Vasc patients had shorter small bowel length (55 vs 92 cm), were more likely to have colon-in-continuity (78% vs 43%), and were less likely to have stoma present (19% vs 61%) compared with SBS-non-Vasc patients. SBS-Vasc patients received more colostomies (14.1 vs 0.5/mo) compared with SBS-non-Vasc patients. After 24 weeks, 53% (CI, 27%–79%) of SBS-Vasc patients and 70% (CI, 50%–86%) of SBS-non-Vasc patients were responders to TED. In the PBO groups, 35% (CI, 14%–62%) of SBS-Vasc patients and 27% (CI, 11%–48%) of SBS-non-Vasc patients met the response criteria. In the TED groups, reduction in mean PS volume (change and percentage change) took longer in the SBS-Vasc group (Week 12: 1.9 [CI, 0.3–3.5], 12% [CI, 3%–20%]; Week 24, 3.6 [CI, 1.5–5.7], 25% [CI, 15%–35%]) compared with the SBS-non-Vasc group (Week 12: 4.0 [CI, 2.0–5.9], 24% [CI, 16%–33%]; Week 24: 5.5 [CI, 3.4–7.6], 36% [CI, 29%–43%]). The overall TED safety profile was generally similar between the 2 groups. Specifically, >15% of SBS-Vasc patients reported abdominal pain, dyspepsia, fatigue, nausea, and peripheral oedema, whereas >15% of SBS-non-Vasc patients reported nausea, abdominal distension, abdominal pain, stoma complication, and peripheral oedema.

Conclusion: To our knowledge, this post hoc analysis is the first to compare baseline characteristics and response to treatment in patients with SBS resulting from vascular catastrophes and nonvascular diseases. In this group of patients, SBS-IF patients with vascular catastrophes were more likely to have colon-in-continuity, less likely to have stoma present, and had less baseline PS volume than in patients with nonvascular causes of SBS-IF. SBS-IF patients with vascular catastrophes took longer to respond to tegdulitide in the observed PS volume reduction.

Table: Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SBS-Vasc (n=17)</th>
<th>PBO (n=26)</th>
<th>TED (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>56.6 (13.3)</td>
<td>52.3 (13.5)</td>
<td>45.2 (15.3)</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (47)</td>
<td>9 (60)</td>
<td>11 (42)</td>
</tr>
</tbody>
</table>
Aims & Methods: currently there is limited data on their nutritional outcome.

Introduction: multivisceral transplants performed in the UK over the past 10 years. Despite

Results: Patient characteristics: Transplants included 12 isolated small bowel (SBT), 5 liver and small bowel (LSBT), 12 modified multivisceral (small bowel, stomach, pancreas, liver-MVT) and 22 multivisceral (small bowel, stomach, pancreas, liver-MVT). 7 patients were re-transplanted. Recently, donor colon has been included in the graft to help with fluid balance. Mean age at transplant was 43.9 years. Patients were followed up for a median of 30 months, to April 2016 or death (n 10). Primary outcomes: Out of the 30 long-term survivors, 73.3% (22) of them are maintained on oral diet alone at the end of follow up. The other 5 patients require ONS, 2 require IV fluids and 1 patient continues on PN. Most patients (95.5%, 21/22) who achieved nutritional autonomy were previously dependent on nutritional support (2 ONS; 1 EN; 18 EN; 10% of patients who were listed super-urgently. Of the patients who died, 3 out of 14 were requiring PN. The mean BMI pre-transplant was 21.7 (SD = 3.5). Post-operatively, the majority of patients (86.7%) lost weight (mean 14.3%; range 10–30%) with their nadir weight occurring at a mean of 10.7 months. 11 lost ≥20% of their pre-transplant weight. However more than half (26/44) of the patients weights improved over time. Compared to the time of assessment, their BMI improved by 1 kg/m² (SD = 4.3) in the median (11 months) and increased further by 1.4 kg/m² (SD = 4.3) at the end of the follow up. The most recent mean BMI in 30 survivors was 23.3 kg/m² (SD = 5.2). Further analysis revealed 20 patients have healthy weight (BMI 18.5–25), 4 underweight (BMI <18.5), 3 overweight (BMI >25) and 3 obese (BMI >30). Significant outcome: 77% of patients achieved nutritional autonomy more than 2 years post-transplant, PN was given for a median of 22 days (range 2-241) and 39.5 days (range 11–262) of EN. At the end of the follow up, those who have nutritional autonomy required a considerably shorter duration of nutritional support post-transplant. Comparing those who are nutrition independent (mean of 65.3 vs 120.7) days, this suggests that the duration on nutritional support post-transplant may predict nutritional autonomy. Of the patients who have colon (graft or continuity), 64% have nutritional autonomy. However those without functioning colon are less likely to (47.4%) (P = 0.36). Handgrip strength was measured in 31 patients pre and post-transplant. At median of 9 months (range from 2–32), there was a slight reduction by 6% of expected value which correlates with their weight loss. 18 patients had further handgrip strength test and they improved with a mean of 7% at last follow up (median 16 months).

Conclusion: The majority of patients achieved nutritional autonomy post-transplant and a colon-containing graft may be beneficial. It is common for patients to lose a moderate amount of weight, up to 30% post-operatively. Therefore timely referral is crucial to allow optimisation of perioperative nutritional status.

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

Table

Disclosure of Interest: P.B. Jeppesen: Has received grant/research support and served as a consultant, advisory board member, and consultant 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 Frentus in Germany. K. Iyer: Has received grant/research support and served as an advisory board member and consultant for NPS Pharmaceuticals, Inc and Shire plc. H. Lee: Employee and stockholder of Shire plc. C. Olivier: Employee and stockholder of Shire plc. The clinical trial was funded by NPS Pharmaceuticals, Inc., Bedminster, NJ, NPS Pharmaceuticals, Inc., is a wholly owned indirect subsidiary of Shire plc. This analysis research was funded by Shire plc.

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 Frentus in Germany. K. Iyer: Has received grant/research support and served as an advisory board member and consultant for NPS Pharmaceuticals, Inc and Shire plc. H. Lee: Employee and stockholder of Shire plc. C. Olivier: Employee and stockholder of Shire plc. The clinical trial was funded by NPS Pharmaceuticals, Inc., Bedminster, NJ, NPS Pharmaceuticals, Inc., is a wholly owned indirect subsidiary of Shire plc. This analysis research was funded by Shire plc.

OP266 SUBANALYSIS OF TEDUGLUTIDE EFFICACY AND SAFETY DATA FROM PATIENTS WITH CROHN’S DISEASE AND ULCERATIVE COLITIS IN THE STEPS STUDY

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-IBD) vs those with noninflammatory causes of SBS–IF (SBS–non-IBD). STEPS (NCT00798967, EndraCT2008–006193–15) was a 24-week, phase III, placebo-controlled study of 0.05 mg/kg/day TED in patients with SBS–IF. Patients with CD were included in a predefined 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.

Conclusion: The Table details patient characteristics (SBS–IBD, n = 19; SBS–non-IBD, n = 67). Patients with SBS–IBD had lower colon-in-continuity, higher starch intake, and higher baseline PS volume than those with SBS–non-IBD. After 24 weeks, 73% (95% CI, 39%–94%) of patients with SBS–IBD and 59% (95% CI, 41%–76%) with SBS–non-IBD were respondents to TED in the patients, mean PS volume was reduced by 45% (95% CI, 31%–59%) in patients with SBS–IBD and 29% (95% CI, 22%–35%) in those with SBS–non-IBD. Two of 9 (22%) patients with SBS–IBD and 6/20 (30%) 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 of a TEF (TED) of colitis.

**Conclusion:** In this analysis, the subgroup of patients with inflammatory bowel disease (SBS-IBD) had evidence of more severe disease based on a higher frequency of stoma presence, higher PS requirements, and lower colon-in-continuity. Despite this, clinical responses to TED were equally strong.

### Table: Demographic and Disease History Data

<table>
<thead>
<tr>
<th></th>
<th>SBS-IBD</th>
<th>Placebo</th>
<th>SBS-Non-IBD</th>
<th>SBS-Non-IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 8)</td>
<td>(n = 11)</td>
<td>(n = 35)</td>
<td>(n = 32)</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>48 (7)</td>
<td>48 (7)</td>
<td>50 (17)</td>
<td>52 (14)</td>
</tr>
<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, 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.

H. Lee: Employee and stockholder of Shire plc.

A.A. Grimm: Employee of Shire plc.

S.J. O’Keefe: Has received research funding support from NPS Pharmaceuticals, Inc.

This clinical trial was funded by NPS Pharmaceuticals, Inc., Bedminster, NJ.

NPS Pharmaceuticals, Inc., is a wholly owned indirect subsidiary of Shire plc.

This analysis research was funded by Shire plc, and Fresenius Kabi GmbH; served as a study investigator for NPS Pharmaceuticals, Inc.

This analysis was funded by Shire plc.

**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 3 years. Some recent transplants have been performed ‘superurgently’ for acute wide-spread splachnic ischaemia. Longstanding indications include complications of bowel resection in patients with type 3 Intestinal failure (IF-associated liver disease (IFALD), recurrent catheter-related infections and loss of vascular access, cirrhosis with extensive portomenteric venous thrombosis precluding an isolated liver transplant and the need for extensive evisceration due to benign tumour. Re-transplantation is indicated for loss of previous graft due to rejection, ischaemia or primary non-function.

**Aims & Methods:** We describe here the indications and outcomes for Intestinal and Multivisceral transplant at Addenbrooke’s Hospital, Cambridge, UK Data was collected prospectively on an internal database of all patients transplanted from January 2006 to April 2016. All patients considered for an intestine-containing graft require ratification at a national forum (NASIT). Grafts which include liver or kidney are also discussed at local listing committees. Induction therapy is tacrolimus and steroids. If complications related to tacrolimus occur, patients are switched to ciclosporin or sirolimus. An antithrombotic is added to aid steroid withdrawal post discharge.

**Result:** In the study period, 66 transplants were performed in 61 patients (33 Multivisceral, MVT; 7 Liver/small bowel, LSB; 9 Modified multivisceral, MMV; 17 small bowel, SB). Grafts can also contain colon and pancreas. 26 patients (39%) received a transplant for complications relating to intestinal failure (ever IFALD), 11, impending IFALD, 4, recurrent sepsis = 1, loss of vascular access = 10). 14 patients (21%) received a multivisceral graft because an isolated liver transplant was not possible due to extensive portomenteric venous thrombosis. An increasing indication is that of acute abdominal catastrophes – 9 patients were transplanted for this including 5 with widespread splachnic ischaemia. Less frequent indications included desmoid tumours (4), re-transplant (6), short bowel and renal failure (2). The median length of hospital stay post transplant is 77 days. 7 patients had a proven episode of acute cellular rejection (ACR) within 90 days, 12 patients had an episode between 90 days and 1 year and 7 had ACR after 1 year. The vast majority of episodes were treated with pulsed methyl-prednisolone (23/26, 88%). Subsequent treatments given were Alemtuzumab (n = 9), Infliximab (n = 1), second pulse of ATG (n = 4), 3 grafts required removal due to rejection and all 3 patients have been re-transplanted. Within our cohort, there have been 5 cases of graft versus host disease (GVHD) and 6 cases of post-transplant lymphoproliferative disorder (PTLD). Infections continued to be a problem. We have seen increasing rate of vancomycin resistant enterococcus (VRE) and carbapenem resistant pseudomonaous. Cytopherovirus is the most common viral infection. Overall rates are 37.5% but this increases to 91% when seropositive donor is given to a seronegative recipient. 1 year patient survival for SB recipients is 91%, for MMV is 89% and for MVT/LSB is 69%. 3 year patient survival for SB recipients is 81%, for MMV is 89% and for MVT/LSB is 52%.

**Conclusion:** Transplantation of intestinal-containing grafts is technically challenging and recipients have a higher rate of complications compared to other solid organ transplants. However, with advances in surgical techniques and increasing experience of the management of medical complications, survival is improving. Intestinal or Multivisceral transplant should be considered for certain patients who have suffered an abdominal catastrophe, are unable to have a liver transplant due to extensive portomenteric thrombosis, or have complications arising from intestinal failure. Timely referral to a transplant centre and careful follow-up is essential to continue improvement in outcomes.

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

**TUESDAY, OCTOBER 18, 2016 14:00-15:30**

**PROGNOSTIC FACTORS IN LOWER GI CANCER – ROOM LB**

**OP268 EXPRESSION OF DDR2 CORRELATES WITH HIGH FREQUENCY OF PERITONEAL DISSEMINATION AND POOR PROGNOSIS IN COLORECTAL CANCER**

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**Introduction:** In the previous study, our colleagues identified that discordin domain receptor 2 (DDR2) is a promising driver gene of peritoneal dissemination in gastric cancer by a comprehensive expression assay. We found DDR2 expression was associated with high frequency of peritoneal dissemination and poor prognosis in gastric cancer, and also revealed that the DDR2 was upregulated by the loss of DNA methylation and that DDR2 knockdown reduced peritoneal dissemination in a xenograft. Furthermore, we found dasatinib, an inhibitor of the DDR2 signaling pathway, suppressed peritoneal dissemination. In colorectal cancer, peritoneal dissemination is second popular site for colorectal cancer metastasis, next to the liver. Its frequency is estimated to be 4-7% of patients with colorectal cancer at primary surgery, and approximately 4-19% of patients during follow-up after curative surgery. Peritoneal dissemination is one of the most frequent non-curative clinical factors also in colorectal cancer.

**Aims & Methods:** In this study, we analyzed correlations of DDR2 expression with clinicopathological factors in colorectal cancer, especially peritoneal dissemination. We selected 63 cases with colorectal cancer who had an operation in the critical period between 2009 and 2014. Among them, 13 cases had synchronous or metachronous peritoneal dissemination. We performed immunohistochemical examinations for 63 primary colorectal cancers and 12 peritoneal dissemination cases in 11 cases with anti-DDR2 antibody. We evaluated histological localizations of DDR2 expressions, divided 63 cases into two groups by the degree of DDR2 expressions, and compared various clinicopathological factors and overall survival between these two groups.

**Result:** In primary lesions, DDR2 was expressed more preferentially in cancer cells at invasive front of tumors. The group with high DDR2 expression had significantly more proportion of T4, lymph node metastasis, and peritoneal dissemination than the group with low DDR2 expression (p = 0.0025, 0.012, and 0.012, respectively), and the prognosis of the former was significantly poorer than the prognosis of the latter (p = 0.0164). In peritoneal dissemination lesions, 11 out of 12 exhibited intense DDR2 expressions.

**Conclusion:** High DDR2 expression correlates with peritoneal expression and poor prognosis in colorectal cancer as well as in gastric cancer. DDR2 might be one of promising driver genes of peritoneal dissemination universally in gastrointestinal peritoneal dissemination.

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

**Reference**

OP209 GENETIC SUSCEPTIBILITY AND FAMILY HISTORY OF COLORECTAL CANCER: RELATIONSHIP OF SINGLE NUCLEOTIDE POLYMORPHISMS IN THE DEVELOPMENT OF COLORECTAL PNEUMOPLASMS

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

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

Result: Average age of participants was 54.5 ± 9.4 years with a slight predominance of women (51.7%). In 57% of patients, no preneoplastic lesions were found. By contrast, 288 patients (144 cases and 144 controls) showed non-advanced adenomas (NAA), and 354 patients (177 cases and 177 controls) had advanced adenomas (AA). Concerning gene variation, 2 SNPs (rs10505477 A > G and rs6838267 G > T) located in the CASC8 gene were associated with the development of adenomas. Thus, the rs10505477A and the rs6838267T alleles were associated with a reduced risk of adenomas in patients with a positive family history of CRC (controls) (log-additive models, OR: 0.67, 95% CI:0.54–0.84, respectively). However, such a protective effect was not observed in FDR of patients with CRC (cases). In the stratified analysis, only the rs10505477G and the rs6983267T alleles were significantly associated with a reduced risk of both, NAA and AA in controls. Although this effect was stronger on the risk of developing NAA (recessive models, OR: 0.50, 95% CI:0.34–0.75 for rs10795668, and OR:0.52, 95% CI:0.34–0.84, respectively).

Conclusion: Genetic variants in the CASC8 gene may be involved in the development of colorectal adenomas or specific histological subtypes.

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

OP210 PREDICTION OF COMPLETE RESECTIONS AFTER CYTODUCTIVE SURGERY BASED ON THE EXTENT OF COLORECTAL PERITONEAL CARCINOMATOSIS


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Introduction: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (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 results were compared with CT results.

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. Regarding disease recurrence, patients with fewer than 29.19 mm of IQR (9.1-24.7) and 44.6 mm (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 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 PREDICTION OF COMPLETE RESECTIONS AFTER CYTODUCTIVE SURGERY BASED ON THE EXTENT OF COLORECTAL PERITONEAL CARCINOMATOSIS


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Conclusion: Patients with four or less involved abdominal regions with PC 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.

OP272 PREVALENCE OF LYMHPH NODE METAESTASIS AND LONG TERM SURVIVAL OF TI RECTAL CARCINOID 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 excision) is effective for ≤10mm 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 Beijing and 62.0% (29/46) of CRC patients from cohort III by Copy Number Assay. The copy number gain was positively correlated with its mRNA overexpression both in cohort I (r sq = 0.327, p < 0.0001) and in cohort III (r sq = 0.619, p < 0.0001). Biological functional investigation of PCID2 revealed that mRNA overexpression of PCID2 in colorectal cancer cell lines (DLD1 and HT29) significantly increased cell proliferation (p < 0.01 in DLD1 and p < 0.001 in HT29), G1-S cell cycle transition (p < 0.01 and p < 0.05, respectively), invasion (p < 0.01 and p < 0.01, respectively) and migration (p < 0.01 and p < 0.05, respectively). 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.

Conclusion: PCID2 plays a pivotal oncogenic role in colorectal carcinogenesis by promoting tumor cell proliferation and invasion in human colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.
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, and 3) evaluate the long-term survival of patients with T1N0M0 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. T2 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 (F3) was found in 49.9%. Overall, 12% (12% (1.5%) had N1 in 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 (N1) distant metastasis. Mean follow-up for 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 T1N0M0 rectal carcinoids <10 mm in size and >6 months, 527 (94.5%) 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 T1N0M0 rectal carcinoids 11–19 mm in size [39 (84.8%) who underwent local excision and 7 (15.2%) underwent radical surgery], there were no tumor-related deaths after a median follow-up of 28 months (range 8–122). The overall survival of T1N0M0 rectal carcinoid 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 with N0/M0 with excellent outcomes in addition to clinical examination and endoscopy imaging – mainly MRI – plays a important role. Given the novelty of the ‘watch-and-wait’ approach, limited data exists yet on what we can expect to see on MRI during long-term follow-up after chemoradiotherapy. A pilot study described various patterns of a complete response during watch-and-wait in a small group of 19 patients.

**Aims & Methods:** Aim of this study was to follow-up on this previous research in a larger patient cohort. Objectives are to describe the morphology of the rectal wall, obtain complete response rates and follow-up in the evolution in rectal wall morphology during long-term clinical follow-up in these patients. 68 patients with a sustained complete response (i.e. no evidence of recurrence on sequential endoscopic examinations (abnormal endoscopic findings) were analyzed during long-term follow-up within the scope of a watch-and-wait protocol. Patients underwent MRI (as well as corresponding clinical examination and endoscopy) 3-monthly in the first year and 6 monthly during the second to fifth year. Two readers assessed the rectal wall morphology post-chemoradiotherapy MRI scan and studied the evolution in morphology on the various sequential follow-up MRIs. MRIs were performed at 1.5 T. Routine T2-weighted sequences in sagittal, transverse and coronal plane were analyzed. Median follow-up time was 30 months (range 6–96). A total of 512 MRIs was analyzed (median 7, range 3–15 patient). In 7% of patients the rectal wall completely normalised post-CRT. The other 93% showed a fibrotic remnant (60% minimal fibrosis limited to the bowel wall, 21% thick/mass-like fibrosis and 12% irregular/spicular fibrosis). In 94% the rectal wall morphology remained unchanged during long-term follow-up, in 2% initial fibrosis later developed into a normalised wall, in 3% the fibrosis slightly diminished (without evidence of recurrence).

**Conclusion:** In the majority of patients with a complete response residual fibrosis is present post-chemoradiotherapy which remains unchanged during long-term follow-up in almost all patients. A completely normalised wall is observed in approximately 1–10% of the patients. This 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 watch-and-wait policy.

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

Reference
elastographic reference method: Transient Elastography (TE)- FibroScan, EchoSens). Reliable liver LS measurements were defined as follows: for 2D-SWE: the median value of 10 measurements acquired in a homogenous area and an interquartile range (IQR) <30% (1), for 2D-SWE: the median value of 3 measurements acquired in an homogenous area and an interquartile range value of >50% and an interquartile range <30% (3). Spearman’s rank correlation coefficient (r) was used to assess the correlation of LS measurements by means of 2D-SWE, 2D-SWE.SSI and TE.

Result: Valid measurements were obtained in 94.6% (123/130) for 2D-SWE, 90.7% (118/130) for 2D-SWE.SSI, 89.2% (116/130) for TE (p = 0.05). Reliable liver stiffness results were obtained in 107 subjects by means of 2D-SWE.SSI, 2D-SWE.GE and TE. The values ranged from 4.17 to 20.48 kPa for 2D-SWE and 2.38 to 82.4 kPa for 2D-SWE.SSI. The mean LS values by 2D-SWE.SSI were significantly higher than for 2D-SWE: 19 ± 12.3 kPa vs. 12.1 ± 3.7 kPa (p < 0.0001). There was a significant correlation between 2D-SWE.SSI and 2D-SWE.GE LS values (r = 0.712, p < 0.0001). The correlation between 2D-SWE.SSI and TE was r = 0.746, p < 0.0001 and between 2D-SWE.SSI and TE was r = 0.604, p < 0.0001 with no significant differences between them (p = 0.056). Taking TE as the reference method, both 2D-SWE.SSI and 2D-SWE.GE had a good value to differentiate between different stages of liver fibrosis and liver cirrhosis. For 2D-SWE.SSI the best liver stiffness cut-off value to differentiate between liver cirrhosis and other stages of fibosis was >13.7 kPa with 88.37% Se, 75.68% Sp, 87.3% positive predictive value (PPV) and 77.8% negative predictive value (NPV) (AUROC = 0.831, p < 0.0001). For a liver stiffness cut-off value >10.7 kPa, 2D-SWE.GE had 91.43% Se, 78.38 Sp, 88.9% PPV, 82.9% NPV (AUROC = 0.904, p < 0.0001) for differentiating liver cirrhosis. The AUROCs of 2D-SWE.SSI and 2D-SWE.GE for predicting the presence of liver cirrhosis were similar (p = 0.09).

Conclusion: Both 2D-SWE techniques have a very good feasibility for the non-invasive liver fibrosis assessment and both have a strong correlation with TE. Both 2D-SWE techniques have a very good feasibility for the non-invasive liver fibrosis assessment and both have a strong correlation with TE.

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

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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 play a crucial role in the recognition and response to diverse microbial molecules and enable the innate immune system to discriminate among groups of pathogens and to induce an appropriate cascade of effector responses. HCV has different effects upon TLR pathway stimulation which results in the activation of different pro-inflammatory cytokine production leading to liver damage and evade immune responses to establish viral persistence.

Aims & Methods: The aim of this work is to investigate the associations of TLR SNPs with the outcome of the HCV infection. Four SNPs of TLR1 and TLR4 were genotyped by real time PCR using TaqMan® allelic discrimination kit (Applied Biosystems) according to the manufacturer’s protocol. A total 392 families (1176 individuals) were recruited in this study from upper & lower Egypt (east & west desert). we compared the risk of allele carriage of selected markers in different patient groups. These groups included spontaneous virus clearance (SVC) (108 subject), chronic HCV patients (549), and negative control (519) individuals. The rs121917864 (C/T) allele of TLR2 was genotyped by Taqman allelic discrimination assay.

Results: As regard TLR2, The T allele of rs121917864 (C/T) is significantly higher in SVC group compared to that control group and spontaneous (SVC) group (OR = 2.2071 (95% CI 1.2056 to 4.0404 P = 0.007) and 2.635 (95% CI 2.184 to 4.115 P = 0.0001)) respectively. As regard TLR4, The T allele of rs4986791 (C/T) is significantly higher in SVC group compared to that control group and spontaneous (SVC) group (OR = 2.8474 (95% CI 1.3808 to 6.4666 P = 0.0449) and 5.08 (95% CI 2.552 to 9.2754. P = 0.0001)) respectively. The T allele of rs4986791 (C/T) is significantly higher in SVC group compared to that control group and spontaneous (SVC) group (OR = 2.8474 (95% CI 1.3808 to 6.4666 P = 0.0449) and 5.08 (95% CI 2.552 to 9.2754. P = 0.0001)) respectively. On the other hand the TLR4 genotyping revealed that the carriage of C allele of rs4986791 was significantly higher in negative and spontaneous (SVC) group compared to that of chronic HCV group (OR = 0.4835 (95% CI 0.3380 to 0.6646 P = 0.4449 and 95% CI: 0.2917-0.6787) simultaneously indicating that the C allele act as protective allele against HCV infection and development of chronic HCV. Linkage Disequilibrium of rs4986791 and rs6252260 SNPs indicating that the carriage of TA haplotype was significantly higher in chronic HCV compared to that of SVC group (OR = 2.906 (95% CI 1.01-8.54 P = 0.049). No one of spontaneous group was carriage for TA haplotype, this revealing the role of TA haplotype as a risk indicator for HCV infection.

Conclusion: Current study demonstrated that spontaneous clearance of HCV was associated with The allele C of rs4986791 of TLR4 and chronicity of HCV infection is associated with the risk haplotype (TA) of TLR4 & The allele C of rs4986791 of TLR4 and chronicity of HCV infection is associated with the risk haplotype (TA) of TLR4-8 & TLR4-3 Alleles with the Hepatitis C Virus Infection Outcome in Egyptian Population: A Multicentre Family Based Study.

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

This Research Was Funded By Science, Technology Development Foundation (Stdf), Project No.1784 (Te-2/health/2009/hep-1.3).
new-onset diabetes mellitus after kidney transplantation. From previous studies we cannot reasonably infer that adiponectin protein in the development of NODAT. However, there have been no reports to describe the association between ADIPOQ gene polymorphism and new-onset diabetes mellitus after liver transplantation.

**Aims & 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 transplantation 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.

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

**References**


**TUESDAY, OCTOBER 18, 2016 15:55-17:15**

**MANAGEMENT OF REFRACTORY CROHNS DISEASE - ROOM A**

**OP220 DISAPPEARANCE OF ANTI-DI-DRUG ANTIBODIES TO INFliximab AND Adalimumab AFTER ADDITION OF AN IMMUNOMODULATOR IN PATIENTS WITH INFAMMATORY BOWEL DISEASE**

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**Introduction:** Since therapeutic options for patients with inflammatory bowel disease (IBD) who lose response to anti-TNF therapy are limited, optimal use of these agents is crucial. Loss of response can be caused by anti-drug antibody (ADA) formation and subsequent neutralization of the effect of the drug. Addition of an immunomodulator (IM) to anti-TNF therapy has been proposed as an approach to reduce antibody formation, increase serum concentrations and to regain clinical response.

**Aims & Methods:** We investigated whether addition of an IM to anti-TNF mono-therapy can lead to a decrease of ADA levels and regained clinical response. Therefore, we retrospectively collected measurements of infliximab (IFX) and adalimumab (ADL) serum concentrations together with ADA levels from 602 patients at our IBD centre (September 2005-September 2015). ADA levels were determined with a drug sensitive assay by Sanquin Biologicals Laboratory. As a next step, we identified all ADA positive patients with secondary loss of response and added a second IM in an attempt to eliminate ADA and to...
regain clinical response. Detailed documentation of disease activity was unavailable.

Result: In 98/376 patients ADA directed against IFX and in 61/226 patients ADA against ADL were detectable. From all 159 ADA positive patients, 17 patients had received an IM, either a thiopurine or MTX, because of secondary loss of response. Seven patients received MTX, ten a thiopurine (4 azathioprine, 4 mercaptopurine and 2 6-TG). In 7 out of 8 patients treated with IFX, addition of an IM resulted in an increase of serum drug levels accompanied with a decrease of ADA till they were undetectable. The median time for ADA to IFX to become undetectable was 11 months (IQR 6–28). For patients treated with ADL, an increase of the serum drug concentrations, together with a decrease of ADA levels, was reached in 6 out of 7 patients after addition of an IM. The median time for the ADA levels to be undetectable was also 11 months (IQR 2–27). 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 Abbott laboratories, Merck Sharp & Dohme and Ferring Pharmaceuticals. He has received research grants from Abbott laboratories, Merck Sharp & Dohme and Ferring Pharmaceuticals. He has received research grants from Abbott laboratories, Merck Sharp & Dohme and Ferring Pharmaceuticals. M. Lowenberg; M. Lowenberg has served as speaker for AbbVie, Coviden, Dr. Falk, Ferring Pharmaceuticals, Merck Sharp & Dohme, Receptos, Takeda, Tillots and Tramedico. He has received research grants from AbbVie, Merck Sharp & Dohme, Novartis healthcare and JANSsen. G. D’Haens; G. D’Haens reports having received consulting fees from AbbVie, Boehringer, Ferring, Jansen Biologics, Merck Sharp & Dohme, Takeda, Pfizer, Tillots Pharma and reports receiving research grants from Abbott Laboratories, Jansen Biologics, MSD, DyFalk Pharma. All other authors have declared no conflicts of interest.
small bowel diseases. Secondary objectives: procedural success, - time, depth of mucosal trauma, therapeutic adverse events. Patients with occult gastro-intestinal bleeding (OGB) or indeterminate iron-deficiency anemia (IDA) or positive findings of small bowel imaging examinations were included in a two-center prospective clinical trial. In total 132 cases were enrolled to determine the efficacy yield. A rate of 0.5% would be considered as clinically efficacious under consideration of a two-sided non-inferiority margin of 20% in comparison to conventional enteroscopy. A novel reusable endoscope (Olympus Corp.) with an integral motor was used for rotating a disposable short spiral overtube mounted on the insertion tube. Rotation of the spiral overtube offers “pleat” or “unpleat” the bowel either on or off the insertion tube as the spiral is advancing or retracted. Additionally, it is possible to apply a consensal pressure on the small bowel. The feasibility of this approach was proved in a pilot study. In a prospective clinical trial we assessed the efficacy and safety of peroral Motorized Spiral Endoscopy (NMSE) in patients with indications for small-bowel enteroscopy. Methods: A prospective, single-center, nonrandomized trial comparing efficacy and safety of peroral NMSE to conventional enteroscopy was conducted. Primary endpoints were efficacy (target deep bowel segment reached), and safety (serious adverse events). Secondary endpoints included duration of the procedure, patient satisfaction, diagnostic yield, and the need for further diagnostic procedures. Results: From November 2015 to April 2016, 22 patients (14 male, mean age 58 years) with indications for small-bowel enteroscopy were enrolled. After a median of 3 months (range 1-6 months), 15 patients (69%) reached the ileum, 8 (36%) the cecum. 1 patient was not able to be evaluated because of a perforation. No adverse events were reported. Conclusion: Small-bowel enteroscopy with peroral NMSE is feasible and safe. However, the clinical utility is limited by the technical complexity of the procedure. Further studies are needed to identify patients who may benefit from this approach.
Activity of sucrase and maltase was reduced in 50% and activity of lactase was decreased in 37.5%. However, even in normal small intestine mucosa the reduction of glucoamylase and maltase, and in 81.8% of cases we observed a decreased activity of sucrase. The activity of all enzymes in all patients; whereas all patients with Marsh IIIb atrophy had a reduced activity of all enzymes. Objective: To determine the activity of enzymes (glucoamylase, maltase, sucrase and lactase) in CD patients. Objective: To determine the activity of enzymes (glucoamylase, maltase, sucrase and lactase) in CD patients.

**Aims & Methods:**

Patients with celiac disease (CD), who have followed gluten-free diet (GFD) and have a normal histological structure of small intestine were observed in 26.6%. The enzyme activity was a gradual increase in the severity of IBS symptoms (p = 0.0001) and somatic quality of life (SF-36). Four days prospective dietary intake records at baseline and 6 weeks, compliance and satisfaction after 6 weeks, and 1 month later. Dietist Net Free was used for FODMAP calculations. Statistics: paired T-tests and Wilcoxon’s.

**Result:** 20 patients were included in each group: A (18F/2M, age 39 ± 13) and B (15F/5M, age 43 ± 12). 42.5% had constipation, 27.5% diarrhea and 30% both. The mean total IBS-SSS score was significantly reduced: Group A from 260 to 204 (p = 0.0022), group B from 263 to 145 (p < 0.0001), p = 0.0247, group B vs. A. In group A 10% reached remission, in Group B 25% (p = 0.0081), group B vs. A. In group A 10% reached remission, in Group B 25% (p = 0.0081), but it was also more challenging to follow their diet (p = 0.0008).

**Conclusion:** Patients with celiac disease and IBS-symptoms had significant improvement in abdominal symptoms and physical health from a low FODMAP diet for 6 weeks. A gluten-free diet with reduced FODMAP content was more effective than a more strict gluten-free diet, and should be offered to coeliac patients with refractory IBS-symptoms on a gluten-free diet.
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 of neuroimaging studies support a crucial role of rACC in altered pain processing, including the rostral anterior cingulate cortex (rACC) as a unique processing area, and support the importance of microbiota as a major factor in the pathophysiology of IBS.

Aims & Methods: We compared IBS patients and healthy controls (HC) regarding concentrations of glutamate (Glu) and γ-Aminobutyric acid (GABA+) in rACC using quantitative magnetic resonance spectroscopy (qMRS). We further addressed associations with anxiety and depression as the most common psychiatric disorders in IBS. We included a combined MRS study; GABA+ concentrations in 38 female IBS and 19 age-matched female HC were measured using a Philips Ingenia 3T scanner and a MEGA-PRESS sequence with a 3x3x3 cm³ voxel placed in the rACC, localized based on individual T1-weighted images. Symptoms of anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS) and correlated with metabolite concentrations in IBS, the biochemical basis of these alterations remains unknown.

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subjects ingested 400 ml of water containing 10 g lactulose and 5 g mannitol, after an overnight fast. Total urine for the following 4 hours was collected and rapidly frozen for analysis. Both groups started with oral intake of 75 mg diclofenac daily for 7 days. Thereafter, the lubiprostone group was treated by oral intake of 24 mg lubiprostone daily for 28 days, while the control group did not receive any medicine after diclofenac. Permeability was expressed as lactulose/mannitol ratio (LMR), calculated from urinary excretion of the initial administered dose of each sugar.

**Result:** Fourteen subjects for each group with a median age of 23.5 (range, 21–32) completed the study. The background characteristics including baseline LMR between the two groups showed no significant difference. Treatment after 28 days of lubiprostone showed significant improvement of LMR (p = 0.0047), 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 control group (n = 14)</th>
<th>LMR lubiprostone group (n = 14)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline 0.019 (0.016-0.022)</td>
<td>0.021 (0.017-0.025)</td>
<td>0.097</td>
</tr>
<tr>
<td>day14 0.055 (0.053-0.047)</td>
<td>0.035 (0.019-0.059)</td>
<td>0.403</td>
</tr>
<tr>
<td>day28 0.028 (0.023-0.033)</td>
<td>0.017 (0.015-0.019)</td>
<td>0.0497</td>
</tr>
</tbody>
</table>

**Conclusion:** In our study, 28 days treatment with lubiprostone demonstrated an improvement of increased intestinal permeability after 1-week administration of diclofenac in healthy volunteers. This is the first study to demonstrate a significant effect of a medication for treatment of increased intestinal permeability, and suggests a new approach towards several diseases associated to “leaky gut”.

**References**
administration, consisting of a once daily oral gavage for 2 weeks prior to experi-
ment. Groups, which four week old mice, were divided into three groups: control, 5% DMSO, and 200 mg/kg lincamot peptide. The results showed that lincamot peptide significantly increased the percentage of mature CD4+ CD25+ cells in the spleen, indicating that it could induce regulatory T cells (Tregs) activation.

Conclusion: Our study demonstrated that lincamot peptide can effectively induce Tregs activation. This effect may be beneficial for the treatment of autoimmune diseases and other conditions where Tregs depletion is required. Further studies are needed to investigate the mechanisms underlying this effect and to determine its potential clinical applications.

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

References

TUESDAY, OCTOBER 18, 2016
15:45–17:15
OP294 DIAGNOSING RARE INHERITED DISORDERS USING TARGETED NEXT GENERATION SEQUENCING IN PATIENTS WITH EARLY-ONSET INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY

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2Gastroenterology Unit & Epimad Registre, Amiens University and Hospital, Amiens/France
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5Gastroenterology Pediatric Unit And Institut Leric Unr 99 Universite & Hospital, Lille/France
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Introduction: Several recent referral center studies showed that a significant proportion (3-10%) of children with an early-onset (EO, defined by an age at diagnosis less than 12 years) inflammatory bowel disease (IBD) present with an underlying monogenic disorder. Currently, more than sixty disorders of this type have been identified and their pathophysiological mechanisms are very heterogeneous. Most of them affecting the intestinal epithelial barrier, are associated with defects in phagocytosis or immune deficiency, or are hyper- and auto-inflammatory diseases. However, they all share the ability to present in the form of an array of intestinal inflammation with EO.

Aims & Methods: Using a next-generation sequencing (NGS) of the 63 genes whose abnormalities are responsible for these disorders, and a targeted CGH analysis of copy number chromosomal loci, 91 patients with an initial diagnosis of EO-IBD between 1988 and 2004 (54% of the whole EO-IBD cohort) issued from EPIMAD population-based registry were screened; 71 had a Crohn’s disease and 20 an ulcerative colitis.

Result: Analysis of 24 patients (26.4%) with very rare or not yet reported potential pathogenic variants in 17 genes. Seven of them (7/9; 7.6%) had a genotype compatible with one of the tested disorders: Burton agammaglobulinemia, familial diarrhea, familial C2 defect, hyper-IgM syndrome or Omenn syndrome. The remaining 17 patients (17/9; 18.7%) were heterozygous carriers of these genes variants involved in autosomal recessive trait. The genotype identified in these patients was thus probably not likely to be the underlying cause of one of these disorders, however, one cannot exclude that it may contribute to IBD as suggested by the unusually high prevalence of these genotypes.

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

References
OP296 EPIGENETIC ALTERATIONS IN INFLAMMATORY BOWEL DISEASE - THE INFLUENCE OF GERMLINE VARIATION (MEQTLS) ON GENOME-WIDE METHYLATION ALTERATIONS


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8Servicio De Aparato Digestivo, Hospital Clinico Universitario Lozano Blesa, Zaragoza/Spain
9Cruz Centre For Genomic Regulation, Barcelona Institute Of Science and Technology, Barcelona/Spain
10Unit Of Molecular Genetics Of Digestive Diseases, Biocrues Health Research Institute, Bilbao/Spain

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 (meQTLs).

Aims & Methods: Genome-wide methylation was measured in 641 DNA samples from peripheral blood mononuclear cells (PBMCs, 150 Crohn's disease (CD), 150 ulcerative colitis (UC), 26 IBD unclassified (IBDU)) using the Illumina 450k platform with covariates of age, sex, and differential cell counts, deconvoluted by the Houseman method; genotyping was performed using Illumina HumanExome-8-8 BeadChips. Samples were obtained from new onset IBD cases in six European centres as part of the European Commission funded IBD-Charity project.

Result: 195 probes exhibited Bonferroni significant IBD-associated methylation differences, including VMP1/MIR21 (p =3.7 x 10^-9), RPS6K2 (1.1 x 10^-9), SBN2O (2.7 x 10^-9), and TNFSF10 (1.1 x 10^-8); data which provide important replication and confirmation of methylation differences previously reported in paediatric CD and adult IBD. Novel findings include PHOSPHO1 (1.3 x 10^-9), ATG16L1 (5.5 x 10^-13), and CDH24 (1.7 x 10^-16), 179 differentially methylated regions of consecutive FDR significant probes were defined in genes including VMP1/MIR21, ITGB2, TNF, and at multiple sites throughout the HLA region. Results were highly similar in CD and UC, with only one probe showing a significant methylation difference between diagnoses (NAV2, 6.82 x 10^-7). Paired genetic and methylation data showed 2327 FDR significant MeQTLs indicating a genetic influence on key methylation loci such as RPS6K2 (8.6 x 10^-4), and ITGB2 (3.3 x 10^-9), and a replication of two SNPs previously described as correlated to VMP1/MIR21 methylation (rs7087424, p = 4.4 x 10^-22, rs1053015, p = 7.4 x 10^-21). There was an enrichment of highly significant IBD-associated methylation changes in proximity to IBD GWAS loci. Results were highly similar in paediatric CD cohort accurately distinguished IBD from controls in this new onset adult cohort (AUC =0.82).

Conclusion: These data allow methylene profiling in a large multinational cohort of IBD patients, showing novel disease-associated methylation changes, important unequivocal replication of recent discoveries, together with insight into the genetic contribution to epigenetic alterations in complex disease, and the utility of peripheral blood DNA methylation as a biomarker.

Disclosure of Interest: R. Kalla: Received funding from the EU FP7 (2858546) and served as a speaker for Ferring J. Jahnsen: Served as a speaker and a advisory board member for MSD, Tillot, Ferring, AbbVie, Celldition, Orion Pharma, Takeda, Napp Pharm, Meda, AstroPharma, Hikma and Pfizer.

F. Gomollon: Advisor: Grifols, Abbvie, MS. Travel Grants: Abbvie,MSD. Research funding (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.

References

Table 1. (OP297)

<table>
<thead>
<tr>
<th>Feature</th>
<th>CCD n = 19</th>
<th>UC n = 32</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at testing (mean ± SD, y)</td>
<td>32.0 ± 14.9</td>
<td>36.0 ± 10.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Age at diagnosis (mean ± SD, y)</td>
<td>25.7 ± 15.5</td>
<td>25.3 ± 10.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Disease Duration at testing (mean ± SD, y)</td>
<td>6.2 ± 4.8</td>
<td>10.5 ± 8.4</td>
<td>0.047</td>
</tr>
<tr>
<td>Gender (%), n</td>
<td>42 %,</td>
<td>50 (16)</td>
<td>0.44</td>
</tr>
<tr>
<td>Clinically active (%), n</td>
<td>58 (11)</td>
<td>66 (21)</td>
<td>0.77</td>
</tr>
<tr>
<td>Endoscopically active (%), n</td>
<td>89 (17)</td>
<td>71 (25)</td>
<td>0.45</td>
</tr>
<tr>
<td>Histologically active (%), n</td>
<td>79 (15)</td>
<td>63 (20)</td>
<td>0.35</td>
</tr>
<tr>
<td>Treatment (%), n</td>
<td>Biologic Azathioprine ASA Steroid Antibiotic</td>
<td>15.8 (3)</td>
<td>15.8 (3) 0 0</td>
</tr>
<tr>
<td>CRP (mean ± SD, mg/mL)</td>
<td>16.1 ± 21.1</td>
<td>8.7 ± 16.3</td>
<td>0.2</td>
</tr>
<tr>
<td>WCC (mean ± SDX 10^11)</td>
<td>6.5 ± 2.0</td>
<td>6.3 ± 1.3</td>
<td>0.7</td>
</tr>
</tbody>
</table>

OP297 AN AUTOPHAGY-RELATED PERIPHERAL BLOOD MICRORNA SIGNATURE DIFFERENTIATES COLONIC CROHN'S DISEASE FROM ULCERATIVE COLITIS

A. Mohammad, O. Kelly, B. Kabakchiev, K. Borowski, M. I. Smith, D. Kevans, M.S. Silverberg
Mount Sinai Hospital, Toronto/Canada

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Introduction: Phenotypic expression of colonic inflammation in inflammatory bowel disease (IBD) in patients with colonic Crohn’s disease (CD) and ulcerative colitis (UC) can sometimes have a similar appearance and be difficult to differentiate. MicroRNAs (miRNAs) may offer a method of distinguishing 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 UC and CD. In the cohort with UC and CD was prospectively accrued. Colonoscopy was performed and patients with CD (Montreal Classification L2/L3) or left-sided UC (Montreal Classification E2/E3) were enrolled. Colonoscopy were reviewed by IBD endoscopists and scored for presence/absence, severity and rate of inflammation. Pathology reports were reviewed for presence/absence and severity of inflammation. On the day of endoscopy, C-reactive protein (CRP) was measured and blood was collected in PAXgene tubes (Qiagen). Total RNA was extracted from blood using the PAXgene Blood miRNA kit (Qiagen) and miRNA counts from 798 probes were measured using the Human v3 miRNA nCounter Platform (NanoString Technologies). Raw counts were normalized, log2 transformed and batch corrected. Non-parametric Kruskal-Wallis tests assessed differential miRNA expression across phenotypes. Raw p-values were corrected for multiple testing by the Benjamin-Hochberg false discovery rate method. Target prediction and gene ontology biological process (GO BP) enrichment analyses were performed with miRWalk 2.0. Receiver operating characteristic (ROC) curves were generated following logistic regression through 5-fold cross validation repeated 10 times. Area under the curve (AUC) values for the ROCs were derived in order to evaluate the discriminating capacity of the differentially expressed miRNAs in CD versus UC.

Result: 51 subjects, 32 UC (50% male, 36 yrs mean age), 19 CCD (42% male, 32 yrs mean age) were included in the analysis (see Table 1). There were no significant differences in mean CRP or among clinical, endoscopic or histologic disease activity between the CD and UC groups suggesting that the degree of inflammation was similar in both groups. Comparing CCD and UC, 5 miRNAs were differentially expressed: miR-129-5p, miR-603, miR-619-3p, miR-874-3p, miR-933 (FDRp = 0.0214 all probes), all of which were upregulated in CCD vs UC. In the ROC analysis, the AUC for CCD vs UC for the combined expression of the 5 miRNAs was 0.89 (95% CI: 0.86-0.92). 2 out of 5 miRNAs putatively target the Autophagy Related 16-Like 1 (ATG16L1) gene, and 4 out of 5 miRNAs had significant GO BPs on putative target genes in the regulation of autophagy pathway (FDRp < 0.05). Conclusion: A PBMC-derived miRNA panel of markers identified here differentiates CD from UC with similar degrees of inflammation. All of these differentially expressed miRNAs are upregulated in CCD compared to UC, and...
been reported in CD patients' peripheral blood. Exosomes are small endosomal-disease (CD) patients. A deregulated microRNA (miRNA) expression profile has (adherent-invasive burden in NR. To anti-TNF treatment recapitulating the observation of a higher inflammatory rated diseased BL from NHV samples. It also clustered R PT samples with the higher inflammatory burden in NR. Indeed, specific macrophage, innate lym- bleomycin signatures, representing acute inflammation and a complex mix of T cells, monocytes, macrophages or neutrophil signatures as well as poly:IC and response, in clinical R and in clinical NR respectively compared to NHV. 59% of p Disclosure of Interest:

centrating on subsets of patients sharing similar underlying molecular pathology targeted design of clinical studies to test therapeutics under development, con- be defined by their overall inflammatory burden correlating with their response and UC supporting the notion of a disease continuum rather than two distinct

Gene set signatures whose ES differed significantly (ES change (NR) was queried. Hierarchical clustering on enrichment scores (ES) from gene set variation analysis (GSVA) was used probing a normal healthy volunteer (NHV), CD, UC, and C. difficile colonization signatures (GSE16879) with a library of gene set signatures representative of various immunological and inflammatory processes as well as specific activated cell types. Patient stratification at baseline (BL) or after anti-TNF treatment (PT) in either clinical responders (R) or non-responders (NR) was assurred.

Result: Gene set signatures whose ES differed significantly (ES change ≥ 0.2, p ≤ 0.05) between comparisons were identified from general linear model analyses. Comparisons were made at BL in all participants irrespective of clinical response compared to clinical NR responses 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 beclin1 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 lymphocyte or leukocyte signatures were specifically enriched in NR. Hierarchical clustering of the ES that significantly differed in the comparisons clearly sepa- rated 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, con- centrating 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, United States

C. Monast: Employee of Janssen Research & Development LLC, Spring House, United States

A. Rowe: Employee of Janssen Research & Development Ltd, High Wycombe, UK


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 Implanted Medicated Microreservoirs in the Treatment of Colorectal Cancer. The Good Effects of a Simple Procedure. Early Results

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Introduction: Colorectal cancer (CRC) is the third most common in the world of men, and the second - in women. In Europe remains steady increase in incidence and mortality according to Globocan 2012 and source EuroCaPolon. The main problem after surgery is local recurrences that often develop even after resection R0, for which a five-year survival is less than 50%. In a developed stage of the disease and after the second recurrence, the survival is about 10-15% [4]. We have presented a method of supporting intraoperative chemotherapy with 5-fluorouracil (5FU) supported on polyvinylpyrrolidone (PVP) tablets, which could be a modified system. The innovative modification surgery. Materials and methods: We have investigated the number of CRC recurrence for patients without metastases. The study included 56 patients operated in the Dnipropetrovsk regional proctology centre from February 2014 to February 2015. The control group (42 patients, 16 men and 25 women) per- formance surgery in standard volume according to guidelines. In the test group (45 patients, 16 men and 29 females) before the anoscopy were formed medicated microreservoirs with 5-fluorouracil (5FU) supported on polyvinylpyrrolidone (PVP). As a result, it was a mixture of 30% PVP solution 5ml and 5ml 5FU (250 mg). This mixture was introduced into the muscle layer from the side of mucosa the 1 ml syringe with needle 0,40 x 10 mm 27G 1/2 at a distance of 1.5-1.5 cm from the edge of the intestine. In one procedure was introduced approxi- mately 10 ml of the mixture. The central part of the rectum was 0.5 cm. 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 hydrophilic and biocompatible matrix polymer and drug release dependence on the concentration of sodium and potassium chloride. The polymer is not dangerous for the carrier polymer. An important advantage is the fact that the drug is practically not destroyed at pH of less than 7.0, 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-formation to act against and is quite effective on condition that trigger a pro-inflammatory response and an increased bacterial intracellular replication in recipient cells.

Aims & Methods: Here, we investigated whether exosomal miRNAs are involved in such processes. Exosomes were purified using ExoQuick Exosome Precipitation kit. miRNA signatures were analyzed by qRT-PCR.

In vivo infection with AIEC bacteria was performed using ileal loop assays and exosomes were purified. Purified exosomes were then intravenously injected in naïve mice (10 μg/mouse).

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We recently showed that AIEC-infected human macrophages released exosomes that trigger a pro-inflammatory response and an increased bacterial intracellular replication in recipient cells.

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

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Result: In the control group, local recurrence was detected in 12 cases (28.6%). The following postoperative complications were found: early adverse intestinal obstruction in 2 (4.8%) cases of postoperative pneumonia in 1 (2.4%) case. Within 8 months after surgery 1 patient died of acute coronary syndrome. In the studied group of local recurrence was detected in 8 cases (17.8%). The following postoperative complications were found: early adverse intestinal obstruction in 1 (2.2%) case, even one patient has been observed intestinal obstruction in 3 months after the operation, which resulted in the death of the patient on 2 day after the re-operation due to acute of cardiovascular failure.

Conclusion: 1. Intraoperative implantation of medicated microsorvehas is a safe and effective procedure for the prevention of early recurrent CRC. 2. Notwithstanding the low total dose, good effect can be achieved due to the high concentration of the drug in the tissues. 3. This procedure avoids many resorptive effects of the chemotherapeutic drug, associated with systemic administration and high doses required to achieve therapeutic concentrations in tissues. 4. Obviously, it is necessary to continue the monitoring of these patients. 5. It is possible to consider a combination of other drugs and carrier polymers.

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

OP301 ENDOSCOPIC SUBMUCOSAL DISSECTION IN LATERALLY SPREADING TUMORS: EXPERIENCE OF 282 CASES FROM A TERTIARY REFERENCE CENTER IN TURKEY

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Introduction: Endoscopic submucosal dissection (ESD) is a minimally invasive technique, providing en-bloc resection of premalignant and malignant lesions in early stage gastrointestinal (GI) cancers. Lateral Spreading 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]

| Tissue size, mm, mean (SD) (median; range) | 49.81 (28.9) |
| Duration of procedure, min, mean (SD) (median; range) | 79.5 (71.1) |
| Dissection speed, mm²/min, mean (SD) (median; range) | 24.46 (15.41) |
| En-Bloc resection rate, N (%) | 257 (91.1) |
| Complete Resection, N (%) | 255 (90.4) |
| Paris Classification, N (%) | 1s 1s 1s 1s 1s 1s |
| Adverse Events, N Delayed bleeding | 2 9 |
| Localisation, N Rectum Sigmoid colon | 133 42 |
| Descending colon Splenic flexura | 16 6 |
| Transverse colon Hepatic flexura | 15 5 |
| Ascending colon Cecum Ileocecal valve | 25 14 |
| Pathology, N (%) Carcinoma Intramucosal Sm1 invasion Sm2 invasion Tubular Adenoma Tubulovillous Adenoma Villous Adenoma Serrated Adenoma | 124 (44) 99 (35.2) 2 (1.4) 21 (7.4) 28 (9.9) 102 (36.2) 17 (6.0) 11 (3.9) 3 |
| Location, N LST-G LST-NG | 236 46 |

ESMR-L group, 88.9% (16 of 18) in the CSI-EMR group, and 95.2% (20 of 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 (n=18) in the CSI-EMR group, and 95.2% (20 of 21).
21) in the ESD group, respectively (p = 0.354). Perforation or delayed bleeding did not occur in any of the ESMR-L were significantly shorter than in the other groups and procedure time increased in order of ESMR-L, CSI-EMR, and ESD group (4.3 ± 2.0 min, 11.2 ± 12.5 min, 18.6 ± 3.9 min, respectively, p = 0.000).

Conclusions: All endoscopic resection method, including ESMR-L, CSI-EMR, and ESD were effective and safe for the treatment of rectal NET, compared with CSI-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 in this patient group.

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

OP304 ANAL CYTOLOGY, HISTOPATHOLOGY, AND ANOSCOPIC VISUAL IMPRESSION IN AN ANAL DYSPLASIA SCREENING PROGRAM: IS ANAL CYTOLOGY ENOUGH?

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Introduction: The human papilloma virus (HPV) is the leading cause of anal squamous cell carcinoma. The cytological screening can reduce morbidity and mortality associated with this cancer, although current recommendations are based on expert opinion.

Aims & Methods: The authors intend to estimate agreement between anal cytology examination, histopathology, and anoscopy visual impression. 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.

Results: During the period of the study, 141 patients (91% men, mean age 37 ± 14 years, 87% with HIV infection) underwent 175 anal cytology tests: 33% negative for intraepithelial lesion or malignancy (NILM), 87% with HIV infection) underwent 175 anal cytology tests: 33% negative for intraepithelial lesion or malignancy (NILM), 33% low-grade squamous intraepithelial lesion (LSIL), 10% high-grade squamous intraepithelial lesion (HSIL), and 1% atypical squamous cells of uncertain significance (ASCUS), 33% low-grade squamous intraepithelial lesion (LSIL), 10% high-grade squamous intraepithelial lesion (HSIL), and 1% atypical squamous cells of uncertain significance (ASCUS).

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

ELISA. Arg16l1 ΔIEC and Arg16l1 ΔIEC/Xbp1ΔIEC mice were treated with recombinant IL-22 for 6 or 12 days before sacrificing. Result: IL-22 induces transient self-limiting ER stress in the intestinal epithelium. While IL-22 improves wound healing in the absence of ER stress, IL-22 leads to impaired wound closure and increased cell death under ER stress conditions. This effect is dependent on STAT3 and autophagy as pharmacological STAT3 inhibition or autophagy induction with Rapamycin completely restores IL-22 dependent ER stress induction. On the contrary, impairment of the autophagic flux by Baf10inv C provokes inflammatory features as well, which are aggravation of transient ER stress is dependent on STAT3 and Arg16l1 as IL-22 treatment of intestinal organs derived from Arg16l1 ΔIEC and Xbp1 ΔIEC mice induces a dramatic increase of inducible ER stress and pro-inflammatory gene expression. In addition, mRNA transcriptome analysis reveals differential expression of several IBD related risk genes in Xbp1 ΔIEC and Arg16l1 ΔIEC organoids in response to IL-22 stimulation. Arg16l1 ΔIEC mice display defective autophagy in the intestinal epithelium and spontaneous cell death in intestinal crypts which exacerbates after IL-22 treatment. Finally, IL-22 induces autophagy spontaneous intestinal inflammatory infiltrates in Arg16l1 ΔIEC/Xbp1ΔIEC 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.

Conclusion: These data suggest an unexpected role of the IBD risk gene ATG16L1 and XBP1 in coordinating regenerative IL-22 function in intestinal epithelium and may contribute to the development of genotype-based personalization medicine. However, further studies are necessary to decipher the molecular link between IL-22 signaling and the ER stress/autophagy axis.

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

References

**OP307**

**HOXA9 IS OVEREXPRESSED IN COLONIC ADENOMAS AND CAUSES AN INCREASE IN CELL GROWTH**

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Introduction: Colonic adenomas are premalignant tumors with glandular origin. Identifying the molecular aberrations in this tissue may help to understand its malignant potential and could lead to better understanding of colorectal cancer development. The mammalian HOX clusters encode regulators of embryonic anterior to posterior specification and are important for the formation of tissues, structures, and organs. Besides having a function in embryology, HOX genes have pro-oncogenic activity in various malignant diseases. For example, HOXA13 overexpression predicts poor outcome for patients with the esophagus, stomach, and liver. In a portion of acute myeloid leukemias (AML), a translocation encoding the NUP98-HOXA9 oncogene gives overexpression of HOXA9. HOXA9 overexpression is the molecular mechanism associated with poor prognosis in AML. HOX gene aberrations are strongly correlated with poor prognosis in ovarian epithelial cancer. HOX gene aberrations are reported in colorectal cancer, however, it is unclear whether HOX gene aberrations are present at a premalignant stage and could, thus, contribute to cancer formation.

Aims & Methods: This study firstly aimed to assess the expression of HOXA9 in colorectal adenoma tissue and location matched control tissue. Secondly, it aimed to investigate the functional effects of increased HOXA9 expression, both in terms of its influence in anterior to posterior specification and its oncogenic properties. We collected biopsies from colorectal polyps and matched normal colorectal tissue in patients undergoing colonoscopy. A pathologist classified the colorectal polyps and we only included tubular adenomas. We used RT-qPCR to quantify the expression of HOXA9 in relation to UBC, TPT1 and GAPDH using the efficiency 2ΔΔCT method. In addition, we transduced Caco2 cells with a lentiviral vector containing HOXA9 and a lentiviral vector without a HOXA9 insert, enabling inducible expression. Subsequently, we analyzed transcription of Xbp1 and HOXA9 in Caco2 cells with a lentiviral vector containing HOXA9 and a lentiviral vector without a HOXA9 insert, enabling inducible expression. Results were analyzed with a TMT assay. Finally, we assessed the expression of genes implicated in oncological transformation and epithelial to mesenchymal transition.

Result: HOXA9 expression in tubular adenomas of the colon is increased compared to location matched control tissue (p = 0.04). HOXA9 overexpression in Caco2 cells led to a decrease in FGF2 mRNA levels (p = 0.002). Additionally, when assessed with a METT assay (p < 0.001), HOXA9 overexpression led to increased cell number and cell growth when assessed in an adherent cell assay (p < 0.001).

Conclusion: HOXA9 overexpression led to increased cell number and cell growth when assessed in an adherent cell assay (p < 0.001). Additionally, when assessed with a METT assay (p < 0.001), HOXA9 overexpression led to increased total cell pool. The growth factor IGF1 increased significantly (p = 0.02) as a result of HOXA9 overexpression. Genes important for epithelial to mesenchymal transition were not found to have significantly changed.

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

**Reference**

western blot analysis. The gene expression of transformed organoids was assessed by real-time 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 DUOXA2 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 reversibly activated by long-term stimulation. Moreover, the organoids required either R-spondin nor Wnt3a after the treatment with GSK3 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-mediated carcinogenesis.

**Conclusion:** Long-term inflammation and nuclear accumulation of β-catenin leads to irreversible cell transformation, which is an important 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**


**OP310 THE RIBONUCLEASE RNASEH2B CONTROLS INTESTINAL STEM CELL INTEGRITY**

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**Introduction:** The stability of genomic DNA is under a tightly controlled surveillance. Especially in highly proliferating cells, as e.g. intestinal stem cells, the stability of genomic DNA is under a tightly controlled surveillance, as shown by acid ß-galactosidase staining in intestinal crypts in the majority of cases. AP is a self-limited process, yet 20% of patients (WT) BALB/c mice were intraperitoneally injected with either Cerulein (50 mg/kg, 5 times, at 1 hour apart) or vehicle, with or without low and high doses of AP.

**Result:** We generated RNAseH2bfl/fl and RNAseH2b−/− mice to investigate the impact of RNAseH2b on intestinal cell transformation during inflammation-related carcinogenesis in UC.

**Conclusion:** Commensal fungi and their cell-wall glycans induce autophagy in IECs. Inflammation-dependent autophagy in the involvement of antifungal receptors such as Dectin-1. Fungal-induced autophagy may play a role in mucosal sensing of luminal microorganisms, and contribute to fungal tolerance. Thus, imbalanced response to commensal fungi (recognition, autophagy or downstream processes), may impair homeostasis and contribute to the pathogenesis of CD.

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

**ABSTRACTS ON FIRE: ACUTE PANCREATITIS: FROM MECHANISMS TO DISEASE – HOTSPOT**

**OP312 HEPARANASE IN ACUTE PANCREATITIS: NEW INSIGHTS INTO PATHOGENESIS AND THERAPY**

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**Introduction:** Despite advances in understanding the pathogenesis of acute pancreatitis (AP), the mechanisms underlying this disease have not been fully determined. In the majority of cases, AP is a self-limited process, yet 20% of patients develop a severe form of AP with pancreatic necrosis, multi-organ involvement, (e.g. WIT), ACS, hypotension. Heparanase (HPSE) is an enzyme produced by several agents which cleaves heparan sulfate, degrades and remodels the extracellular matrix. HPSE is preferentially expressed in human tumors, including pancreatic adenocarcinoma. While the role of HPSE in cancer has been extensively studied, the involvement of this enzyme in inflammation and in AP in particular remains obscure. Therefore, this current study examines if HPSE is involved in the pathogenesis of Cerulein-induced AP in mice.

**Aims & Methods:** HPSE over-expressing transgenic mice (hps2-TG) and wild-type (WT) BALB/c mice were intraperitoneally injected with either Cerulein (50mg/kg, 5 times, at 1 hour apart) or vehicle, with or without low and high doses of R0neoparstat (SST001, HPSE inhibitor) pretreatment. The animals were sacrificed 24 hours following the treatment of pancreatitis. The pancreatic response analysis was performed by pancreatic HPSE activity (determined by NaN2/3SO4-labeled ECM), pancreatic edema index (determined by organ to animal weight ratio), tissue inflammatory response (determined by histopathological analysis), autophagy response (determined by electron microscopy and immunohistochemistry staining) and serum pancreatic enzymes (amylase and lipase) levels.

**Result:** Cerulein-induced AP in wild type mice was associated with significant rises in the serum levels of amylase and lipase. These increases were characterized by an enhancement of HPSE activity, a higher pancreatic edema index, tissue inflammation and autophagy response. All types of responses to administration of Cerulein were profoundly exaggerated in hps2-TG mice. In contrast, when vehicle was injected in WT BALB/c mice, the severity of AP was...
attenuated as compared with their wild type controls. Importantly, pretreatment with Roneparstat significantly reduced, in a dose-related manner, the HSPE activity, the tissue inflammatory response, autophagy and serum amyloid and lipase levels.

Conclusion: HSPE appears to play an important role in the pathogenesis of AP. The HSPE inhibitor (Roneparstat) significantly reduced the severity of the AP in an animal model. This new concept may provide a basis for prophylaxis and treatment of AP.

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

OP313 CIGARETTE SMOKE EXTRACT INHIBITS FLUID AND HC03- 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 HC03- 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 ductal ducts were isolated from guinea pig pancreas. Cigarette smoke extract (CSE) was prepared by smoking of 15 cigarettes into 10 ml distilled water by a smoking machine. Three different concentration (20, 40 and 80 µg/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 HC03- secretion in guinea pig pancreatic ductal ducts and forskolin-stimulated CT current of CFTR CT channel (20 µg/ml by 44.5%, 80 µg/ml by 69.3% and 80 µg/ml by 91.3%).

Conclusion: Cigarette smoking and CSE inhibits pancreatic ductal fluid and HC03- secretion and the activity of CFTR which may play role in the smoke-induced pancreatic damage. This study was supported by OTKA, MTA and TAMOP.

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

OP314 GHRELIN INHIBITS TNF-ALPHA PRODUCTION IN ACUTE Pancreatitis

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Introduction: Ghrelin (GHRL), a 28-amino acid polypeptide, that was originally isolated from the stomach, was shown to protect the pancreas from caerulein-induced pancreatitis (AP) [1–3].

Aims & Methods: To determine the effects of GHRL on tumor necrosis factor-alpha (TNF-α) production in AP and on the signals for growth hormone secretagogues receptor type 1a (GHS-R1a) and TNF-α in the pancreatic acini. AP was induced by caerulein infusion (25 µg/kg s.c.). GHRL (12.5; 25; 50 µg/kg p.i.) was given to the control rats and prior to the start of inflammation in vivo. Plasma TNF-α concentration was measured by ELISA. Pancreatic acini were isolated from control, GHRL rats and then hyperstimulated by caerulein (10–8 M) in vitro. The gene expressions were determined by RT-PCR and the protein contents by Western-blot.

Result: Administration of GHRL to the control rats failed to affect TNF-α concentration in plasma. AP significantly increased its, but application of GHRL prior to the inflammation significantly dose-dependently reduced this pro-inflammatory cytokine. Protein expressions and mRNA signals for GHS-R1a and TNF-α were detected in pancreatic acini under basal conditions and GHRL resulted in a statistically increase of GHS-R1a without changing signals of TNF-α. Caerulein significantly changes the test signals: downregulated receptor and upregulated cytokine. These adverse effects were reversed by GHRL.

Conclusion: Caerulein upregulated molecular signals for TNF-α and downregulated that for GHS-R1a in the pancreatic acini. This effect could be prevented by pretreatment of the AP rats with GHRL. Above mechanism could be implicated in the protective action of AP.

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

References

OP315 IDENTIFICATION AND CHARACTERISATION OF A NOVEL EARLY ONSET DIABETES GENE USING HUMAN PLURIPOTENT STEM CELLS

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Introduction: Diabetes represents one of the major burdens in the 21st century with 350 million people affected worldwide. Monogenic diabetes such as juvenile onset insulin-dependent diabetes (JOD) or maturity onset diabetes of the young (MODY) accounts for approximately 1–2% of diabetes cases and results from mutations that primarily reduce β-cell function. The identification of the genetic cause of these diseases has thus translated into novel avenues of personalized medicine in the diabetes field, but only few of these genes have been identified to date.

Aims & Methods: Based on published data, we hypothesize that a proportion of the variability contribution to type 1 diabetes (T1D) and type 2 diabetes (T2D) 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 genes.

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, Nkx.6 and Pax4, all belonging to the core suite of islet transcription factors. Importantly, this gene co-occupies the enhancer and promoter regions of the latter genes together with Foxa2, Pax4 and Gap46.

Finally, we engineered human embryonic stem cells with previously identified mutations in JOD patients. Directed differentiation studies of these cells shows a different binding pattern of Krox22, Nkx2.2, Nkx.6 and Pax4 ultimately 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 personalisation drug-testing but also sheds light on the mechanism how our JOD gene regulates pancreatic development and leads to diabetes in case of certain mutations in humans.

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

OP316 LACK OF CFTR RESULTS IN THE IMPAIRED FUNCTION OF THE PLASMA MEMBRANE CA2+ PUMP THAT CAUSES INTRACELLULAR CA2+ OVERLOAD AND MITOCHONDRIAL DAMAGE IN THE PANCREATIC DUCTAL EPITHELIAL CELLS OF CFTR KNOCK OUT MICE

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Introduction: The cystic fibrosis transmembrane conductance regulator (CFTR) has a significant role in pancreatic ductal epithelial secretion and it’s genetic defects damage the pancreas. The exact mechanism of this pancreatic damage is only partially known. The toxic cellular Ca2+ overload is a hallmark of acute pancreatitis and in CFTR-deficient airway epithelial cells the intracellular Ca2+ homeostasis was disturbed. However the Ca2+ homeostasis of CFTR-deficient pancreatic ductal epithelial cells (PDEC) has never been investigated.

Aims & Methods: Our aim was to characterize the Ca2+ homeostasis of CFTR-deficient PDEC. Pancreatic ducts and acinar cells were isolated from wild type (WT) and CFTR knockout (KO) mice. Intracellular Ca2+ concentration ([Ca2+]i) and changes of the mitochondrial membrane potential was measured.

Result: Maximal [Ca2+]i release upon carbachol stimulation showed no difference in WT and CFTR KO PDEC. Notably, the plateau phase of the Ca2+ signal was significantly higher in CFTR-deficient PDEC, but completely normal in pancreatogenic acinar cells. Interestingly, the functional inhibition of CFTR with 10µM CFTR(Rinh)-172 had no effect on the Ca2+ signals. Next we investigated the role of Ca2+ extrusion and found that the Ca2+ extrusion was significantly lower.
in CFTR KO PDEC compared to WT due to the impaired function of the plasma membrane Ca2⁺ pump (PMCA). In addition, the sustained elevation of [Ca2⁺]i caused a drop in mitochondrial membrane potential in CFTR KO PDEC.

Conclusion: Dysfunction of PMCA leads to disturbed Ca2⁺ homeostasis in CFTR-deficient PDEC and the consequent cellular Ca2⁺ 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 ENDOCYTIC 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 pancreaticoduodenectomy. Insertion of multiple plastic stents (MPS) obtained, in a series of 19 patients, symptomatic MPD stricture resolution in 84% of the cases, after 3-year follow-up (1) The aim of this study was to evaluate the results of the MPS strategy in a larger series of CP patients.

Aims & Methods: Forty-eight patients (34 men; mean age 44 years, range 5–86) with severe CP and a symptomatic dominant MPD stricture located in the head of the pancreas, were evaluated. All the patients experienced pain resolution following MPD drainage with a single plastic stent. The MPD stricture was refractory to single plastic stent placement in all cases and patients underwent insertion of MPS according to the following protocol: balloon dilation of the stricture of necessary, insertion of the maximum number of plastic stents allowed by the stricture tightness and pancreatic duct diameter, stents removal after 6 months.

Result: The median number of stents placed through the major or minor papilla was 3 (range 2–5), 8.5 to 11.5 Fr in diameter and 3 to 7 cm in length. MPS were removed after a mean time of 6.7 months (range 2–18). Eight patients (16.6%) had persistence of the MPD stricture after MPS removal and underwent replacement of an increased number of stents; 3/8 patients had a dilatation of the stricture and 5/8 patients had a stent placement (overall success 89.5%). Following a mean follow-up of 9.5 years (range 0.3–15.5) after MPS removal, 77.1% of patients were asymptomatic. Symptomatic MPD stricture recurrence was reported in 11 patients (22.9%), after a mean time of 26.4 months (range 5–108) from MPS removal. No major complications were recorded.

Conclusion: Endoscopic dilation of CP-related dominant MPD strictures seems possible with the MPS technique. According to this experience on 48 patients, MPS is highly effective even at long-term follow-up in the majority of patients. Disclosure of Interest: J.E. Dominguez-Munizo has acted as speaker and advisor international of Mylan and AbbV. All other authors have declared no conflicts of interest.

Reference

OP319 USE OF THE URINARY TRYPsinogen-2 DIPSTICK TEST IN EARLY DIAGNOSIS OF PANCREATITIS AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY
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Introduction: One of the most common complications (ERC) is acute pancreatitis. The reported incidence varies from 1.3% to 24.4% [1]. Measurement of serum amylase and lipase levels after the procedure may have a possible role for early recognition of post-ERC pancreatitis [3]. Asymptomatic elevation in serum amylase and lipase activities after ERC is common, occurring in approximately 25% to 75% of all patients. A rapid test strip has been developed for the detection of trypsinogen-2 in urine (The urinary trypsinogen-2 dipstick test—UT2DST test) (Pancreas 2007; 36: 6). The aim of this study was to assess the diagnostic value of the urinary trypsinogen-2 dipstick test for early diagnosis of post-ERC pancreatitis.

Aims & Methods: After an informed consent by the patients the selected patients were divided to: Full clinical examination (history-taking and clinical examination), laboratory investigations including (complete blood count (CBC), Bilirubin (total and direct), (ALT), (AST), alkaline phosphatase (ALP), Prothrombin time and internationalization (PT & PC), urea, creatinine, serum amylase, serum lipase, urinary trypsinogen-2 dipstick test (UT2DST).

Result: Post ERC UT2DST was negative in 30 patients of the non pancreatitis group (96.8%) and positive in one of them (3.2%). The test was positive in all patients with ERCP Pancreatitis (100%). UT2DST test was 100% the Specificity was 97% with PPV 86%, NPV 100% and the P value was <0.01. Comparison between serum lipase and amylase levels post ERCP in relation to UT2DST test shows that positive UT2DST test was significantly associated with higher amylase and lipase serum levels after ERCP (post amylase and post lipase) (P<0.01).

Conclusion: The urinary trypsinogen-2 dipstick test can be used as an easy and rapid test for early diagnosis of post-ERC pancreatitis with high sensitivity and specificity and can help clinicians to provide intensive care and possible medical treatment as early as possible.

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

References

OP337 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 malnutrition secondary to CP, but if PEI secondary to CP is associated with the risk of CVD and cardiovascular (CV) events is unknown.

Aims & Methods: Aim 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, with and without PEI, was carried out. Unit of diagnosis of CP was based on endoscopic ultrasound (EUS), magnetic resonance cholangio-pancreatoctrophy (MRCP) and pancreatic MRI. PEI was defined as the need of pancreatic enzyme replacement therapy due to the presence of malabsorption-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, 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 5 patients (9.5%). 22 patients (4.8%) suffered from a major 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=5, 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-Munizo has acted as speaker and advisor international of Mylan and AbbV. All other authors have declared no conflicts of interest.

References
Conclusion: Aggressive hydration with lactated Ringer's solution is more effective than standard hydration for prevention of post-ERCP pancreatitis.

Result: 13% (9/70) in the aggressive hydration with physiologic saline group (6.7%, 9/134) and 11.6% (15/129) in the standard hydration group (11.6%, 15/129, P = 0.167, 15/129, P = 0.167, 15/129, P = 0.167, 15/129, P = 0.167, 15/129, P = 0.167, 15/129, P = 0.167, 15/129, P = 0.167). The intention-to-treat and PP post-ERCP pancreatitis were not found between the aggressive hydration with physiologic saline group (6.7%, 9/134) and 11.6% (15/129) in the standard hydration group (11.6%, 15/129, P = 0.167). No significant differences in the intention-to-treat and PP post-ERCP pancreatitis were found between the three groups.

Conclusion: Aggressive hydration with lactated Ringer’s solution is more effective than standard hydration for prevention of post-ERCP pancreatitis.

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Disclosure of Interest: D Domagk: Dirk Domagk has received research support from Merck, honoraria for lectures from Olympus Europe and Dr. Falk Foundation, and has served as consultant for Hitachi Medical Systems and AbbVie Inc.

A. Antonini: Angelo Antonini has received research support from Mundipharma and compensation fromUCB, Boston Scientific, Boheringer-Ingehelm, AbbVie Inc., and Zambon for serving as a consultant and lecturer.

L. Bergmann: Lars Bergmann is an employee of AbbVie Inc. and hold stock or stock options.

A. Yegin: Ashley Yegin is an employee of AbbVie Inc. and holds stock or stock options.

P. Poeewe: Dr. Poeewe: royalties from Thieme, Wiley Blackwell, Oxford University Press; compensation decreased from AbbVie, Astra Zeneca, Teva, Novartis, GSK, Boehringer-Ingehelm, UCB, Orion Pharma, Zambon, Merz Pharmaceuticals for consulting and lecturing.

All other authors have declared no conflicts of interest.

References


OP322 ENDOSCOPICALLY ASSISTED PERCUTANEOUS TRANSGASTROEPHAGEAL GASTROTUBING (PTEG) AND THE PROGRESS

M Murakami1, K Nishino2, S Murakami2, K Mori2, B Murakami2, M Azuma2, S Tanabe1, M Kida1, W Koizumi1, J, and 258 (68%) completed the 24 month follow-up. The median [range] duration of exposure via NJ was 6.0 [1, 53] days (n = 307) and via PEG-J was 722 [1, 957] days (n = 351). During titration via NJ, there were 3 patients (0.8%) who had ≥ 1 GI related ADR. Within the 24 months of treatment post-PEG-J placement (n = 356) ≥ 1 GI related ADR was reported in 139 patients (39%), of which procedure-related ADRs were reported in 35 patients (9.8%), device-related in 93 (26%), other GI events in 63 (18%); the ADRs in all GI categories reported for ≥ 1 patients were weight decreased (6.7%), device related infection (5.9%), device dislocation (4.8%), device issue (4.8%); and the serious ADRs reported for ≥ 2% patients were device dislocation (2.2%) and device issue (2.0%). During the 28-day follow up period, there were 4 patients (1.1%) who had ≥ 1 GI related ADR. The device was discontinued in the discontinuation of 10 patients (2.8%) overall, 2 of whom discontinued due to a procedure-related ADR, 5 due to a device-related ADR, and 3 due to another type of GI ADR. Of the 29 deaths reported, 23 were deemed unrelated to treatment, 5 possibly related (to device) and 1 probably related (to tubing). Of the possibly/probably related deaths, 2 had GI related events, 1 had a small bowel obstruction and died approximately 3 weeks later of unknown causes, and 1 had a small bowel perforation and peritonitis.

Conclusion: Most GI-related ADRs were related to the device in this registry. The incidence of GI-related ADRs and discontinuations due to GI-related ADRs were relatively low, which is supportive of the overall tolerability of LCIG and consistent with previous studies.

Disclosure of Interest: D Domagk: Dirk Domagk has received research support from Merck, honoraria for lectures from Olympus Europe and Dr. Falk Foundation, and has served as consultant for Hitachi Medical Systems and AbbVie Inc.

A. Antonini: Angelo Antonini has received research support from Mundipharma and compensation from UCB, Boston Scientific, Boheringer-Ingehelm, AbbVie Inc., and Zambon for serving as a consultant and lecturer. L. Bergmann: Lars Bergmann is an employee of AbbVie Inc. and hold stock or stock options.

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All other authors have declared no conflicts of interest.

References


OP324 INCREASED MUCOSAL EXPRESSION OF TOLL-LIKE RECEPTORS IN ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: An adaptive Th2-type immune response to food antigens is involved in eosinophilic esophagitis (EoE). Evidences of a potential role for the innate immune system in the pathogenesis of EoE are emerging. Our study analysed the role of Toll-like receptors (TLRs) in adult patients with eosinophilic esophagitis (EoE) and compared them with healthy controls.

Aim: To evaluate the expression of TLRs in the esophageal mucosa of adult patients with EoE compared to healthy controls.

Methods: We included 60 adult patients with EoE (35 male, 25 female, mean age of 43 years) and 60 healthy controls (HC; 35 male, 25 female, mean age of 42 years). A four-food elimination diet (SFED) was performed to rule out any food trigger in both groups. Thereafter, endoscopic biopsies were obtained from the mid-oesophagus and submucosa, and expression of TLR1, TLR2, TLR3, TLR4, TLR6, and TLR9 was analyzed by qRT-PCR. Differences were assessed by non-parametric methods (Mann-Whitney U test).

Results: Expression of TLR1 and TLR9 was significantly higher in EoE patients compared to HC controls (p < 0.001). No significant differences were observed for TLR2, TLR3, TLR4, and TLR6.

Conclusion: Our findings indicate that the expression of TLR1 and TLR9 is increased in the esophageal mucosa of adult patients with EoE compared to healthy controls. This study highlights the potential role of TLR1 and TLR9 in the pathogenesis of EoE and suggests that targeting these receptors could be a potential therapeutic strategy.
**OP325 A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF COMBINATION TREATMENT WITH THE INTERLEUKIN-13 MONOCONAL ANTIBODY (RPC4046) IN PATIENTS WITH ACTIVE EOSINOPHILIC OESOPHAGITIS: RESULTS OF THE HEROES STUDY**

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**Introduction:** Interleukin-13 (IL-13) has been implicated in the pathogenesis of eosinophilic oesophagitis (EOE). RPC4046 prevents the binding of IL-13 to both the IL-13Rα1 and IL-13Rα2 receptors. This study evaluated the efficacy and safety of 2 dose levels of RPC4046 compared to placebo (PBO).

**Aims & Methods:** Patients were randomized 1:1:1 to receive either RPC4046 180 mg (LD) (n = 31), RPC4046 360 mg (HD) (n = 34), or PBO (n = 34). An IV day on Day 1 was followed by weekly subcutaneous doses. Oesophageal biopsies, read by a central blinded pathologist, were obtained at baseline (BL) and Weeks 4 and 16. In mean eosinophil counts, 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 127.2 (HD). HD showed a mean count was significantly reduced from BL, for both RPC4046 dose levels compared to PBO (mean change: PBO –4.4, LD –94.8, and HD –99.9 [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 –6.4, LD –5.3 [p = 0.006 vs PBO], and HD –13.3 [p = 0.073 vs PBO]). There were 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 –1.5, LD –2.0, HD –2.8 [HD p = 0.0107 vs PBO]). The rates of overall adverse events (AEs) were 64.7% (PBO), 64.5% (LD), and 85.3% (HD). The most frequent AEs were headache (PBO 14.7%, LD 20.6%, HD 20.6%), upper respiratory infection (PBO 5.8%, LD 16.1%, HD 14.7%), and arthralgia (PBO 6%, LD 12.9%, HD 5.9%).

**Conclusion:** RPC4046 demonstrated significant reductions in eosinophilic inflammation and improvements in endoscopic features at both dose levels in subjects with EOE, and HD had greater symptom improvement than LD in this phase of study. 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 to Receptos, Regeneron, Shire Pharma
M. Collins: I have received research funds (through contracts) from Receptos, Shire Pharma and Meritage Pharma,
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; AstraZeneca, AG; Apteos Pharma; GSK, AG; Nestle S. A.; Novartis, AG; Pfizer, AG, and Regeneron
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**Introduction:** Hypersensitive esophagus (HE) is defined by endoscopy-negative heartburn with normal esophageal acid exposure time (EAET) but positive symptom-reflux association probability (SAP) and symptom index (SI) at reflux monitoring, and/or heartburn suppression with proton pump inhibitor (PPI) therapy. Functional heartburn (FH) is distinguished by PPI-refractoriness and negative SAP/SI. However, diagnostic accuracy of SAP and SI has been recently questioned. We aimed to investigate whether HE was hyperacidity and HE distinguished from FH/HE based on symptom-reflux association analysis only.

**Aims & Methods:** We aimed to investigate whether diagnostic clear- express, by post-reflux swallow-induced peristaltic wave (PSPW) index, and/or mucosal baseline impedance (MBNI), distinguish FH from HE independently from SAP and SI. Impedance-pH tracings from 303 patients with PPI-dependent (i.e. heartburn repeatedly abolished by 4-week PPI-therapy and repeatedly recurring after PPI withdrawal) or PPI-refractory (i.e. ≤ 50% of symptom relief after 8-week high-dose 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), characteristics of reflux episodes (acid/weakly acidic) and symptom-reflux association using both SAP (positive if ≥95%) and SI (positive if ≤0.50). MBNI values were calculated as the mean NBI over 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.

**Conclusion:** HE, FH, normal EAET HE (normal EAET, but positive symptom-reflux correlation) and symptom index (SI) with normal EAET HE (normal EAET, but positive symptom-reflux correlation) and symptom index (SI) were the most sensitive impedance parameters; at multivariate analysis, they were independent predictors of HE. At receiver operating characteristic analysis, PSPW index with MBNI efficiently separated HE from FH the area under the curve (AUC) was 0.943 (P < 0.0001 vs PBO). There was a significant improvement in Subject's Global Assessment of Disease Severity as determined by the reduction in the mean EREF score with both RPC4046 dose levels (mean change: PBO –9.0, LD –4.2, and HD –4.8 [both p < 0.0004 vs PBO]). There was a significant improvement in Subject's Global Assessment of Disease Severity at the HD (PBO –1.5, LD –2.0, HD –2.8 [HD p = 0.0107 vs PBO]). The rates of overall adverse events (AEs) were 64.7% (PBO), 64.5% (LD), and 85.3% (HD). The most frequent AEs were headache (PBO 14.7%, LD 20.6%, HD 20.6%), upper respiratory infection (PBO 5.8%, LD 16.1%, HD 14.7%), and arthralgia (PBO 6%, LD 12.9%, HD 5.9%).

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

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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 (MBNI), were the most sensitive impedance parameters; at multivariate analysis, they were independent predictors of HE. At receiver operating characteristic analysis, PSPW index with MBNI efficiently separated HE from FH the area under the curve (AUC) was 0.943 (P < 0.0001 vs PBO). There was a significant improvement in Subject's Global Assessment of Disease Severity as determined by the reduction in the mean EREF score with both RPC4046 dose levels (mean change: PBO –9.0, LD –4.2, and HD –4.8 [both p < 0.0004 vs PBO]). There was a significant improvement in Subject's Global Assessment of Disease Severity at the HD (PBO –1.5, LD –2.0, HD –2.8 [HD p = 0.0107 vs PBO]). The rates of overall adverse events (AEs) were 64.7% (PBO), 64.5% (LD), and 85.3% (HD). The most frequent AEs were headache (PBO 14.7%, LD 20.6%, HD 20.6%), upper respiratory infection (PBO 5.8%, LD 16.1%, HD 14.7%), and arthralgia (PBO 6%, LD 12.9%, HD 5.9%).

**Conclusion:** RPC4046 demonstrated significant reductions in eosinophilic inflammation and improvements in endoscopic features at both dose levels in subjects with EOE, and HD had greater symptom improvement than LD in this phase of study. These phase 2 data support the further study of RPC4046 as a novel treatment for EOE. (clinicaltrials.gov ID: NCT02098473)
investigating PPI-refractory patients studied off-therapy, further improving the management of these patients.

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-thrapy impedance-pH tracings from consecutive patients referred for PPI-refractory heartburn with/without regurgitation (< 50% of symptoms resolved) healing after blank high-dosage PPI therapy were blindly reviewed. All tracings were manually analyzed to detect: acid exposure time (AET; abnormal if > 12.5% over 24 hours), characteristics of reflux episodes (acid/weakly acidic and symptom-reflux association using both symptom association probability (SAP; positive if > 35%) 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 found to be abnormal on acid and peristaltic waves with the number of total refluxes. Patients were subdivided into refractory reflux esophagitis (RRE), healed reflux esophagitis (HRE), non-erosive reflux disease (NERD; defined by abnormal acid exposure time or normal AET but positive symptom-reflux correlation) and functional heartburn (defined by hyperacidity and negative symptom-reflux correlation) according to endoscopy and conventional impedance-pH variables.

Result: Median PSPW index and MNBI were significantly lower in 39 RRE (16%; 1145 Ohms) than in 41 HRE (25%; 1741 Ohms) and in 68 NERD (29%; 2374 Ohms) patients, and in all three GERD subgroups compared to 41 FH cases (67%; 3488 Ohms) (P = 0.0001). Comparing NERD to FH, PSPW index and MNBI increased more than more than those in RRE and NERD at 6 months in patients with alcoholic-related greater than those in NERD at recurrence according to a characteristic analysis (0.886 vs. 0.867, P = 0.005). PSPS 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 9.03, P = 0.01).

Conclusion: At on-therapy impedance-pH monitoring, impaired chemical clearance and mucosal integrity characterize PPI-refractory typical GERD. PSPW index and MNBI efficiently distinguish PPI-refractory NERD from FH and PSPW index is recommended for selecting surgical candidates.

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

OP328 PRELIMINARY RESULTS OF A PROSPECTIVE MULTI-CENTER REGISTRY OF LOWER ESOPHAGEAL SPHINCTER STIMULATION FOR GERD: THE LESS-GERD REGISTRY

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Introduction: Safety and effectiveness of electrical stimulation of the lower esophageal sphincter (LES) using the EndoStim® LES Stimulation System (The Hague, The Netherlands) was 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), structural and symptomatic outcomes, use of proton pump inhibitors (PPIs) and physiological data (esophageal pH/mannometry) are collected when available.

Result: Data was available in 50 patients enrolled in eleven sites with 6 months post-op follow up from 28 patients with 12 months follow-up. Ninety-five (43/44% of patients) had no or minimal improvement in their heartburn symptoms 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 22 (15.5-25) at baseline to 5 (0-10.5) at 6 months (P < 0.001) and from 20 (12.5-22.5) 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) in 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 from 40 patients who had hospitalization data available for their 6 visit (<1 m). Annualized hospitalization rates due to GERD were 1/100 patient-years (n = 40) and 15 (18.4%) reported at least one hospitalization due to GERD which at last follow up decreased to 0.3 days/year with 83% of patients who were required hospitalization pre-op reporting no hospitalization post-op. All patients were on long-term PPI at baseline. Seventy-one (45/63) patients at 6 month and 75% (27/36) patients at 12 months were completely off PPI. Data on 24h esophageal pH at 6 m showed a non-statistically significant improvement. Safety data was adjudicated by an independent DSMB. Four serious adverse events in the whole cohort were reported which were considered unrelated to the LES stimulation procedure.
Conclusion: In our 16-year cohort with long-term surveillance, the incidence of PanIN was highest in moderately differentiated MCNs but majority of detected cancers were asymptomatic and resectable. Surveillance also detects early stage PanNETs and HCPLCs. 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 pancreatic parenchyma (atrophy/inflammation/fibrosis) was also examined.

Result: Among patients with EUS-CP findings, invasive intraductal papillary mucinous carcinoma (IPMC) was significantly more frequent than among patients without EUS-CP findings (42.5% (17/40) vs. 3.4% (1/29), p = 0.0002). In addition, patients with EUS-CP findings had higher grades of pancreatic atrophy and inflammation than patients without EUS-CP findings (atrophy: 72.5% (29/40) vs. 34.5% (10/29), p = 0.003, inflammation: 45.0% (18/40) vs. 20.7% (6/29), p = 0.04).

Conclusion: In IPMN patients, detection of EUS-CP findings in the background pancreatic parenchyma was associated with a higher prevalence of invasive IPMC. Accordingly, EUS examination should not only assess the morphological features of the lesion itself, but also EUS-CP findings in the background parenchyma.

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

OP331 NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY (nCLE) FOR THE DIAGNOSIS OF SOLITARY PANCREATIC CYSTS: A PROSPECTIVE MULTICENTER STUDY

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Introduction: Diagnosis of solitary pancreatic cysts is clinically challenging due to the malignant potential of several cyst subtypes. nCLE is emerging as a powerful tool for the diagnosis of solitary pancreatic cysts. This study aims to prospectively evaluate the diagnostic performance of nCLE for the diagnosis of solitary non-communicating PCL which represent the main diagnostic issue. Being able to precisely discriminate between benign (sCA) or malignant cysts (sMCN), nCLE procedure would improve patient management by avoiding either repeated follow-up procedures or unnecessary resections due to diagnosis uncertainties. nCLE procedures should now be included in the guidelines.

Aims & Methods: Clinical data for 69 consecutive patients with IPMNs who underwent preoperative EUS and surgical resection between April 2010 and October 2014 were collected prospectively. The association of EUS-CP findings (total number of EUS-CP findings: 0 vs. ≥1) with invasive IPMN was examined. The association of EUS-CP findings with pathological changes of the background pancreatic parenchyma (atrophy/inflammation/fibrosis) was also examined.

Result: Among patients with EUS-CP findings, invasive intraductal papillary mucinous carcinoma (IPMC) was significantly more frequent than among patients without EUS-CP findings (42.5% (17/40) vs. 3.4% (1/29), p = 0.0002). In addition, patients with EUS-CP findings had higher grades of pancreatic atrophy and inflammation than patients without EUS-CP findings (atrophy: 72.5% (29/40) vs. 34.5% (10/29), p = 0.003, inflammation: 45.0% (18/40) vs. 20.7% (6/29), p = 0.04).

Conclusion: In IPMN patients, detection of EUS-CP findings in the background pancreatic parenchyma was associated with a higher prevalence of invasive IPMC. Accordingly, EUS examination should not only assess the morphological features of the lesion itself, but also EUS-CP findings in the background parenchyma.

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

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 or black particles” for Pseudocyst (PC). In case of doubt between IPMN and MCN, un-determined Macron cystic lesion (UML) was proposed. The absence of criteria led to inconclusive nCLE diagnosis considered as false-negative. Nine patients were withdrawn for screen failure (n = 6) or procedure failure (n = 3). Among the 208 analyzable patients, final diagnosis was proven in 90 cases by cytopathological analysis of cystic fluid obtained by FNA (n = 50) or by surgical histopathology (n = 31). Statistical analysis of nCLE performance was done for cysts sufficiently represented.

Result: Among the 217 nCLE procedures, 98.6% were successfully performed. Two patients were lost to further follow up in the cohort. nCLE procedure improves patient management by avoiding either repeated follow-up procedures or unnecessary resections due to diagnosis uncertainties. nCLE procedures should now be included in the guidelines.

Disclosure of Interest: B. Napoleon: Dr. Napoleon reports non financial support from Mauna Kea Technologies, Grants from Mauna Kea Technologies; personal fees from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work. L. Palazzo: Dr. Palazzo reports non financial support from Mauna Kea Technologies, during the conduct of the study. B. Pujol: Dr. Pujol reports non financial support from Mauna Kea Technologies, Grants from Mauna Kea Technologies; personal fees from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work. M. Giovannini: Dr. Giovannini reports non financial support from Mauna Kea Technologies, Grants from Mauna Kea Technologies, during the conduct of the study; personal fees from Mauna Kea Technologies, outside the submitted work.

References

surveillance. Our aim was to understand which baseline cyst and patient features predict disease progression and malignant transformation.

Aims & Methods: Patients with clinically suspected IPMN who did not meet consensus criteria for resection at diagnosis and were surveyed for at least 12 months or underwent surgery after a minimum surveillance of 3 months were included. All patients evaluated by radiologic studies or endoscopic ultrasound between 1998 and 2015 were included. We defined progression as either an increase in size of the dominant cyst ≥20% or ≥2mm or the development of worrisome features (mural nodule or mass, thick septations, main duct involvement or high grade dysplasia or cancer on cystic or surgical pathology). Statistical analysis was performed with the Chi square and Fisher exact tests. There were no baseline predictors of cyst size increase alone. Baseline characteristics such as race, smoking or alcohol use, a strong family history of PDAC, multifocality and location of cysts were not associated with increased disease progression.

Conclusion: In the largest multicenter surveillance study of low risk IPMNs to date, we showed that 41% of suspected IPMNs increased in size only, 9% developed worrisome features and 2% developed high-grade dysplasia or cancer. Among baseline characteristics, none were predictive of size increase. A personal history of prostate cancer and weight loss were the strongest predictors of the development of worrisome features.

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

OP333 MULTIMODALITY TREATMENT OF LOCALLY ADVANCED Pancreatic cancer, including FOLFIRINOX CHEMOTHERAPY, SURGICAL EXPLORATION AND IRREVERSIBLE 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 chemotherapy (59% FOLFIRINOX). After 3 months, 59 (45%) had non-progressive disease and 36 (27%) were IRE-eligible and underwent laparotomy, resulting in 14 (11%) pancreatic resections and 15 (11%) IREs. In 36 patients who underwent laparotomy, IRE-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.

Contact: This is the first prospective study on multimodality treatment, including FOLFIRINOX and IRE, in a consecutive LAPC-cohort. An 11% resection-rate with a median overall survival of 34 months seems highly promising where no clear survival benefit was seen after IRE. This study highlights the importance of reporting on unselected LAPC-cohorts.

Disclosure of Interest: R.C. Martin: Prof. Dr. Marin is a paid consultant for AngioDynamics. K.P. van Lienden: Dr. Krijn van Lienden is a paid consultant for AngioDynamics. All other authors have declared no conflicts of interest.
WP334-WORLDWIDE MULTIDISCIPLINARY ONLINE EXPERT PANEL FOR PRACTICAL CLINICAL RESEARCH RESULTS

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Introduction: Gastrointestinal disorders can be debilitating and may have a significant impact on the quality of life of patients. The centralization of care in gastroenterology may improve patient outcomes. The Dutch Pancreatic Cancer Group (DPCG) aimed to develop an online expert panel to facilitate and tailor rapid expert advice for patients with (locally advanced) pancreatic cancer. In collaboration with Aexist (The Hague, the Netherlands) we developed the ImageHub system which allows for secure review of CT scans. Next, a nationwide multidisciplinary expert panel for pancreatic cancer consisting of surgeons, (interventional) radiologists and medical oncologists was installed. This study prospectively analyses the first patients who were referred to the online expert panel between June 2015 and February 2016.

Result: A total of 59 patients from 7 centers were referred to the expert panel. All had locally advanced pancreatic cancer and in 46% (27/59) of the patients this led to an additional treatment or a change in treatment strategy. A resection with curative intent was performed in 5 patients (8%) and 21 patients (42%) were included in a clinical trial, investigating local ablative therapies. In all cases the expert panel advice was provided within one week.

Conclusion: The results show that an online expert panel is feasible and changed the treatment strategy in almost half of the patients with locally advanced pancreatic cancer. Future studies have to determine the impact of an online expert panel on the accessibility of new treatment strategies, survival and quality of life.

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

Wednesday, October 19, 2016 08:30–10:00

CONSTITUTION AND FECAL INCONTINENCE: FROM BENCH TO BEDSIDE – ROOM N2

OP335 ORAL ADMINISTRATION OF THE GUT-RESTRICTED GLYCLATE CYCLASE-C AGONIST, LINACLOTIDE, REDUCES ENDOMETRIOSIS-INDUCED VAGINAL HYPERALGESIA

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Introduction: Linacotide, a guanylate cyclase-C (GC-C) agonist, reduces abdominal pain and improves constipation in patients with Irritable Bowel Syndrome with Constipation (IBS-C). We have shown that linacotide activates GC-C expressed on intestinal epithelial cells, resulting in the production and release of cyclic GMP (cGMP), which accelerates gastrointestinal transit and inhibits the development of intestinal secretory alterations. As key components of 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. 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 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 (GUC2A, GUC2B), PDZ3 proteins regulating GC-C activity (PDZD33), CGMP-dependent protein kinases (PRKG2), phosphodiesterases (PDE3A, PDE3B), components involved in ionic secretion (PDZK1, SLC9A2, SLC9A3, SLC26A3, CFTR) and transporters of cGMP (ABCC3, ABCC5).

Result: We compared female healthy controls (N = 12, mean age 36.4 yrs) with IBS patients with constipation (N = 12, mean age 36.2 yrs), IBS patients with diarrhea (N = 12, mean age 36.2 yrs) and patients with chronic idiopathic constipation (CIC) (N = 12, mean age 36.3 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/GMP pathway components compared with healthy controls (P > 0.05). Similarly, biopsies from IBS-D and IBS-M patients did not display any significant alterations 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 protein kinase activity which may be related to the reduced cGMP 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 pathophiology associated with IBS-C.

Disclosure of Interest: G. Hannig: Employee, stock holder and stock options from Ironwood Pharmaceuticals Inc.

C.B. Kurtz: Employee, 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 (e.g. gastroenterologists, 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 constipated) and 534 GI specialists were surveyed. The majority 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 manual disimpaction (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</th>
<th>Constipation</th>
<th>Constipation specialists</th>
<th>GPs</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrequent bowel movements</td>
<td>28%</td>
<td>26%</td>
<td>65%</td>
<td>41%&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hard stool</td>
<td>26%</td>
<td>32%</td>
<td>57%</td>
<td>66%&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Straining</td>
<td>43%</td>
<td>40%</td>
<td>53%</td>
<td>61%&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sense of incomplete evacuation</td>
<td>15%</td>
<td>24%</td>
<td>21%</td>
<td>13%&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual disimpaction</td>
<td>14%</td>
<td>15%</td>
<td>32%</td>
<td>34%&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Rome III symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long time on toilet without stool</td>
<td>42%</td>
<td>29%</td>
<td>33%</td>
<td>23%&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laxative use</td>
<td>37%</td>
<td>33%</td>
<td>56%</td>
<td>40%&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The symptoms most frequently considered to be bothersome were different for each of the groups: manual disimpaction for the constipated general population, bloating for GI specialists and straining for GPs. In the 10 case studies, correct diagnoses were made by doctors (GPs and GI specialists) on 79–80% of occasions. However, on average, the patients’ diagnosis was correctly identified by doctors in 85–92% of the six cases without constipation, whereas the presence of constipation was correctly identified in only 60–70% of the four cases with constipation.

Conclusion: There are striking differences in the perceived definition and burden of symptoms of constipation between the general population, GI specialists and GPs, and variable agreement with the Rome III criteria. These differences have major implications for patient care, management and satisfaction with treatment. The findings reinforce the need to re-evaluate current diagnostic criteria for constipation in clinical practice and to ensure these are communicated widely.

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

OP338 EFFICACY AND SAFETY OF NALDEMEDINE FOR THE TREATMENT OF OPPIED-INDUCED CONSTIPATION IN SUBJECTS WITH CHRONIC NON-CANCER PAIN RECEIVING OPIOID THERAPY: RESULTS FROM TWO PHASE 3 CLINICAL TRIALS

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Introduction: Opioids effectively treat pain but their use is limited by side effects including opioid-induced constipation (OIC). Naldemedine is an oral, peripherally-acting mu-opioid receptor antagonist that is being evaluated for the treatment of OIC.

Aims & Methods: Two identical Phase-3, double-blind, randomized, placebo-controlled 12-week studies were conducted. In both studies, subjects 18 to 80 years old with chronic non-cancer pain and OIC, taking opioids for ≥3 months and on a stable regimen for ≥1 month, not on laxatives, and meeting all other eligibility criteria were randomized (1:1) to naldemedine 0.2 mg taken orally QD or placebo. The primary objective was to evaluate the efficacy of naldemedine vs. placebo as assessed by the proportion of responders. A responder was defined as someone who had ≥9 positive response weeks (PRW) out of 12 weeks and ≥3 PRW out of the last 4 weeks. A PRW was defined as ≥3 spontaneous bowel movements (SBMs)week and ≥1 SBM week increase from baseline. The safety and tolerability of naldemedine was also assessed. Studies were approved by an IRB prior to randomization of subjects and conducted in accordance with GCP Guideline (ClinicalTrials.gov identifier NCT01963518 and NCT01993940).

Results: 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 = 0.0001). Naldemedine resulted in a greater increase in the frequency of SBMs per week from baseline to Week 1 was observed with naldemedine relative to placebo and this difference remained generally stable between the two groups throughout the 12-week study period. The responder group also showed a significantly greater increase, relative to the placebo group, from baseline to the last 2 weeks of the study period in the frequency of complete SBMs and the frequency of SBMs without straining. Summary measures of treatment-emergent adverse events (TEAEs) were generally similar between naldemedine and placebo groups in both studies. The TEAEs reported for >5% of subjects and at a higher frequency in naldemedine relative to placebo were abdominal pain and diarrhea. In both studies, treatment with naldemedine was not associated with signs or symptoms of opioid withdrawal, and the analgesic effect of opioids was not affected.

Conclusion: Results from two identically designed Phase 3 studies demonstrated a consistent efficacy and safety profile of naldemedine as a treatment for OIC in subjects with chronic non-cancer pain. Naldemedine treatment resulted in a significantly greater proportion of responders than placebo, with improvement early on and throughout the 12-week study period. Naldemedine was generally well tolerated in these two studies.

Disclosure of Interest: M.E. Hale: I was a Principle Investigator for the Clinical Trials, and a consultant for Shionogi. J. Wild: 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 the clinic nurse, we suggested three screening questions. We also gave


A. Silos-Santiago: Employee, stock holder, and stock options from Ironwood Pharmaceuticals Inc and Devcel Therapeutics.
L. Chang: Scientific advisory boards or consultation for AstraZeneca, Synergy, Ardelyx, Ironwood, Bioamerica, Takeda, Allergan, Commonwealth Labs, QOL Medical, Salix, and Drais.
S.M. Bierley: Research support: Ironwood Pharmaceuticals Inc., Takeda Pharmaceuticals Inc., Key Pharmaceuticals Inc. All other authors have declared no conflicts of interest.

S.M. Bierley: Research support: Ironwood Pharmaceuticals Inc., Takeda Pharmaceuticals Inc., Key Pharmaceuticals Inc. All other authors have declared no conflicts of interest.

Pharmaceuticals Inc., Key Pharmaceuticals Inc. Takeda, Allergan, Commonwealth, Devcel Therapeutics.
L. Chang: Scientific advisory boards or consultation for AstraZeneca, Synergy, Ardelyx, Ironwood, Bioamerica, Takeda, Allergan, Commonwealth Labs, QOL Medical, Salix, and Drais.
S.M. Bierley: Research support: Ironwood Pharmaceuticals Inc., Takeda Pharmaceuticals Inc., Key Pharmaceuticals Inc. All other authors have declared no conflicts of interest.
Faecal incontinence (FI) is a common and devastating condition that significantly impacts 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, and the perceived overall effectiveness of individuals' coping strategies. The study employed a cross-sectional survey approach among a sample of 182 consecutive patients attending a community-based gastroenterology clinic in 2016 who reported symptoms of FI occurring at least twice per month. The symptom severity was defined as mild (3.32 for non-consulters vs. 4.28 for consulters, p < 0.001), moderate, and severe (4.17 for consulters). The impact of FI severity on ways of coping was examined using a list of 15 coping strategies and free-text fields. Symptom severity was defined as mild (3.32 for non-consulters vs. 4.28 for consulters), moderate, and severe (4.17 for consulters).

Results: Of 182 consecutive patients attending a community-based gastroenterology clinic in 2016 who reported symptoms of FI occurring at least twice per month, 136 (75%) were female and the mean age was 51.3 years. The median number of coping strategies used was 3 (range: 1–13). The most commonly reported strategies were the use of pads (111/182, 61%), but the strategy reported by 61% of patients was using pads, of whom had been during their clinic visit. A p-value of < 0.10 accepted as significant in this small pilot study.

Conclusion: Systematically encouraging geriatric medicine providers to screen for FI significantly increased the number of patients receiving a new diagnosis of FI compared to baseline. Most geriatricians perceived the benefits outweighing the burden. Distributing a GI symptom checklist in the clinic was rated least burdensome and was as effective as direct screening by the geriatrician. However, these interventions to improve screening were only partially effective: 37.5% of patients remained uncertain about being asked to consult a physician at their clinic visit.

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

References

Disclosure of Interest: results in better management of intraprocedural and early complications. There is a higher rate of intraprocedural and early complications in HER, p = 0.001. Early complications (Haemorrhage, perforation, pancreatitis) occurred in 46% of ESD/HER vs 23% in EMR (p = 0.07). Intra-procedural complications occurred in terms of age, sex, location of lesions or length of hospitalization. adenocarcinomas, 34% HGD, and 60% LGD. No significant differences were observed in an Australian tertiary center. apartmenting in a single tertiary center, we cross-examined our database of endoscopic procedures to identify patients with duodenal adenoma treated by ESD, HER and EMR between 2006 and 2016. We included patients with non-ampullary lesions and familial adenomatous polyposis. Procedure was qualified as ESD when an endoscopic knife was used. When resection was achieved with endoscopic knife and resection loop, the procedure was considered as HER. We divided complications in 3 groups (ASGE and ESGE recommendations): intra-procedural, early complications (occurring within 15 days) and late complications (occurring after 15 days). Results were expressed as medians, and compared with Student’s-t test, Pearson’s chi-squared test. Results: Thirty-eight patients underwent ESD/HER procedure out of a total of 111 patients. The resection was complete in 38/39 lesions in ESD/HER group, and 141/149 lesions in EMR group (p = 0.182). Histological finding showed 4% adenocarcinomas, 34% HGD, and 60% LGD. No significant differences were observed in terms of age, sex, location of lesions or length of hospitalization. There were significant differences in the procedure time (108 min ESD/HER, 79 min EMR), 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 in 25.6%, EMR 20.1% and perforation (ESD 20.5%, EMR 3.4%, p = 0.07). In HER, perforations occurred between 2006 and 2010. Early complications (Haemorrhage, perforation, pancreatitis) occurred in 23% ESD/HER vs 9% in EMR (p = 0.001), managed either by medical treatment. Five cases of perforation occurred (4 ESD/HER, p = 0.001) and 2 cases needed surgery. Three cases of late complications (stenosis) occurred in the EMR group. No mortality reported during the study. Conclusion: There is a higher rate of intra-procedural and early complications in the ESD/HER group, especially in case of perforation. Those events can be well managed in a tertiary center, experienced in ESD and HER. Perforation rate tends to decrease over time, reflecting the experience acquired in our team. This highlight the importance of a learning process in ESD/HER procedure, which results in better a graspment of intra-procedural and early complications.

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

References
OP344 WATERJET SUBMUCOSAL DISSECTION OF PORCINE ESOPHAGUS WITH THE HYBRIDKNIFE® AND ERBEJECT® 2 SYSTEM


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Introduction: The recent advancement of endoscopic submucosal dissection (ESD) is technically difficult because of narrow working spaces and ease of perforation due to the lack of serosa. HybridKnife® is a recently developed ESD device that is combined with the high-pressure waterjet ERBEJECT® 2 system to lift mucosa. We hypothesized that this waterjet could make submucosal dissection safer and studied this in porcine esophagus.

Aims & Methods: Water pressures of 30–70 bar were tested to determine the 1.1, 0.5, and 1.0 cm2/min in C-ESD, respectively. Minor bleeding Water pressures of 30–70 bar were tested to determine the died this in porcine esophagus.

Conclusion: WJ-ESD (4, 6, and 8%) compared with C-ESD (14, 16, and 7%).

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

References:

of 69% for lymph node involvement when restaging, inferior to what was found for EUS and for the initial staging (p < 0.0001).

### TABLE 1: Accuracy of EUS and PET vs Histology

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>50%</td>
<td>98.5%</td>
<td>75%</td>
<td>95.7%</td>
<td>94.5%</td>
</tr>
<tr>
<td>T2</td>
<td>41.7%</td>
<td>88.5%</td>
<td>41.7%</td>
<td>88.5%</td>
<td>80.8%</td>
</tr>
<tr>
<td>T3</td>
<td>38.5%</td>
<td>86.5%</td>
<td>50%</td>
<td>80%</td>
<td>74%</td>
</tr>
<tr>
<td>T4</td>
<td>77.3%</td>
<td>61%</td>
<td>61%</td>
<td>77.3%</td>
<td>68%</td>
</tr>
<tr>
<td>T4a</td>
<td>76.2%</td>
<td>65.5%</td>
<td>61.5%</td>
<td>75%</td>
<td>70%</td>
</tr>
<tr>
<td>T1-T2/T3-T4</td>
<td>87.3%</td>
<td>50%</td>
<td>84.2%</td>
<td>56.3%</td>
<td>78.1%</td>
</tr>
<tr>
<td>N0</td>
<td>73.9%</td>
<td>78.9%</td>
<td>81%</td>
<td>71.4%</td>
<td>76.2%</td>
</tr>
<tr>
<td>N1</td>
<td>50%</td>
<td>83.3%</td>
<td>33.3%</td>
<td>90.9%</td>
<td>78.6%</td>
</tr>
<tr>
<td>N2</td>
<td>55.6%</td>
<td>81.8%</td>
<td>45.5%</td>
<td>87.1%</td>
<td>76.2%</td>
</tr>
<tr>
<td>N3</td>
<td>97.4%</td>
<td>90.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N+/N−</td>
<td>78.9%</td>
<td>73.9%</td>
<td>71.4%</td>
<td>81%</td>
<td>76.2%</td>
</tr>
<tr>
<td>PET N+/N−</td>
<td>50%</td>
<td>90.9%</td>
<td>81.8%</td>
<td>69%</td>
<td>72.5%</td>
</tr>
</tbody>
</table>

**Conclusion:** Our results, obtained from a real clinical practice, showed that the overall accuracies of EUS and PET-CT for preoperative N staging were 76.2% and 72.5%, with significant differences between both techniques. The overall accuracy of EUS for T staging was 78% and 80.2% for restaging. More importantly, our results show a significant advantage of EUS over PET-CT in restaging, even in our series, in which the vast majority of suspicious lymph nodes were not sampled. Conclusion: EUS performance in gastric cancer N staging and restaging is better than PET-CT. Both procedures showed suboptimal accuracies when considered alone, and more than one single staging method should be used.

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

**References**


**OP348 SORTEILIN DEFICIENCY REDUCES DUCTURAL REACTION, HEPATOCYTE APOPTOSIS AND LIVER FIBROSIS IN CHOLESTATIC-INDUCED LIVER INJURY**

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

**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 activity and 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-IL-6 antibody to WT mice and BDL. Results: Sortilin-/- mice displayed strongly attenuated liver fibrosis following BDL and CCl4 treatment, accompanied by an attenuated in vitro activation phenotype of Sortilin-/- HSC. Restoring 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. Shifting the treatment of bile duct ligation WT mice with a neutralizing antibody to IL-6 attenuated hepatic inflammation and expression of reactive cholangio-cyte-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 NECROSIS IN HUMAN AND EXPERIMENTAL CHOLESTASIS**

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

**Introduction:** Targeting necroptosis, a programmed necrotic cell death pathway regulated by receptor-interacting protein 3 (RIP3), is being considered as a potential therapeutic approach for inflammation-driven liver diseases. Still, the role on the expression of membrane markers EpCAM and TROP-2 in HPCs. Human liver is not 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/β-catenin and Notch pathways, known for their role in proliferation and differentiation of HPCs. In addition we identified several novel pathways activated in human HPC-enriched cultures such as the TNF and IL17A pathways. Moreover, comparison of the different isolation methods indicates some slight differences between the different HPC populations, e.g. the ErbB signalling pathway is activated in the TROP-2 positive cells while this is not the case in the EpCAM-positive or SP cell populations.

**Conclusions:** Our results indicate that signature molecules of human HPCs are enriched in pathways already known to be involved in HPC activation in human and in animal models, but we also identify previously unknown pathways like TNF, IL17A and ErbB signalling pathways. Comparison of the 3 isolation methods shed light on the possible existence of different HPC populations existing in the human liver. The isolated HPC populations will be used to further characterize human HPCs and to understand the molecular mechanisms underlying their activation and differentiation, with the ultimate goal of using HPCs for the treatment of liver diseases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
of necrosis in the pathogenesis of cholestatic liver injury has been poorly explored.

**Aims & Methods:** We aimed to evaluate the role of necroptosis in patients with primary biliary cirrhosis (PBC), a cholestatic chronic liver disease, and in mice after common bile duct ligation (BDL), a classic experimental model of acute cholestasis. We used non-model and cholestatic liver fibrosis. Thioflavin T staining and immunohistochemistry of RIP3 and its target phosphorylated-mixed lineage kinase domain protein (p-MLKL) were performed in liver biopsies of patients with PBC and healthy controls. C57BL/6N wild-type (WT) or RIP3-deficient (RIP3-/-) mice were subjected to BDL or sham surgeries for 3 and 14 days, with subsequent histological and biochemical analysis of hepatic damage. Necrotic markers and the functional crossstalk between RIP3, antioxidant response and iron homeostasis were investigated in vivo and in vitro.

**Result:** In PBC patients, expression of RIP3 and p-MLKL was found increased in hepatocytes surrounded by lymphocytic infiltrates and also in cells morphologically resembling bile duct cells. Moreover, p-MLKL fluorescence co-localized in cells with increased thioflavin T staining, suggesting necroosome assembly and necroptosis activation. BDL in mice resulted in progressive bile duct hyperplasia, multifocal necrosis, fibrosis and inflammation. Concomitantly, necroptosis was activated as evidenced by increased RIP3 expression and activity and sequestration of RIP3 and MLKL in the insoluble protein fraction of the liver. Remarkably, RIP3 deficiency blocked BDL-induced necroinflammation at 3 and 14 days post-BDL. Serum hepatic enzymes, fibrogenic liver gene expression and oxidative stress decreased in RIP3-/- mice at 3 days after BDL. However, at 14 days, cholestasis aggravated and fibrosis was not ameliorated. RIP3 deficiency was further associated with increased hepatic expression of heme oxygenase-1 (HO-1) and accumulation of iron in BDL mice. The functional link between HO-1 activity and bile acid toxicity was established in RIP3-deficient primary hepatocytes. The necroptotic activity of RIP3 and its target p-MLKL 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, necroptosis is triggered in PBC patients and mediates hepatic necroinflammation in BDL-induced cholestasis. Targeting necroptosis may provide an opportunity to develop novel therapeutic strategies to attenuate chronic 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 HMS-P:ICT/008:2011, SFRH/BD/9119/2012, SFRH/BD/88212/2012 and SFRH/BD/104160/2014, FCT, Portugal).

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

**References:**

**OP350 PROTECTIVE ROLE OF SPECIFIC PATHOGEN FREE MICROBIOTA IN BILE DUCT LIGATION 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 development of liver fibrosis remain largely unknown. We hypothesized that fibrosis could be attenuated in a gnotobiotic model of limited intestinal colonization (altered Schaedler flora, ASF) compared to a more complex colonization with specific pathogen free flora (SPF).

**Aims & Methods:** We aimed to investigate the development of fibrosis and portal hypertension in ASF and SPF mice. Liver fibrosis was induced by common bile duct ligation (BDL) for 14 days or intraperitoneal injection of 20% (dilution in olive oil) tetrachloride (CCL4) for 10 weeks in ASF or SPF mice. Liver histology and collagen deposition were evaluated using Sirius red staining for determination of fibrosis degree. To assess bacterial translocation, mesenteric lymph nodes, spleen and liver were dissected aseptically and then cultured on plates, On the other hand, the balance of gut microbiota of SPF mice was significantly different from ASF mice, with more complex intestinal bacterial flora may play a hepato-protective role. Our results are in line with studies showing that germ free mice are more susceptible to liver injury.

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

**References:**
to liver injury and fibrosis suggesting the beneficial role of intestinal microbiota in preventing diseases.

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

References

OP52 IMPROVING METABOLIC PARAMETERS IN NAFLD BY TARGETING NUCLEAR RECEPTORS
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1Research Institute for Health Sciences (IMed/Lisboa), Faculty of Pharmacy, Universidade de Lisboa, Lisbon/Portugal
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Introduction: Non-alcoholic fatty liver disease (NAFLD) pathogenesis and treatment remain unsolved. microRNAs and bile acids were recently suggested to participate in disease pathogenesis and, as such, constitute potential therapeutic tools and targets. Moreover, nuclear receptors, namely peroxisome proliferator-activated receptors (PPARs) and the retinoic acid receptor (RAR) are currently under scrutiny as modulators of lipid and glucose metabolism in non-alcoholic steatohepatitis (NASH).

Aims & Methods: We aimed to elucidate the role of the miR-21/PPAR pathway in liver and muscle tissues of murine NASH models and ascertain the therapeutic potential of miR-21 abrogation alone or in combination with obeticholic acid (OCA). Wild-type (WT) and miR-21 KO mice were fed with chow (n = 10) or methionine and choline-deficient (MCD; n = 10) diets for 2 and 8 weeks. Alternately, mice were fed either chow (n = 12) or fast food diet (FF; n = 12) for 25 weeks. Six animals from each group had their diet supplemented with OCA 10 mg/kg/day (Intercept Pharmaceuticals, Inc.). Human liver biopsies were obtained from morbid obese NAFLD patients (n = 28). Liver/muscle samples were processed for histological analysis and assessment of miR-21, pro-inflammatory/pro-fibrogenic cytokines, PPARs and metabolic relevant genes, by qRT-PCR and immunoblotting. A Taqman® Array was performed to evaluate modulation of lipid regulated genes. ROS levels were analysed through the use of 2',7'- dichlorodihydrofluorescein diacetate.

Results: WT mice fed with the MCD diet developed steatohepatitis and fibrosis, displaying increased levels of apoptosis, necroinflammation and serum ALT and AST. In contrast, miR-21 KO mice displayed a significant decrease in steatosis severity, liver fibrosis and inflammation and did not develop fibrosis. WT FF-fed mice developed hepatomegaly, macrovesicular steatosis, inflammatory infiltrates and increased oxidative stress. miR-21 levels were increased in WT FF-fed mice, in liver and muscle, concomitantly with decreased expression of PPARα, a key miR-21 target, in FF-fed mice in comparison with WT mice. In contrast, miR-21 KO mice displayed decreased ROS levels, together with decreased protein and mRNA levels of PPARs and the metabolic targets, including PCK-1 and ACOX2. Finally, lipid regulated genes such as ACAT1, ALOX5 and FABP5 were found to be severely deregulated in WT FF-fed mice and reverted to control levels in KO FF-OCA-fed mice.

Conclusion: In conclusion, activation of PPARα as a result of miR-21 abrogation, together with FXR activation by OCA, significantly improves metabolic parameters in NASH, highlighting the therapeutic potential of multi-targeting therapies for NAFLD. (Supported by PTDC/BIM-MEC/087312/2012, SFRH/BDE/88212/2012, FCT, Portugal).

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

Wednesday, October 19, 2016
8:30-10:00
MURINE MODELS OF INTESTINAL INFLAMMATION – ROOM 1.66

OP53 AN AUTOMMUNITY-ASSOCIATED VARIANT IN PTTPN22 PROTECTS FROM DISEASE ONSET IN MOUSE MODELS OF COLITIS
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Introduction: Presence of the single nucleotide polymorphism (SNP) rs2476601 in the gene encoding protein tyrosine phosphatase non-receptor type 2 (PTPN22) results in an altered-function PTP22 protein product and is associated with increased risk to develop autoimmune disorders, including rheumatoid arthritis, systemic lupus erythematosus. However, the same variant reduces the risk for Crohn’s disease (CD) onset. We have previously shown that protein and mRNA levels of PTP22 are reduced in intestinal biopsies from CD patients, and that loss of PTTPN22 results in enhanced inflammatory cytokine secretion from mononuclear cells treated with interferon-gamma or the bacterial product muramyl dipeptide.

Aims & Methods: In this study, we addressed how presence of the altered-function variant in PTP22 influences the susceptibility to intestinal inflammation in mouse models of colitis. For this aim, colitis was induced in 10-12 week old female mice by administration of 2% DSS for 7 days (acute DSS colitis), administration of four cycles of DSS (1.5% DSS for 7 days, followed by 10 days normal diet each week); chronic DSS colitis, or by transferring naive naïve T- cells from Rag2−/− recipients. PTP22 deficient (PTP22−/−) mice, or mice expressing the IBD-associated variant in PTP22 (PTP22−/−:619W mice), and their respective wild-type (WT) littermates were used for the study.

Results: PTP22−/− mice suffered from aggravated acute DSS colitis as characterized by pronounced weight loss, increased endoscopic and histologic colitis scores (p < 0.05), while PTP22−/−:619W mice reacted only weakly to the DSS treat- ment when compared to WT littermates (p < 0.05 for weigh development, p < 0.01 for other parameters). In chronic DSS colitis however, PTP22−/− mice suffered from a milder disease course (reduced weight loss [p < 0.05], decreased histological severity [p < 0.05]) from the third cycle onwards. PTP22−/−:619W mice displayed decreased steatosis and miR-21 expression, compared to PTP22−/− mice, in the first weeks, and later on developed only a mild disease (moderate weight loss [p < 0.01], reduced shortening of the colon [p < 0.05], low histological dis- ease scores [p < 0.05]) when compared to mice receiving WT T cells.

Conclusion: Taken together, we here describe for the first time how the IBD- associated variant in PTP22 affects colitis development. This helps to explain why this variant is associated with a reduced risk for CD onset, although it increases the risk to develop classical autoimmune disorders.

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

OP54 TOLL LIKE RECEPTOR 2 MODULATES THE INHIBITORY MOTOR RESPONSE INDUCED BY HYDROGEN SULPHIDE IN MOUSE COLON
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Introduction: The recognition of intestinal microbiota is in part carried out by 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). CSE is determined by real time-PCR and protein expression of CSE and CBS were quantified by Western blotting in colon from WT and TLR2−/− mice.

Results: The NaHS, as a source of exogenous H2S, reduced the frequency but not the amplitude of the spontaneous contractions in colon from WT mice. The inhibition of CSE or CBS with PAG or AOAA, respectively, increased the frequency but not the amplitude of the spontaneous contractions in colon from WT mice. The NaHS induced a higher reduction of the frequency of the spontaneous contractions in TLR2−−/− compared to WT mice. The PAG and AOAA did not modify the spontaneous contractions in colon from TLR2−/− mice. The mRNA and protein expression of CBS resulted decreased in colon of TLR2−/− compared with WT mice. The mRNA but not the protein expression of CSE resulted decreased in TLR2−/− compared with WT mice.

Conclusion: These results suggest that exogenous and endogenous H2S may regulate the colonic spontaneous contractions in WT mice, reinforcing the hypothesis that H2S is a gaseous inhibitory mediator of intestinal motility, TLR2
OP355 DIRECT INHIBITION OF HMGB1 BY NEUTRALIZING ANTI-BODY AMELIORATES EXPERIMENTAL COLITIS IN MICE VIA TLR4 PATHWAY

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Introduction: Biologics targeting inflammatory cytokines has reveal a new era in inflammatory bowel disease treatment. High mobility group protein B1 (HMGB1) acts as an alarmin in early stage and inflammatory cytokine in late stage during inflammation. Direct blockade of HMGB1 can be protective against intestinal inflammation.

Aims & Methods: 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-β (DSS-C group) or normal control (ctrl group). Colon shortening, disease activity index (DAI), histological score of colitis (HIS), MPO activity and inflammatory cytokines were evaluated to determine the colonic inflammation severity. Mucosa barrier function was assessed by imuno-fluorescent staining of mucus layer (mucin2) and tight-junction (T-J) protein detection. mRNA was detected by qPCR.

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 (3.7±0.5 vs. 3.7±0.3, p<0.05) and HIS (6±0.1 vs. 9±0.5, p<0.05). Besides, MPO activity (2.6±0.8 vs. 4.8±1.0, p<0.05) and TNF-α (1.6±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 (ctrl group). The repression effect of HnAb was more evident in 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-1 (0.30±0.07 vs. 1.00±0.00, p<0.0001) and occludin (0.85±0.09 vs. 0.39±0.01, p<0.0001) was detected. HnAb could also prevent mice to 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. 0.03±0.01, p<0.0001) were all decreased significantly when treated with HnAb 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 interventional target of HMGB1 in ulcerative colitis treatment.

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

OP356 NEW, PEPTIDE INHIBITOR OF DIPEPTIDYL PEPTIDASE IV, EMDB-1 ATTENUATES COLITIS IN MICE AFTER TOPICAL ADMINISTRATION

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Introduction: PETIR (PEptidase-Targeted ImunoRegulation) is a novel therapeutic strategy which takes for the purpose restoration of the immune balance by limiting the activation of immune cells and induction of endogenous protective mechanisms, such as TGFβ and glucagon-like peptide-2 (GLP-2) through inhibition of DPP IV-dependent pathways. Experimental data indicate that PETIR results in suppression of cell proliferation and reduced synthesis of pro-inflammatory cytokines without affecting cellular viability.

Aims & Methods: The objective of this study was to test the anti-inflammatory activity of a novel DPP IV inhibitor EMDB-1 in the mouse models of colitis. The inhibitory effect of EMDB-1 on DPP IV was characterized in vitro using the results in suppression of cell proliferation and reduced synthesis of pro-inflammatory cytokines without affecting cellular viability.

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

OP357 CHROMOFUNGIN (CHR) AMELIORATES EXPERIMENTAL COLITIS IN MICE VIA MODULATION OF MACROPHAGES’ PLASTICITY

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3Internal Medicine, Division of Gastroenterology, University of Manitoba, Winnipeg, Canada

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Introduction: Macrophages play a major role in inflammatory bowel disease (IBD) pathogenesis through an inappropriate response to migration, and an impaired transition from a pro-inflammatory (classical activated macrophages (CAMs)) to an anti-inflammatory (alternative activated macrophages (AAMs)) phenotype. While there is growing awareness of a relationship between Chromogranin (Cg)-A and a susceptibility to inflammatory conditions, the specific interaction between Cg-A derived peptides and macrophage plasticity in IBD is unknown. Recently, we have shown a linear correlation between Cg-A and CAMs markers in normal gut, but with active ulcerative colitis, and colitic Cg-A-deficient mice demonstrated a significant decrease of colitis associated to a modulation of macrophage plasticity. As Cg-A is a prohormone, herein, we assessed the functional role of a specific Cg-A-derived peptides (Chromofungin (CHR); Kcg-A76) in the regulation of acute colitis and the functional plasticity of murine macrophages.

Aims & Methods: Colitis was induced in C57BL/6 mice (7–8 weeks old) by administering dextran sodium sulfate (DSS 3%) in drinking water for 5 days. DSS-C mice were treated with CHR (2.5 μg/kg) or placebo (saline). Macrophage phenotypes started 1 day before induction of colitis and lasted for a total of 6 days. Disease activity index (DAI) was evaluated daily and mice were sacrificed on day 5 post-DSS induction to assess the extent of colitis. At sacrifice macroscopic scores were evaluated. Linear density of C-reactive protein (CRP) was quantified using ELISA, and colonic interleukin (IL)-1β, IL-6, TNF-α, MIP-1α, MIP-1β, and ARG-1 were assessed using ELISA and RT-qPCR.

Results: Preventive treatment with CHR significantly reduced the DAI onset and severity of colitis associated to rectal bleeding, stool consistency and weight loss. Macrophage scores, serum-CRP, colonic IL-1β, IL-6, TNF-α, MIP-1α, MIP-1β, and ARG-1 were significantly increased when treated with ELISA and RT-qPCR. Northern peritoneal macrophages were isolated from BALB/c mice ± Chromofungin (CHR) (200 ng/ml) by centrifugation by CHR (200 ng/ml) then exposed for 6 h to LPS (100 ng/ml) to promote CAMs, or to IL-4/IL-13 (20 ng/ml) to promote AAMS. CAMs markers (IL-6, IL-1β, TNF-α, MIP-1α & MIP-β) and AAMS markers (ARG-1) were quantified by using ELISA and RT-qPCR.

Conclusion: These findings suggest that CHR can modulate the severity of experimental colitis. CHR treatment can attenuate the severity of experimental colitis and the inflammatory process via the modulation of the functional plasticity of murine macrophages and their functions. Targeting Cg-A-derived peptides may lead to novel therapeutic strategies in ulcerative colitis.

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

OP358 DEFICIENCY OF PH-SENSING RECEPTOR TDAG8 AMELIORATES T-CELL TRANSFER COLITIS

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Background: Th17 cells are essential for the immune response against intestinal pathogens. TLR4 regulates the expression of Th17 cells and Th17 response to TNBS-induced colitis in mice. The Th17 response to TNBS was mediated by CCR6 and IL-17A and IL-22. The aim of this study was to test the anti-inflammatory activity of T-cells transfer colitis in the mouse models of colitis. The inhibitory effect of TDAG8 on T-cells transfer colitis was characterized in vitro using the results in suppression of cell proliferation and reduced cytokine production.
Introduction: The adaptive immune system plays a crucial role in the pathogenesis of inflammatory bowel disease (IBD). Colorectal cancer 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 intranasally transferred. Injection of PBS was used in a control group. The results of colitis were evaluated by weight change, colonoscopy score, spleen weight, H&E staining, IHC and mRNA expression.

Results: Induction of colitis was observed after 3 weeks by weight loss, diarrhea and bloody stool. The WT group showed severe weight loss (p = 0.013), whereas the TDAG8-/- group displayed only a minor delay in weight gain. No significant differences were observed in colon length, spleen weight and colonoscopy score between PBS and the TDAG8-/- groups. H&E staining of distal and proximal parts of the colon showed severe infiltration of mononuclear cells without a 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. The regulation 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 FosP, RORy and IL18.

Conclusion: Our data demonstrate that TDAG8 deficiency in T-cells ameliorates the development of colitis suggesting an important physiological role of this pH receptor.

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

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00

SURGERY MEETS ENDOSCOPY IN THE COLON – ROOM F1

OP359 TRANSPORTAL ENDOSCOPIC MICROSURGERY VERSUS ENDOSCOPIC MUCOSAL RESECTION FOR LARGE RECTAL ADENOMAS (META-ANALYSIS)

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Introduction: Non-randomized studies suggest that endoscopic mucosal resection (EMR) is equally effective in removing large rectal adenomas as transportal endoscopic microsurgery (TEM). EMR might be more cost-effective and safer. This trial compares the cost-effectiveness and cost-utility of TEM and EMR for large rectal adenomas.

Aims & Methods: For this randomised controlled non-inferiority trial, patients with rectal adenomas ≥3 cm, without malignant features, from 20 hospitals were included and randomised (1:1) to TEM or EMR, allowing endoscopic removal of residual adenoma at 3 months. Unexpected malignancies were excluded post randomisation. Primary outcomes were recurrence within 24 months and the number of recurrence-free days alive and out of hospital, analysed by intention to treat. The trial was designed to demonstrate non-inferiority of EMR with regards to recurrence rate with an upper limit of 10%. Secondary outcomes were quality of life, anorectal function and costs. This trial is registered in the Dutch Trial Registry (NTR1422).

Results: Between Feb 2009 and Sept 2013, 209 patients were randomised to EMR (n = 106) or TEM (n = 103). 4 patients withdrew consent. 1 patient had prostate carcinoma instead of rectal adenoma. The remaining 204 patients (103 TEM, 101 TEM) were treated; 27% (131) had unexpected cancer and were excluded. One additional patient withdrew consent. Of the remaining 176 (87 EMR, 89 TEM) patients, overall recurrence rates were 15% after EMR and 11% after TEM (relative risk (RR) 1.33, 95% confidence interval (CI) 0.77–2.46). However, EMR was statistically not non-inferior to TEM. The number of recurrence-free days alive and out of hospital was similar (EMR 609 ± 209, TEM 652 ± 188, p = 0.15). Complications (mostly hemorrhage) occurred in 18% (EMR) vs. 26% (TEM) (odds ratio (OR) 0.65 (95% CI 0.32–1.33)). Major complications occurred in 1% (EMR) vs. 8% (TEM) (OR 0.14 (95% CI 0.02–1.13), p = 0.064). Quality adjusted life years were similar in both groups. Although EMR patients scored more favourably on disease specific quality of life questions, mean values were similar and continued improvement after adenoma resection regardless of treatment. EMR was approximately €300 cheaper and therefore more cost-effective.

Conclusion: Due to unexpected high recurrence rates after both TEM and EMR, non-inferiority of EMR could not be demonstrated. Taking into account the high rate of unexpected malignancies, a trend towards more severe complications after TEM and the cost-effectiveness of EMR, EMR is the recommended technique in case of similar expertise of TEM and EMR.

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

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00

UPPER GI BLEEDING – ROOM M

OP361 MEDIUM- AND LONG-TERM RESULTS OF TREATMENT WITH LANREOTIDE IN CASES OF CHRONIC OR RECURRENT OBSCURE GASTROINTESTINAL BLEEDING OR DUE TO GASTROINTESTINAL ANGIODYPLASIAS

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Introduction: Somatostatin analogues have been proposed as a rescue therapy in cases of chronic or recurrent obscure gastrointestinal bleeding (GIB) or attributable to gastrointestinal angiodyplasias (GIADs). The long-term results with lanreotide are still very scarce.

Aims & Methods: Our aim is to determine the medium and long-term benefit of lanreotide in cases of chronic or recurrent refractory obscure gastrointestinal bleeding or due to GIADs, in terms of savings of health resources. This was a retrospective single-center study conducted under conventional clinical practice, following a defined management protocol, between 2003 to 2012. Patients with chronic or recurrent obscure GIB or due to GIADs, refractory to or not candidates for iron therapy, endoscopic, surgical or angiographic treatments, were included. Cirrhotic patients and those ones with very severe comorbidity (IV-V of the American Society of Anesthesiologists Classification-ASA) were excluded. The diagnostic protocol included upper and lower endoscopy, abdominal computed tomography, video capsule endoscopy and/or single balloon enteroscopy. Lanreotide 60 or 90 mg was administered monthly, for at least 6 months. During the previous year and 36 months after starting the drug it was recorded demographics data, comorbidities, chronic use of antiplatelets and anticoagulants, hemostatic treatments, side effects, hospitalisations and use of transfused red cells units, intravenous...
Among patients with angiodyplasias at multiple sites or in the colon, somatostatin analogues are less effective in following its indication. Disclosure of Interest: All authors have declared no conflicts of interest.

Introduction: Cohort studies have shown a beneficial effect of octreotide in gastrointestinal angiodyplasias located at multiple sites or in the colon. Aims & Methods: The aim of this individual patient data meta-analysis is to identify articles reporting the effect of SST in gastrointestinal angiodyplasias. We identified 7 studies and obtained individual data from 6 (n = 50) patients that benefit most from SST. A systematic review was performed to identify articles reporting the effect of SST in gastrointestinal angiodyplasias. We collected individual patient data of included articles. Patients with oral iron dependency were excluded. The primary outcome was response to SST, defined as good: ≥50% reduction of parenteral iron and/or red blood cell (RBC) transfusions; or poor: <50% reduction of parenteral iron and/or RBC transfusions. We used univariate logistic regression to determine the effects of patient and disease characteristics on SST. The variable “study” was included in the univariate analysis to correct for study-effect.

Results: We identified 7 studies and obtained individual data from 6 (n = 180) studies. We analyzed data of 159 patients (mean age 70 years, 55% men) with transfusion dependency due to gastrointestinal angiodyplasia bleeding that were treated with SST. Fifty percent of patients had angiodyplasias at multiple sites (small bowel (75%), stomach (45%), and colon (45%)). Endoscopic treatment prior to SST was started in 48%. Octreotide LAR 20 mg was the most frequent prescribed (81%). Side-effects occurred in 31% (41/131) of the patients, with gastrointestinal symptoms (19.8%) and erythema / pain at the injection site (8%, p = 0.001) the most frequent. In 8 patients (6%) SST was discontinued due to side-effects. There was a high SST response with 99% of the patients having >50% reduction of their parenteral iron and/or RBC transfusion dependency. Sex, age, small bowel and stomach localization, the use of anticoagulants, dose, only parenteral iron dependent and prior endoscopic treatment were not associated with treatment response. Angiodyplasia localization in the colon (OR 0.28, 95% CI 0.09–0.88, p = 0.03) and at multiple sites (OR 0.37, 95% CI 0.17–0.77, p = 0.008) were negatively associated with a good response. Conclusion: Based on this pooled analysis of data from individual patients with transfusion dependent angiodyplasia bleeding, SST is effective and safe in the majority of patients. A decreased SST response is found in patients with angiodyplasias located at multiple sites or in the colon. 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 gastrointestinal service, from January 2003 to December 2015. Controls: EBL treated patients without post-therapeutic ulcer bleeding. Matching was made for Child-Pugh-Turcotte (CPT) score and indication (bleeding vs elective) in a 1 case for 2 controls ratio. Patient’s demographics, comorbidities and endoscopic findings were reviewed from medical records. Endpoints were re-bleeding from post therapeutic ulcer and mortality assessed at 28, 90, 180 and 360 days post-therapeutic.

Results: A total of 50 post-EBL ulcer bleeding cases and 100 controls were included. Mean age (57.1 ± 12.0); male:female ratio (4:1:1). CIRRHOSIS etiologies: alcoholic (30.7%), HCV (29.3%) and HBV (15.7%). CPT distribution: A (36.7%), B (46%) and C (26.7%); mean MELD was 14.5 (17.3). 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, 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: 5.9, p < 0.001) correlated with rebleeding. In multivariate logistic regression analysis HBV cirrhosis, multiple concomitant aetiologies of cirrhosis and endoscopic stigmata of recent bleeding were independently associated with rebleeding. Post-EBL ulcer bleeding did not significantly impacted overall short and long term mortality. However CPT class B patients with post-EBL ulcer bleeding showed a trend for lower survival which was significant at 180 days (16% vs 6% log rank p = 0.04).

Conclusion: We identified both patient’s and endoscopic features correlating with post-EBL ulcer bleeding, namely HBV infection related cirrhosis, higher number of concomitant aetiologies/aggressors, and endoscopic stigmata of recent/active bleeding. Though overall patient’s short and long-term mortality was not affected by post-EBL ulcer bleeding, CPT class B patients showed a trend for
lower survival. Thus, we hypothesize that CPT class B patients may be a cluster of patients with low hepatic reserve, to whom post-EBL bleeding may impose an additional risk for disease progression, that can significantly impact on survival.

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

References

OP364 INTERNATIONAL PROSPECTIVE STUDY OF UPPER GI HAEMORRHAGE: DOES WEEKEND ADMISSION AFFECT OUTCOME? I. A. Murray1, A. Stanley2, H. R. Dalton1, J. H. J. Ng1, S. B. Laursen5
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Introduction: Weekend admissions have been associated with higher mortality. For upper gastrointestinal haemorrhage (UGIH) some studies show significantly increased mortality1 and delayed endoscopy while the UK UGH audit reported no difference2. We studied whether out of hours (OOH) admissions had more morbidity, were less stable and/or had higher mortality.

Aims & Methods: Prospective study over 12 months (from March 2014) from 2 UK and 2 international centres. Admission time, demographics, pulse, BP, lab results, endoscopy findings, further procedures and 30 day mortality were recorded. 3 pre-endoscopy scores (Glasgow Blatchford (GBS), AIMS65 and admission Rockall scores) and 2 post-endoscopy scores (PNED and full Rockall scores) were determined. Chi-squared, Fisher’s exact and the Kruskal-Wallis tests were used as appropriate. A two-tailed significance level of 5% was used.

Results: 2118 consecutive patients, 60% male, median age 66 years were seen. There were no significant differences in mortality, need for endoscopic therapy, splenic embolisation or rebleeding in both UK and non-UK centres. There were no differences in comorbidity, mean ASA 2.3, pulse or BP although weekend admissions had a lower Hb (110 g/l vs 118 g/l (weeknight) vs 117 g/l (weekend) p < 0.001) and higher GBS (p < 0.05). No difference in peptic ulcer disease or various incidence between periods although more weekday admissions had normal endoscopies. No OOH admissions were less likely to have an endoscopy (30% not endoscoped vs 23% for weekday admission p < 0.005). Time to endoscopy was less for weekday admissions (15% vs 17% for weekend and 20h for weekend). Time to rebleeding 75% weeknight and 60% weekend admissions had their endoscopy within 24 hours.

Outcome of patients with UGIH and time of presentation

<table>
<thead>
<tr>
<th>Weekdays: working time</th>
<th>Weekdays: overnight</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>858</td>
<td>603</td>
</tr>
<tr>
<td>Units blood transfused</td>
<td>1.4-6</td>
<td>1.3-6</td>
</tr>
<tr>
<td>Endoscopic therapy</td>
<td>185 (22)</td>
<td>116 (19)</td>
</tr>
<tr>
<td>Surgery/embolisation</td>
<td>4 (0.5)</td>
<td>6 (1.0)</td>
</tr>
<tr>
<td>Rebleeding</td>
<td>49 (5.8)</td>
<td>33 (5.7)</td>
</tr>
<tr>
<td>30d mortality</td>
<td>61 (7.1)</td>
<td>43 (7.1)</td>
</tr>
</tbody>
</table>

2118 consecutive patients admitted March 2014-March 2015 from Glasgow (600), Truro (544), Odense (541) and Singapore (433). Data shown are mean [95% CI] or number (%).

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 PROGNOSTIC FACTORS FOR SECOND ENDOSCOPIC THERAPY FAILURE IN PEPTIC ULCER BLEEDING
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Introduction: According to current guidelines a second endoscopic therapy is generally encouraged for patients with rebleeding secondary to peptic ulcer disease (PUD). Although risk factors for endoscopic hemostasis failure are well defined in the setting of the first endoscopic therapy, literature lacks studies that focused on the risk factors for rebleeding after the second endoscopic therapy.

Aims & Methods: To assess risk factors related to the failure of the second endoscopic therapy in patients with upper gastrointestinal bleeding (UGIB) secondary to PUD, in order to determine which patient may benefit from alternative methods like angiography or surgery. Retrospective analysis of all cases of UGIB secondary to PUD that were submitted to two endoscopic therapies between 2010 and 2014 in a tertiary center. We recorded demographic, clinical, analytical and endoscopic data. Comorbidities were evaluated according to the age adjusted charson comorbidity index (ACCI). The main endpoint was rebleeding, defined as: objective evidence of UGIB, with hemodynamic instability and Hb decrease ≥2 g/dl, or need for more than 3 units of blood in the 72-hour period after the endoscopic treatment.

Results: We identified 56 patients who underwent a second endoscopic therapy. The mean age was 76 years (males: 63% and the mean ACCI was 7 ±3.3). The mean location of PUD was duodenal (80.4%) and 26.8% of cases were classified as having a high-risk location (small gastric curvature / posterior wall of the bulb); the estimated mean size of PUD was 13.3 mm ±6.8). The mean number of blood units transfused was 3 (±2.4). Rebleeding occurred in 23% and in-hospital mortality was 5% (p = 0.041), presence of active non gastroenteral neoplasia (p = 0.021), high-risk location (p = 0.001), large-ulcers (p = 0.045), Idiopathic-PUD (p = 0.006) were associated with hemostatic failure. The number of red blood cells (RBC) transfused within 24h of admission was related to hemostatic failure (p = 0.041), presence of hemodynamic instability (p = 0.004), presence of active non gastroenteral neoplasia (p = 0.021), high-risk location (p = 0.001), large-ulcers (p = 0.045), Idiopathic-PUD (p = 0.006) were associated with hemostatic failure. The number of red blood cells (RBC) transfused within 24h of admission was related to hemostatic failure (p = 0.041), presence of hemodynamic instability (p = 0.004), presence of active non gastroenteral neoplasia (p = 0.021), high-risk location (p = 0.001), large-ulcers (p = 0.045), Idiopathic-PUD (p = 0.006) were associated with hemostatic failure. The number of red blood cells (RBC) transfused within 24h of admission was related to hemostatic failure (p = 0.041), presence of hemodynamic instability (p = 0.004), presence of active non gastroenteral neoplasia (p = 0.021), high-risk location (p = 0.001), large-ulcers (p = 0.045), Idiopathic-PUD (p = 0.006) were associated with hemostatic failure.

Conclusion: In patients with UGIH secondary to PUD that require a second endoscopic therapy for rebleeding, the need for higher blood transfusion (>4) and large ulcers (>20 mm) were independent risk factors for hemostasis failure. Early surgery or angiography should be considered in this group of patients.

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

Reference
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).

Conclusions: 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.

OP368 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.

Aims & Methods: In this study, we aimed to unravel the molecular mechanism underlying tumor angiogenesis in colorectal cancer (CRC). We isolated endothelial and epithelial cells from surgically resected 14 CRC tissues and corresponding normal colonic tissues using antibodies against endothelial (CD146) and epithelial markers (EpCAM). RNA sequencing (RNA-seq) was carried out in 3 pairs of normal and tumor endothelial cells. Gene expression was validated by quantitative RT-PCR (qRT-PCR) and immunohistochemistry. Functions of a selected gene were analyzed by tumor conditioned medium (TCM) experiments, in vitro tube formation assay, cell cycle analysis, gene expression microarray and xenograft experiments.

Results: Through RNA-seq analysis, we identified a series of 18 genes which were upregulated in the endothelial cells isolated from CRC tissues. We further validated the results by qRT-PCR and 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 fibroblasts. 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-implanted CRC cells with HUVECs into nude mice. We found that knockdown of gene A in HUVECs resulted in reduced micro vessel formations in the xenograft tissues. Finally, we evaluated the clinical implication of gene A in colorectal cancer. The Cancer Genome Atlas (TCGA) datasets of primary CRCs (n = 411) revealed that higher expression of gene A is associated with worse overall survival, suggesting that upregulation of gene A in tumor endothelial cells may promote aggressiveness of CRC.

Conclusion: Our results suggested that gene A may play an important role in the angiogenesis in colorectal cancer, and that it could be a potential therapeutic target.

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

OP369 RANDOMIZED CONTROLLED TRIAL OF BACLOFEN IN TREATMENT OF MUSCLE CRAMPS IN PATIENTS WITH LIVER CIRRHOSIS
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Introduction: Muscle cramps adversely influence the quality of life of patients with liver cirrhosis. However, despite the obvious association of muscle cramps with liver disease, there is a paucity of information regarding pathogenesis and treatment in these patients.

Aims & Methods: This is the first randomized placebo controlled trial of baclofen 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 reduction 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 apparent 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 with significant short and long-term morbidity and mortality. With theambulatorization of medical care, the use of antibiotics for primary and secondary prophylaxis of SBP, there is some controversy concerning whether the acquisition site of the infection has an effect on the prognosis of SBP and if the international guidelines for antibiotic therapy (mainly based on the acquisition site) are still considered to be the best practice. Aim: 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 3 tertiary centers that evaluated all cases of SBP between 2010 and 2014. Medical records and laboratory data were reviewed. For defining the acquisition site of the infection, we followed the criteria described by European Center for Disease Prevention and Control (ECDC). Healthcare-Associated infections and Nosocomial infections were analyzed with a different 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 6.36%; 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 SBPs for the variables age, gender, Child-Pugh, MELD, Hb, leukocytes, platelets, CRP, Na, INR, bilirubin, albumin, ascites fluid characteristics, gastrointestinal bleeding, acute kidney injury, diabetes mellitus, and hemodynamic instability (p > 0.05). No complications were recorded. Nosocomial-acquired SBPs were associated with longer hospitalizations (17.8 vs 11.7 days; p = 0.007).

Conclusion: Nosocomial-acquired SBPs were associated with higher rates of MDR-bacteria, longer hospitalization lengths and higher 1 year-mortality. Clinical and laboratorial features were not significantly different between SBP according to the infection acquisition site; 6.36% of community-acquired SBPs were secondary to MDR-bacteria and so in a relevant percentage of our sample, empiric antibiotic therapy according to the current guidelines would eventually fail.

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 female, mean age was 69 years. Significant increases over time were found for ADRs, which rose from a mean of 4.5% in 2008 to 10.7% in 2014 (11.6%) in 2013-2014, corresponding to an average increase of +1.5% per two-year-period (95% confidence interval [95%CI] +0.9%, +2.2%, p < 0.001). Likewise, proximal lesion detection rates rose from 15.8% (95% CI) 21.7% (95% CI), +2.5% per two-year-period, 95% CI (+1.9%, +3.1%, p < 0.001). Adverse events occurred in 0.3%, 63% thereof were associated with polypectomy. There was a decline in complication rates of –7.3 per 10,000 endoscopies per two-year-period (95%CI –13.1, –1.5 per 10,000 endoscopies per two-year-period, p = 0.013). Sedation induced the probability of adverse events 0.24% in sedated and 0.16% in unsedated patients. p = 0.025. Notably, all perforations occurred under sedation.

Conclusion: This study showed a strong improvement in quality of screening colonoscopies performed within a national quality assurance programme in Austria between 2007 and 2014. Overall adenoma detection rate and detection rate of proximal lesions increased strongly in the investigated study period. Interestingly, the detection rate of advanced adenomas decreased.

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

OP372 ENDORINGS™ INCREASES ADR EVEN IN HIGH-RISK SCREENING COLONOSCOPY: RESULTS OF A SINGLE CENTRE PILOT STUDY
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Introduction: Colonoscopy remains the gold standard procedure for screening and polyp detection, with adenoma detection rate (ADR) being a widely accepted key performance indicator (KPI). It has long been recognised that even experienced colonoscopists incur an appreciable ‘miss-rate’ and a number of novel devices have been marketed to assist this aspect of practice. The Endorings™ device is a simple soft silicone, single-use device consisting of a series of rings arranged around a central tubular core. As the colonoscope is inserted the rings fold backward to allow intubation and flare on withdrawal to flatten colonic folds and aid inspection.

Aims & Methods: This was a single-centre pilot study to determine the effect of Endorings used in a high-risk cancer screening population (national), when used by experienced colonoscopists already established ADR and compared the results to outcomes from the previous few months, for the same two colonoscopists when the device was not in use (ie. historical controls).

Results: The ADR without Endorings™ (n = 85) was 49.4% with a per-procedure detection rate (ppr) of 0.97. With the device (n = 66), ADR was 66.7% (p = 0.0006) with ppr of 1.625. This represents a 35% increase in ADR and a 68% increase in the number of polyps detected at any given procedure. There were no significant differences in completion rates, withdrawal time, use of sedation or comfort scores. The device was removed in 5/6 procedures due to interference with intubation (in the presence of either an angulated sigmoid or difficult rectal angle).

Results: 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 device, Endorings™ with three rings which increase intubation and inspection. The three-ring design was felt to interfere with normal intubation and aid inspection.

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 with two rings which increase intubation and aids inspection. Use of the Endorings™ device was associated with a significant increase in ADR and a 68% increase in the number of polyps detected at any given procedure.

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

OP373 THE FIRST RANDOMISED CONTROLLED TRIAL OF ENDOCUFF VISION®-ASSISTED COLONOSCOPY VERSUS STANDARD COLONOSCOPY FOR POLYP DETECTION IN BOWEL CANCER SCREENING PATIENTS (E-CAP STUDY)
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Introduction: Up to 25% of colonic polyps are missed during colonoscopy. The Endocuff Vision™ is a cap with soft flexible arms which unfold at the end of a colonoscope and improves views during withdrawal. We have performed the first randomised controlled trial to identify the role of Endocuff Vision® in improving polyp detection.

Aims & Methods: Our aim was to investigate the impact of Endocuff Vision®-assisted colonoscopy on polyp detection, as compared to standard colonoscopy, in the UK Bowel Cancer Screening Programme (BCSP). This was a single-centre, non-blinded, randomised controlled trial. Ethics approval was obtained (ref. 13/HS/0023).
OP374 INCREASED ADENOMA DETECTION RATE BY G-EYE HIGH DEFINITION COLONOSCOPY IN COMPARISON TO STANDARD HD DEFINITION COLONOSCOPY - A PROSPECTIVE RANDOMIZED MULTICENTRE STUDY


A145

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

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 colonic miss rates and interval cancer incidents.

Disclosure of Interest: H. Jacob: Board of directors

All other authors have declared no conflicts of interest.

OP375 EFFICACY AND SAFETY OF THE NOVEL 1L PEG AND ASCORBATE BOWEL PREPARATION NER1006 VERSUS TRISULFATE SOLUTION IN OVERNIGHT SPLIT-DOSING ADMINISTRATION: RESULTS FROM THE PHASE 3 STUDY NOCT

C. Winkler1,2, R. Vetter1,2, L. Kisselich1,2, S. Heaton3,4, P.M. Krähenbühl5,6, M. Seip1,2, H. Jacob3,4, K. Grass1,2, C. Winkler1,2, K. Grass1,2, C. Winkler1,2, K. Grass1,2, C. Winkler1,2, K. Grass1,2

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Introduction: Successful colon cleansing enables effective colonoscopy. PEG based split dosing preparations are traditionally seen as the gold standard in cleaning, but most still require a high preparation volume intake. NER1006 is a new, low volume (1L), PEG3350 and ascorbate bowel preparation in phase 3 clinical development. The low volume of NER1006 is achieved through the use of ascorbate in the second dose only.

Aims & Methods: This phase 3, randomised, multicentre, colonoscopist-blinded, non-inferiority study assessed the safety, efficacy and tolerability of a 2-day overnight split-dosing regimen of either NER1006 (NER) or trisulfate solution (TS) in patients undergoing colonoscopy. Two alternative primary endpoints were evaluated: overall bowel cleansing success and ‘Excellent plus Good’ cleansing rate in the colon 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 NER2D (n = 310) or TS (n = 311). For NER 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 (51.0%) vs. 152 (49.0%). The prevalence of N2D, N1D and N0D in patients randomized to NER2D was 45.6% (142) vs. 45.7% (142) for TS. High standard overall bowel cleansing efficacy was achieved in both treatment groups (Table 1). NER2D demonstrated non-inferiority (lower CI limit ≥ 10%) to TS for both alternative primary endpoints. Numerically, more patients on NER2D achieved an ‘Excellent plus Good’ cleansing rate in the colon ascends compared with TS. Non-inferiority for NER in adenoma detection rate in the colon ascends was not demonstrated; other key secondary endpoints were not formally tested. Tolerability and acceptability as assessed by the Bowel Cleaning Impact Questionnaire (BCIQ-LIR) Questionnaire were comparable for NER2D and TS (Table 1). Compliance rates were high in both treatment groups. There were no deaths. The study was concluded as non-inferior to TS.

Discussion: NER1006 was not associated with any serious treatment-emergent adverse events (TEAEs). The most frequently reported related TEAEs in both treatment groups were nausea and vomiting.

Conclusion: When administered as a 2-day split dosing regimen, and compared to trisulfate solution, NER1006 was non-inferior in overall bowel cleansing success and in achieving an ‘Excellent plus Good’ cleansing rate in the colon ascends. Both treatments were well tolerated, most TEAEs were mild or moderate in severity and reflected the expected safety profile of respective therapies. The

Table 1: Results Summary

<table>
<thead>
<tr>
<th>SC</th>
<th>G-EYE</th>
<th>% Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR</td>
<td>33.8%</td>
<td>49.2%</td>
</tr>
<tr>
<td>Adenoma per patient</td>
<td>0.57</td>
<td>0.93</td>
</tr>
<tr>
<td>Small adenomas (6-9 mm)</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>Large adenomas (≥10 mm)</td>
<td>26</td>
<td>51</td>
</tr>
<tr>
<td>Advanced adenomas</td>
<td>32</td>
<td>63</td>
</tr>
</tbody>
</table>

Table 1: E-CAP results

<table>
<thead>
<tr>
<th>Standard</th>
<th>Endocuff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>265</td>
</tr>
<tr>
<td>Polyps</td>
<td>470</td>
</tr>
<tr>
<td>Polyps/patient</td>
<td>1.77</td>
</tr>
<tr>
<td>Adenomas</td>
<td>339</td>
</tr>
<tr>
<td>Adenomas/patient</td>
<td>1.35</td>
</tr>
<tr>
<td>PDR</td>
<td>185/265 = 69.8%</td>
</tr>
<tr>
<td>ADR</td>
<td>167/265 = 63%</td>
</tr>
<tr>
<td>Cancer detection rate</td>
<td>15/265 = 5.7%</td>
</tr>
</tbody>
</table>

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

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6Rafi Medical Technologies, Jalisco/Mexico
7R&A Medical, Sydney/Australia
8Kings College London - ISS on November 25, 2016
Primary endpoint: Patients with successful bowel cleansing efficacy (HCS) [n]

Supportive secondary endpoint: Patients with successful overall bowel cleansing efficacy (BBPS) [n]

Key secondary endpoint: Adenoma detection rate, colon ascends

Key secondary endpoint: Adenoma detection rate, overall colon

Key secondary endpoint: Polyp detection rate, colon ascends

Key secondary endpoint: Polyp detection rate, overall colon

Compliance rate (min 75% of both doses taken) [n]

BOCLIR score [mean (SD)]

SAFETY

All treatment-emergent adverse events [n]

Patients with any related treatment-emergent adverse event [n]

Results: During the study period (January–April 2016), 286 patients were enrolled (mean age 59.8 ± 7.1, males 53.7%), 143 in group A and 143 in group B; of them 266 have undergone colonoscopy (group A: 130, group B: 136). The two groups were well balanced as concerns age, gender, education, employment and marriage status. Split-dose was adopted by 106/130 and by 118/136 patients in group A and B, respectively (81.5% vs 86.8%, p = 0.317). Among patients who complied with split-dose the quality of bowel cleansing, as assessed by BBPS, was in each segment of the colon) in 215/224 (96.0%). No significant differences between group A and B were observed with regards to adherence to preparation scheme, which were both optimal, (98.1% vs 97.5%, p = 0.693) and to the adequacy of bowel prep (BBPS > 2 in each segment) (97.2% vs 94.9%, p = 0.785).

In order to evaluate whether additional oral explanation, aimed at reinforcing the benefits of split-dose, may further improve compliance, patients were randomized in two groups: group A-only booklet delivered; group B-oral explanation. This result is relevant in an open-access system, where routine oral education is not applicable.

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A. Andrealli, S. Paggi, A. Amato, E. Rondonotti, G. Imperiali, N. Lenoci, G. Mandelli, N. M. Terreni, G. Spinzi, F. Radaelli

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 adopted in the study. All patients received a low-volume preparatory regimen for colonoscopy. Proportions were compared by chi-squared questionnaire on colonoscopy day. Colon cleansing was evaluated by Boston Bowel Preparation Scale (BBPS) 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].

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 preparatory regimen for colonoscopy. Proportions were compared by chi-squared questionnaire on colonoscopy day. Colon cleansing was evaluated by Boston Bowel Preparation Scale (BBPS) 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].

References

was recorded. Sex distribution of these patients was similar to that of the patients with cirrhosis and enzyme alterations (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 = 1:59; mean age (yrs) = 65.6 vs M:F = 1:67; mean age (yrs) = 65, p = ns], but significantly different (p = 0.0001) compared to the normal population and to subjects with only liver enzyme alterations. Patients with occult and overt cirrhosis presented a similar prevalence of metabolic syndrome profile (49% and 56% respectively), while these figures were lower in patients without signs of liver disease (33%, p < 0.0001).

Conclusion: In conclusion, a large proportion of patients with biochemical signs of chronic hepatitis and cirrhosis are still undiagnosed. Metabolic syndrome seems to be the major risk factor that characterizes patients with more severe liver disease.

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

References


OP378 THE NATIONAL BURDEN IN FRANCE OF HOSPITAL CARE FOR PATIENTS WITH HEPATIC ENCEPHALOPATHY: DATA FROM THE FRENCH NATIONAL HOSPITAL DATABASE (PMSI)

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Introduction: Hepatic encephalopathy (HE) is a complication of cirrhosis characterised by a broad spectrum of neuropsychiatric manifestations. According to the clinical symptoms there are two types of HE: covert and overt HE (OHE). In general, the prevalence of OHE is estimated at 10%–14% in cirrhotic patients, compared to patients with transjugular intrahepatic portosystemic shunt (TIPS). In France, the prevalence of OHE was estimated at 25,000 patients and at 10%–50% in patients with transjugular intrahepatic portosystemic shunt (TIPS). In France, the prevalence of OHE was estimated at 25,000 patients (21,000 to 30,000 patients). Yet little is published on the national burden of hospitalisation of patients with hepatic encephalopathy. The first objective of this study was to use the retrospective national PMSI data (Programme Médicalisé des Systèmes d’Information) to assess the public health burden of this study was to use the retrospective national PMSI database from 2012 and 2013. Given the absence of coding specificity of hepatic encephalopathy, the prevalence of HE was implemented according to a medical expertise from the expression of the main symptoms of the disease. A retrospective cohort was performed from the national PMSI database. Aims & Methods: A retrospective observational study in 11 specialist National Health Service (NHS) centres of 145 patients prescribed RFX for HE between July 2008 and May 2014. Local clinical staff reviewed patients’ medical records for demographics, RFX prescribing and adverse drug reactions (ADRs) to RFX. Details of inpatient hospitalisations and hospital visits in the 12 months pre- and post-RFX initiation were extracted from NHS Trust electronic databases. Ethics reference 14/WS/107.

Results: Of the 145 patients evaluated, 89 (61%) were male. At RFX initiation, mean age was 61 years (standard deviation [SD] = 11), 119 patients (82%) were on lactulose. Child-Pugh score was recorded for 67 (46%) patients (10% Class A, 54% B, 36% C). Resource use in the 6–12 months pre- and post-RFX initiation is shown in Table 1; to avoid nonsurvivor confounding this analysis includes the 114 patients (78%) who were alive at 6 months and 102 (70%) alive at 12 months post-RFX initiation. 3 patients (2%) had ADRs and 4 (3%) developed diffuse infection (including critical care and emergency room visits; reductions are observed within 6 months of treatment initiation and sustained at 12 months. This is the first study to demonstrate a reduction in critical care bed occupancy with RFX.

Disclosure of Interest: R. Aspinall: Consultant and UK advisory board member for Norgine. G. Shaya: Employee of Norgine. R. Cipelli: Consultant for Norgine. Employee of pH Associates which was commissioned by Norgine Pharmaceuticals to provide support with study design and management, data analysis and statistical editorial services. M. Hudson: Consultant for Norgine. Attended advisory board and has given sponsored lectures (national or international) on behalf of Norgine.

Table 1 (OP379): All-cause resource use pre- and post-RFX initiation

<table>
<thead>
<tr>
<th>6 months (n = 114)</th>
<th>12 months (n = 102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>n*</td>
</tr>
<tr>
<td>Hospitals with overnight stay per patient</td>
<td>101</td>
</tr>
<tr>
<td>Total bed days</td>
<td>101</td>
</tr>
<tr>
<td>Total bed days per inpatient</td>
<td>101</td>
</tr>
<tr>
<td>Critical care bed days per inpatient</td>
<td>19</td>
</tr>
<tr>
<td>Emergency room visits per patient</td>
<td>63</td>
</tr>
</tbody>
</table>
**OP382 Pregnancy outcome in more than 5000 births to women with viral hepatitis in a population-based cohort study in Sweden**

J. Stokkeland1, J.F. Ludvigsson2, R. Hultcrantz1, A. Ekbom3, J. Höjér4, M. Botti4, O. Stephansson5

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**Introduction:** Previous studies have shown inconsistent results with respect to hepatitis B (HBV), Hepatitis C (HCV) and pregnancy outcome.

**Aims & Methods:** The aim of this study was to investigate pregnancy outcome in women with HBV or HCV. In a nationwide cohort of pregnancies between 1997 and 2011 we investigated the risks of adverse pregnancy outcomes in 3,077 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 to women with HCV (n = 1,429) were selected as population controls.

**Results:** Women with HCV were more likely to smoke (47.62% vs. 8.65%) and to have alcohol dependence (18.79% vs. 1.07%) compared with population controls. Most women were born in non-Nordic countries. HCV was associated with a decreased risk of preeclampsia (aRR: 0.42, 95% CI: 0.25–0.65), an increased risk of late neonatal death (7–27 days: aRR: 4.47, 95% CI: 1.01–12.44) and an increased risk of preterm birth (aRR: 1.31, 95% CI: 1.08–1.59). HCV was associated with an increased risk for preterm birth (aRR: 1.21, 95% CI: 1.01–1.44).

**Conclusion:** Both HBV and HCV are risk factors for preterm births, while HCV seems to be associated with a protective effect against preeclampsia. Future studies should corroborate these findings.

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

**WEDNESDAY, OCTOBER 19, 2016**

**10:30–12:00**

**TRANSLATIONAL ASPECTS OF IBD – ROOM L8**

**OP383 ALTERATION OF THE RENIN-ANGIOTENSIN SYSTEM IN THE CIRCULATION, TERMINAL ILEUM AND COLON IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A POTENTIAL NOVEL THERAPEUTIC TARGET**


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**Introduction:** The renin-angiotensin system (RAS) has well-recognised roles in cardiovascular and renal homeostasis, but may also regulate inflammation, fibrosis and angiogenesis in multiple other organs, including the gastrointestinal tract. The recently recognised alternative RAS axis comprising angiotensin converting enzyme 2 (ACE2), the effector peptide angiotensin (Ang) (1–7) and the Mas receptor, mediate anti-inflammatory and anti-fibrotic effects as opposed to the classical axis comprising ACE, Ang II and the AT1 receptor. This study aimed to investigate the expression of angiotensin (1–3) fold, ACE (30–40 fold) and ACE2 (10 fold) expressed in the terminal ileum than colon (p < 0.0001 for all). RAS components were closely localised to the epithelium; variably in the lamina propria and submucosa, especially microvascular elements and medium; and circular muscle myocytes. Expression of mRNA of angiotensin II was twofold higher in inflamed IBD and non-inflamed IBD or non-IBD control colonic segments (p = 0.001, Kruskal-Wallis); immunohistochemical staining intensity for ACE2 was higher in the colon in patients with CD (p = 0.001) and that for Ang (1–7) (p = 0.0001) in the colon in patients with IBD than 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).

**Conclusion:** All of the 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) 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.

**OP384 BLOCKADE OF AE7-INTEGRIN CONTACTS TRAFFICKING OF CD8+ AND TH2 LYMPHOCYTES FROM IBD PATIENTS TO THE INFILATED GUT IN VIVO**

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**Introduction:** The anti-ε7 antibody etrolizumab (VDZ), which inhibits homing of lymphocytes via interaction of αε7β Integrin with MAdCAM-1, has greatly increased therapeutic options in patients with IBD. However, lymphocyte homing may also occur via other homing molecules like the α4β1 integrin and a considerable portion of patients does not respond to VDZ therapy. The anti-ε7 antibody etrolizumab (ETZ) is currently tested in phase III trials and additionally blocks the binding of αε7β to E-Cadherin, which is believed to mediate epithelial retention of homed lymphocytes.

**Aims & Methods:** We aimed to compare lymphocyte trafficking upon blocking of β7 vs. αε7β integrin. Hence, αε7β and αε7β expression was determined on peripheral blood and lamina propria lymphocyte subsets in CD and CD patients and healthy donors by flow cytometry or immunofluorescence staining, respectively. The regulation of αε7β expression upon lymphocyte stimulation and incubation with cytokines was studied. In vitro adhesion assays the adhesive capacity of lymphocytes to MAdCAM-1 and E-Cadherin in the presence of VDZ or the ETZ surrogate antibody FIB504 (ETZs) were tested. Finally, lymphocytes from UC patients were treated with either of the compounds. Flow cytometry labelled and injected into the ileocelec area of immuno-suppressed mice. Gut homing was assessed by in vivo confocal microscopy and flow cytometry of lamina propria cells.

**Results:** Aε7β expression was significantly higher on CD8+ lymphocytes than on CD4+ lymphocytes both in the peripheral blood and the gut. Among both subsets αε7β expression was correlated with IL-9 secretion, while CD4+ IL-9 cells expressed less αε7β than other CD4+ subsets. At the same time, CD8+ cells exhibited a notably greater potential to increase αε7β expression upon T cell receptor stimulation and TGF-beta, while decreased αε7β 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 mMAdCAM-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 PL1/11 cells was decreased. The expression of αε7β on CD8+ cells from IBD patients treated with VDZ was higher in the maintenance than in the induction phase of treatment.

**Conclusion:** VDZ may not equally cover all pathogenetically relevant lymphocyte subsets and may not equally influence therapeutic response in UC and CD patients. ETZ seems to offer superior reduction of intestinal lymphocyte infiltration especially concerning CD8+ and TH2 cells.

**Disclosure of Interest:** S. Zundler: The etrolizumab Surrogate antibody was produced at (p = 0.0001) and that for Ang (1–7) (p = 0.0001) in the colon in patients with IBD than 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).
Flow cytometry was used to identify total DC, (HLA-DR response to mucosal antigen. Dendritic cells (DC) are the primary antigen

Introduction:

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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 contribute 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-TNFa 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-TNFa (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)2vitamin D3). Flow cytometry was used to identify total DC, (HLA-DR* cells negative for markers of other cell lines (CD3, CD14, CD16, CD19, CD34)). DC were further subtyped as myeloid (mDC, CD11c+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 for TNFα + vitamin D (58 ng/mL) was lower compared to the TNFα + vitamin D (109 ng/mL). 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/mL was associated with a decrease in myeloid DC TNFα production. Anti-TNF therapy alone induced a significant upregulation of the skin homing marker cutaneous lymphocyte antigen (CLA) on myeloid DC (p = 0.0055), an effect which was not seen in patients receiving adjunctive vitamin D.

Conclusion: High dose parenteral vitamin D, given as an adjunct to anti-TNFα therapy in Crohn’s, promotes down-regulation of circulating myeloid DC production of TNFα. This may influence the subsequent interaction of DC and T cells. TNFα promotes a TH-17 response characteristic of Crohn’s inflammation; thus the ability of vitamin D to further block TNFα production may promote a more regulatory T cell response and improve outcomes when used as an adjunct to anti-TNFα therapy. The upregulation of the skin homing marker CLA following anti-TNFα therapy may explain the high rates of cutaneous side effects to this drug class. The down-regulation of CLA by vitamin D in this setting may be useful in those patients suffering cutaneous sequelae of anti-TNFα therapy.

Disclosure of Interest: P. Hendy: Advisory board: DrFalk; AbbVie

All other authors have declared no conflicts of interest.

OP387 A PROTEOMIC APPROACH TO EXPLORE THE PROTECTIVE ROLE OF INULIN IN PREVENTING LPS-INDUCED HUMAN COLONIC SMOOTH MUSCLE IMPAIRMENT

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Introduction: Fructans, such as inulin, are dietary fibers which stimulate gastro-intestinal function acting as prebiotics. We recently demonstrated the protective effect of inulin on LPS-induced damage of colonic smooth muscle in an ex vivo experimental model, which seems to be related to presence of oxidative stress.

Methods: In the present study, the protective role of inulin against LPS-induced oxidative stress was evaluated on colonic mucosa using a proteomic approach. Human colonic mucosa and submucosa, obtained from disease-free margins of resected segments for cancer, were sealed between two chambers containing Krebs solution, with or without the mucosa overlaid with 5 mL of Krebs, or 100 μg/mL LPS solution, or 100 μg/mL LPS + 100 mg/mL inulin Fructafit IQ (LPS + INU). The biological system was kept oxygenated for 30 min at 37°C. The solutions on the submucosal side were collected following mucosal exposure to Krebs in the absence (N-unendamantant) or presence of LPS (LPS-unendamantant) or LPS + inulin (LPS + INU-unendamantant). Untamantants were tested for the effects on human colonic smooth muscle strips contractility using an organ bath system. Proteomic analysis (iTRAQ based analysis) was used to identify and compare the soluble proteomes from human colonic mucosa and submucosa treated. Each sample was labelled by one of four reagents of the iTRAQ 4-plex and then combined into one aliquote. Triplicate labelling was performed, which showed a high level of reproducibility.

Results: In the presence of inulin exposure was able to restore, in human colonic mucosa, the LPS-dependent alteration of some proteins involved in the host response and in the intestinal smooth muscle contraction (ZG16, CALM1/MlCK/MYL signaling pathway) and to reduce the upregulation of two proteins involved in the radi-based alteration of some proteins involved in the host response and in the intestinal smooth muscle contraction (ZG16, CALM1/MlCK/MYL signaling pathway) and to reduce the upregulation of two proteins involved in the radiation-induced oxidative stress induced by LPS (APEX1, CCT7). Moreover the administration of inulin entails a higher level of some detoxification enzymes (MT2A, GSTK1, and UGT2B4) with respect to LPS treatment. Following exposure to the LPS-unendamantant, a significant decrease in maximal Ach-induced contraction was observed when compared to the control. In contrast, in control muscle strips incubated with the N-unendamantant (49 ± 5% vs 10 ± 1% respectively, P < 0.05) and this was completely prevented by pre-incubation of the LPS with Inulin (12 ± 2%, P = ns versus N-unendamantant).

Conclusion: Our data suggest that the exposure of colonic mucosa to inulin is able to prevent LPS-dependent altered expression of some key proteins which promote intestinal motility and the host response, reducing the radiated-mediated oxidative stress induced by LPS.
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, GOJ4: 5 cm distal to the junction). It is crucial to note that this classification is not distinct for all types of gastro-oesophageal junction (GOJ) tumours; therefore, it is essential to consider the anatomical location and subtypes. GOJ1 tumours are more comparable to intraduodenal tumours, GOJ2 tumours to fundic tumours, GOJ3 tumours to pyloric tumours, and GOJ4 tumours to gastric cardia tumours. 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 of gastro-oesophageal junction (GOJ) was assessed by the Illumina HTv4.0 beadchip array (GOJ: 35; GOJ1: 20; GOJ2: 18; GOJ3: 18; true gastric comparators: gastric fundus/proximal body: 6; distal body: 9; antrum: 8). Only tumours of intestinal Lauren type were included. DNA methylation gene expression analysis was performed using Illumina in R, using unsupervised biclustering analysis. This study provides evidence that different molecular subtypes exist in GOJ and other gastro-oesophageal junction tumours and that these subgroups may have distinct clinical outcomes. Conclusion: The Siewert classification is currently used to determine the molecular phenotype of GOJ tumours, which is then used for prognosis and targeted therapy. However, this classification may not accurately reflect the molecular subtypes of GOJ tumours. Further research is needed to determine the optimal classification for GOJ tumours.

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

References

OP388 TLR4 IS STILL ACTIVE IN GP96-DEFICIENT MACROPHAGES

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Introduction: GP96 is an enolase-like 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 (TLRs), one of the best investigated family of pattern recognition receptors, lead to the phosphorylation of NFκB 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. Aim and Methods: We aim to study the impact of the gp96-knockdown on TLR-function in the human monocytic cell line MM6 and in a conditional gp96−/−LysMCre knock-out mice. MM6 cells were stably transduced with lentiviral gp96-knockdown vector. The lentiviral vector particles were produced by co-transfection of HEK293T cells with transfer, packaging and envelope plasmids using Fugene HD Transfection Kit. After transduction, cells were treated with LPS (100 ng/ml) for 2 hours. Furthermore, in order to analyze the relevance in vivo, conditional LysMCre-gp96 knock-out (KO) mice were also generated after crossing gp96lox-mice with LysMCre mice. 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 NFκB, IkBα, IκBβ, IL-8, IL-6 and TNFα was determined by Western blot, PCR and ELISA. Results are expressed as percentage or fold induction ± SEM. All experiments were performed with n ≥ 3.

Results: After checking that the efficiency of lentiviral knockdown was more than 90%, we performed flow cytometry experiments revealing that the transduction of TLR4 and TLR2+gp96 shRNA transduced cells were slightly decreased, 81% and 77% respectively, compared with mock-transduced MM6 cells. 92% and 97% respectively. In line with this, the analysis of the expression of TLR4 and TLR2 receptors in peritoneal macrophages showed a similar slight decrease in KO mice (74.4% and 77.0% respectively) compared with WT mice (78.2% and 90.5% respectively). The functionality of TLR4 receptor was also analyzed and treatment with LPS induced a significant increase in the ratio p-IκBα/IκBα in gp96−/−MM6 cells (1.6 fold induction) and KO peritoneal macrophages (5.1±1.5), and in protein expression of p-NFκB in both gp96−/−shRNA (1.7) and in KO peritoneal macrophages (1.5±1.0) compared with non-treated mock-transduced cells and WT peritoneal macrophages. Furthermore, LPS induced a significant increase in mRNA expression of IL-6 (2.0 fold induction) and TNFα (3 fold induction) in KO peritoneal macrophages compared with non-treated macrophages.

Conclusion: TLR4 receptor is still active and functional even in the absence of gp96.

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

OP391 SRGAP1, A CO-TARGET OF MIR-340 AND MIR-124, FUNCTIONS AS A POTENTIAL ONCOGENE WITH AMPLIFICATION AND RECURRENT MUTATION IN GASTRIC TUMORIGENESIS

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Introduction: SRGAP1 (Slit-Robo GTPase-activating protein 1) functions as a GAP for Rho-family GTPases and downstream of Rho-signaling. However, the involvement of SRGAP1 activation and functional role in gastric carcinogenesis is unclear. Aim and Methods: We aim to investigate the biological functions of SRGAP1 and comprehensively reveal its regulation by deregulated miRNAs in gastric cancer. This study performed the mRNA and protein expression of SRGAP1 in gastric cancer samples, the expression of SRGAP1 protein showed negative correlation with the expression of miR-340 and miR-124. These findings provided a potentially target SRGAP1 was performed by TargetScan (http://www.targetscan.org/) and miRDB (http://www.mirdb.org). miR-340 and miR-124 were screened out for further validation. The regulation of SRGAP1 by miRNAs was confirmed by qRT-PCR, Western blot and dual luciferase activity assays by ectopic expression of miR-340 and miR-124.

Results: SRGAP1 is over-expressed in 9 out of 12 (75.0%) GC cell lines both from the mRNA and protein level. In clinical samples form TCGA cohort, SRGAP1 shows gene amplification in 5/258 (1.9%) cases and its mRNA upregulation shows positive correlation with the copy number change mutation rate of SRGAP1 in primary GC is 8/258 (3.1%) Knockdown of SRGAP1 in MKN28, MGC-803 and SGC-7901 cells exhibited significant anti-oncogenic effect in vitro. SRGAP1 downregulation suppressed cell proliferation, reduced migration and colony formation, and inhibited at least 50% of the invasion and migration ability. Moreover, luciferase activity experiments revealed SRGAP1 knockdown significantly inhibited Wnt/β-catenin pathway, which was further confirmed by the inactivation of β-catenin and downregulation of CCND1 and c-myc expression. SRGAP1 was confirmed to be a direct target of miR-124 in GC. These two miRNAs showed decreased expression compared with adjacent normal epithelium cells and the downregulation of miR-340 and miR-124 were associated with poor survival. Enforced overexpression of miR-340 and miR-124 in GC cells abolished tumor-suppressive function by inhibiting cell proliferation and inducing G1 phase cell cycle arrest. In paired GC samples, the expression of SRGAP1 protein showed negative correlation with the expression of miR-340 and miR-124.

Conclusion: SRGAP1 is over-expressed and plays an oncogenic role in GC through activating Wnt/β-catenin pathway. Apart from gene amplification and mutation, the activation of SRGAP1 in GC is partly due to the downregulation of miR-340 and miR-124. These findings provided clear evidence that SRGAP1 could be a potential therapeutic target for GC.

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

Wednesday, October 19, 2016
10:30 - 12:00
Gastric and Jugalional Cancers - Room 1.86

OP389 A NEW, BIOLOGICALLY RELEVANT CLASSIFICATION FOR ADENOCARCINOMA AT THE GASTRO-OESOPHAEGAL JUNCTION


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Introduction: Adenocarcinomas at the gastro-oesophageal junction (GOJ) are currently stratified according to the Siewert classification by location of the main tumour mass (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, GOJ4: 5 cm distal to the junction). It is unclear whether this also reflects the molecular phenotype and hence how this stratification might influence therapy and prognosis in an era of personalised medicine.

Aims & Methods: The aim of this study was to determine the molecular phenotypes of GOJ tumours and to relate this to the Siewert classification. The gene expression profile of 107 tumours of gastro-oesophageal junction (GOJ) was assessed by the Illumina HTv4.0 beadchip array (GOJ: 35; GOJ1: 20; GOJ2: 18; GOJ3: 18; true gastric comparators: gastric fundus/proximal body: 6; distal body: 9; antrum: 8). Only tumours of intestinal Lauren type were included. DNA methylation gene expression analysis was performed using Illumina in R, using unsupervised biclustering analysis. This study provides evidence that different molecular subtypes exist in GOJ and other gastro-oesophageal junction tumours and that these subgroups may have distinct clinical outcomes. Conclusion: The Siewert classification is currently used to determine the molecular phenotype of GOJ tumours, which is then used for prognosis and targeted therapy. However, this classification may not accurately reflect the molecular subtypes of GOJ tumours. Further research is needed to determine the optimal classification for GOJ tumours.
Disclosure of Interest: All authors have declared no conflicts of interest.

OFP393 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 develop the risk development of colorectal neoplasms in patients with gastric cancer. The study group included a total of 209 patients with gastric cancer and 270 patients with colorectal cancer as control group. The patients were divided into five groups. The statistical analysis was performed using the SPSS program. The results were statistically significant with a p-value less than 0.05.

Results: There were 27 patients with colorectal cancer in the study group and 43 patients in the control group. The incidence of colorectal cancer in patients with gastric cancer was 10.4% (27/262). The incidence of colorectal cancer in control group was 15.9% (43/270). The difference between the two groups was statistically significant (p=0.047).

Conclusion: The results of this study suggest that colorectal cancer may have a higher risk in patients with gastric cancer. Further studies are needed to confirm these findings.

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

OFP394 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 full version is expected to be published in the journal. A systematic search was performed using the Cochrane 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 with therapy and/or combination treatment versus BSC or versus a control arm, in patients with esophageal or gastro-esophageal junction cancer were included. Two authors independently extracted data.

Results: For the comparison of palliative chemotherapy or targeted therapy versus BSC, five trials with a total of 751 patients were included in the meta-analysis for overall survival (OS). This analysis demonstrated a significant benefit in OS in favor of the group receiving palliative chemotherapy and/or targeted therapy compared to BSC (hazard ratio (HR) 0.81 (0.71 to 0.92)). A similar trend was observed for progression free survival (PFS), including two trials and 542 participants, with a HR of 0.58 (95%CI 0.28 to 1.18). For the comparison of adding a cytostatic and/or targeted agent to a control arm, ten trials, with 1288 patients in total were included for the meta-analysis of OS. This analysis demonstrated a significant benefit in OS in favor of the arm with an additional cytostatic or targeted therapeutic with a HR of 0.77 (95% CI 0.70 to 0.85). The median increased survival time was limited, one month for adding an additional cytostatic or targeted therapeutic to the control arm. Subanalysis with second line therapies showed a similar benefit as first line therapies. Marucciarum 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 toxicities did not occur frequently. Quality of life studies that reported this outcome, often improved in the arm with an additional agent.

Conclusion: Palliative chemotherapy and/or targeted therapy significantly increase OS compared to BSC in patients with esophageal or gastro-esophageal junction cancer. Additional patients with esophageal chemotherapeutic 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 the 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.
Introduction: Appendectomy has been the standard treatment for acute appendicitis and is performed annually in the United States1. Although appendectomy is generally well tolerated, it is a major surgical intervention and can be associated with postoperative morbidity. Our APPAC trial2 comparing antibiotic therapy with appendectomy for the treatment of acute complicated appendicitis was performed in a 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 included in six Finnish hospitals. Patients were randomly allocated in a 1:1 ratio. The study was stopped early because of increasing difficulties in recruitment. Fifty-three patients were randomized to resection and 56 to conservative treatment. The GIQLI score was measured after six months. A total of 109 patients were randomized to resection and 56 to conservative treatment. The GIQLI score was measured after six months. To our knowledge, this is the first randomized study comparing antibiotic therapy and appendectomy for uncomplicated acute appendicitis to result in further analysis. Avoiding appendectomy in our study resulted in major cost savings. Although 27% of the antibiotic group patients underwent surgery, the differences in costs between 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.

References

OP397 PREVALENCE OF SESSILE SERRATED ADENOMAS/POLYPS IN DISTAL COLON DURING SCREENING COLONOSCOPY: FLEXIBLE SIGMOIDOSCOPY: A SINGLE BOWEL CANCER SCREENING CENTRE EXPERIENCE FROM UK

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Introduction: Sessile Serrated Adenomas/Polyps (SSA/P) are responsible for nearly 20% of colorectal cancer (CRC). Despite the utility of novel image enhancing techniques including narrow band imaging it is difficult to differentiate hyperplastic (HP) polyps from SSA/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 detected and 97.6% of flexible sigmoidoscopy procedures were completed. Screening colonoscopy detected 1006 polyps and FS detected and polyps. Polyp size ranged between 1–80 mm. Colonoscopy detected 43 SSA/Ps (4.3%) with SSA/Ps detected in 6 mm, SD 7.2 mm; FS mean 3.4 mm, SD 3.9 mm). While colonoscopy detected 43 SSA/Ps (4.3%), FS detected only 6 SSA/Ps (2.4%) which equates to an overall prevalence of 3.9% (49/1255). Table 1 summarises the SSA/P prevalence data from our cohort. In rectum there were 8 SSA/Ps detected and resected which equals to a 3.6% of all rectal polyps. All SSA/Ps detected in rectum were less than 10 mm in size (range 2–9 mm). Prevalence of SSA/Ps in proximal colon was 4.5%.

<table>
<thead>
<tr>
<th>Site</th>
<th>Total number of polyps</th>
<th>Number of SSA/Ps</th>
<th>Prevalence of SSA/Ps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectum</td>
<td>222</td>
<td>08</td>
<td>3.6%</td>
</tr>
<tr>
<td>Sigmoid colon</td>
<td>320</td>
<td>13</td>
<td>4%</td>
</tr>
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<td>Descending colon</td>
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<td>Splenic flexure</td>
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<td>217</td>
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</tr>
<tr>
<td>Ascending colon</td>
<td>168</td>
<td>09</td>
<td>5.4%</td>
</tr>
<tr>
<td>Rectum site unspecified</td>
<td>114</td>
<td>09</td>
<td>7.9%</td>
</tr>
</tbody>
</table>

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.
OP398 SERRATED POLYPOSIS SYNDROME: A SURGICAL PERSPECTIVE


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Introduction: Serrated Polyposis Syndrome (SPS) is associated with an increased risk of colorectal cancer (CRC). Some patients may require colonic surgery but the literature regarding indication, procedure performed, outcomes and surgical decision making is sparse. We aimed to address these issues.

Aims & Methods: 434 patients with SPS, were retrospectively enrolled from 7 centers in the Netherlands and 2 in the UK. Data were retrieved from medical charts, pathology and endoscopy reports and collected in a centralized database. Data relating to surgical resection and surveillance outcomes were assessed.

Results: A total of 164 (38%) patients underwent colorectal surgery; 114 (70%) for CRC, 31 (19%) for high polyp burden and 14 (9%) for unresolvable polyps. Surgery for SPS Cancer Twenty seven (25%) SPS cancers were managed with total colectomy and ileorectal anastomosis (IRA), with the remaining 87 (75%) patients having a more limited resection. 90% of those undergoing IRA had a formal diagnosis of SPS at the time of their surgery compared with only 39% of those undergoing more conservative resections. Fifty eight (90%) patients had a resection for cancer before a diagnosis of SPS was made. Total polyp burden (median 40 v 22.5, p = 0.01) and proximal polyp numbers (median 20 v 12, p = 0.019) were significantly higher in those having more extensive surgery. In the limited resection group eight (9%) patients developed metachronous cancers: 2.2; 95% CI 1.1–4.3. In the IRA group 15 (13%) patients developed metachronous cancers with adequate bowel cleansing and caecum intubation in the Polish National Colorectal Cancer Screening Program between January 2000 and December 2008. They were followed for colorectal cancer incidence and death through the national registries until December 2013. We estimated adjusted hazard ratios (HR) for individuals with different adenoma characteristics compared to individuals without adenomas and derived a novel risk classification system. Results: Among 159,928 individuals (median age 56 years; 37.8% 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 1.50–11.43), and >5 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 –1.1–1.963).

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 endoscopies without increasing the risk for overlooked cancer.

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

OP399 IMPROVED RISK CLASSIFICATION FOLLOWING COLORECTAL ADENOMA REMOVAL

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Introduction: Current colonoscopy surveillance recommendations after polyp removal are arbitrary and resource demanding. We developed a novel risk classification system for colorectal cancer following adenoma removal.

Aims & Methods: We included 82 colorectal cancer cases identified in individuals who underwent colonoscopy with adequate bowel cleansing and caecum intubation in the Polish National Colorectal Cancer Screening Program between January 2000 and December 2008. They were followed for colorectal cancer incidence and death through the national registries until December 2013. We estimated adjusted hazard ratios (HR) for individuals with different adenoma characteristics compared to individuals without adenomas and derived a novel risk classification system.

Conclusion: Among 159,928 individuals (median age 56 years; 37.8% 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 1.50–11.43), and >5 adenomas (HR: 3.13; 95% CI 1.60–6.12, P = 0.001).

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

OP400 COST-EFFECTIVENESS ANALYSIS OF POST-POLYPECTOMY COLONOSCOPY SURVEILLANCE USING JAPANESE DATA: RISK-STRATIFIED SURVEILLANCE BASED ON POLYP RESULTS IS MORE COST-EFFECTIVE

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Introduction: To maximize the usefulness of total colonoscopy (CS) in reducing deaths from colorectal cancer (CRC), it is essential that cost-effective post-polypectomy CS surveillance programs are implemented. However, this has not been well examined. European Union and United States guidelines for post-polypectomy surveillance recommend risk-stratified programs based on initial CS results.1,2 Japanese guidelines, however, recommend that post-polypectomy surveillance should be performed within 3 years of polypectomy, regardless of the results of resected polyps.3 Given that different surveillance programs are recommended in different settings, it is important to determine the most cost-effective surveillance program.

Aims & Methods: The aim of this study was to determine the most cost-effective post-polypectomy CS surveillance program by performing a Markov model analysis using Japanese data. The model was developed by simulating the clinical course of CRC as a transition from normal epithelium, low-risk adenomatoses polyps sized 1–4 mm and 5–9 mm, high-risk adenomatous polyps, CRC, and finally to death from CRC.4 High-risk polyps included 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 accuracies were determined 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 were as follows: strategy 1, 23.004 QALYs and US$1,024.88; strategy 2, 23.000 QALYs and $1,009.02; strategy 3, 23.013 QALYs and $977.40; strategy 4, 23.046 QALYs and $970.31. The required numbers of CS procedures per person in strategy 1, 2, 3, and 4 were 2.143, 1.664, 1.617 and 2.548, respectively. Risk-stratified strategies (strategies 3 and 4) yielded higher QALYs with lower costs than strategies 1 and 2. Comparing strategy 3 with strategy 4, yielded QALYs were higher and required cost was lower in strategy 4. Strategy 4 was most-cost-effective, showing simple dominance over the other strategies, followed by strategy 3; however, strategy 4 required the most CS procedures. The PSA showed that the probability of strategy 4 being chosen as the most cost-effective at the willingness-to-pay value of $50,000 was 67.8%.

Conclusion: After polypectomy, risk-stratified CS surveillance programs based on the polyp results should be recommended owing to higher expected effectiveness and cost-effectiveness. Furthermore, more intense use of CS procedures in risk-stratified surveillance can heighten the effectiveness and cost-effectiveness in the Japanese setting. However, it does require a larger number of CS procedures; thus, it would be preferable to determine the most appropriate use of CS procedures in risk-stratified surveillance programs depending on the nationwide availability of CS resources.

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

References

OP401 NEW NBI MAGNIFYING ENDOCOSCOPIC CLASSIFICATION FOR COLORECTAL TUMORS PROPOSED BY THE JAPAN NBI EXPERT TEAM (JNET)

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Introduction: There have been many narrowband 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 poly/ sessile serrated poly (SSP), low grade intramusosal neoplasia, high grade intramusosal neoplasia/shallow submucosal invasive cancer, and deep submucosal invasive cancer, respectively. A web image interpretation study using the modified Delphi (UMIN000010292: Multicenter study for developing universal NBI magnifying endoscopic classification of colorectal tumors in Japan) was conducted. 25 specialists in magnification evaluated NBI magnifying findings and histology with 100 NBI still images on the web.

Results: Univariate and multivariate analyses and analysis on diagnosability from 5 candidate NBI magnifying findings such as i) loose vessel areas, ii) interruption of thick vessels, iii) scattered vessels, iv) thick, linearized/meandering atypical vessels in the tumor, and 5) amorphous areas of surface patterns for Type 3, and i) variable caliber of vessels, ii) thick vessels iii) irregular distribution of vessels, iv) vessel meandering, and v) irregular or obscure surface pattern for type 2B. Among the five candidate NBI findings, three findings such as 1) loose vessel areas, 2) interruption of thick vessels, and 5) amorphous areas of surface patterns were identified as the diagnosis of type 3. In addition, three findings such as i) variable caliber of vessels, ii) irregular distribution of vessels, and iii) irregular or obscure surface pattern in Type 2B. Among the five candidate NBI findings, three findings such as 1) loose vessel areas, 2) interruption of thick vessels, and 5) amorphous areas of surface patterns were identified as the diagnosis of type 3. In addition, three findings such as i) variable caliber of vessels, ii) irregular distribution of vessels, and iii) 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 intramusosal neoplasia and high grade intramusosal neoplasia/shallow submucosal invasive cancer.

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

Table (OP401)

<table>
<thead>
<tr>
<th>JNET</th>
<th>Type 1</th>
<th>Type 2A</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessel pattern</td>
<td>Invisible</td>
<td>Regular caliber</td>
<td>Variable caliber</td>
</tr>
<tr>
<td>Surface pattern</td>
<td>Regular or white spots</td>
<td>Regular (tubular/branched / papillary)</td>
<td>Irregular or obscure</td>
</tr>
<tr>
<td>Most likely histology</td>
<td>Hyperplastic poly/ Sessile serrated poly</td>
<td>Low grade intramusosal neoplasia</td>
<td>High grade intramusosal neoplasia/Shallow submucosal invasive cancer</td>
</tr>
</tbody>
</table>

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OP402 SUBCLASSES OF TYPE-II PIT PATTERN REVEAL ALTERNATIVE TUMORIGENIC PATHWAYS OF COLORECTAL SERRATED LESIONS

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Introduction: Colorectal serrated lesions (SLs) include hyperplastic polypl (HP), traditional serrated adenoma (TSA) and sessile serrated adenoma/polyp (SSA/P). Emerging evidences suggest that SSA/Ps are precursor lesions of colorectal cancers (CRCs) with BRAF mutation and the CpG island methylator phenotype (CIMP). We have previously reported that Type II-Open (Type II-O) pit patterns, which is highly specific to SSA/P. However, clinicopathological and molecular features of SLs without Type II-O pits remain unclear.

Aims & Methods: We aimed to identify clinicopathological and molecular features of SLs without Type II-O pits. We analyzed the methylation of CIMP markers (MINT1, −2, −12, −31, p16 and MLH1) and BRAF and KRAS mutation in 448 premalignant and malignant colorectal tumors. By using magnifying endoscopy, surface microstructures of colorectal lesions were classified into Type II pit or tumor pit (Type III, IV or V pit) according to the Kudo’s pit pattern classification system. Type II pit was subclassified into classical Type-II pit, Type II-O pit, Type II 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-Open plus tumor pit. Progression of Type II-L pit lesions to TSA was associated with KRAS mutation and accumulation of moderate DNA methylation. In contrast, BRAF mutation was frequently observed in colonic tumors with Type II plus tumor pit. These results suggest that lesions with Type II-L pit and those with Type II-Open plus tumor pit are useful hallmark of the premalignant stage of CRCs with KRAS mutation and CIMP-low.

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

OP403 ARTIFICIAL INTELLIGENCE (AI) IN ENDOSCOPY–DEEP LEARNING FOR OPTICAL BIOPSY OF COLORECTAL POLYPS IN REAL-TIME ON UNALTERED ENDOSCOPIC VIDEOS

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Introduction: ASGE-PIVI guidelines support a “resect and discard” strategy for diminutive colon polyps, provided that the predictive value of technology allowing for “optical biopsy” depicts at least 90% agreement in assignment of post-polypectomy surveillance intervals using pathology as standard. In addition, in order for a technology to be used to guide the decision to leave suspected diminutive rectosigmoid hyperplastic polyps in place (without resection), the technology should provide 90% negative predictive value for adenomatous histology. Such standards with optical biopsy might be achievable with experts (although even that is unclear) but do not cross over into general clinical practice. Several groups have looked at supporting the process of optical biopsy decision making on endoscopic assessment of the histology of diminutive colorectal polyps using traditional machine learning, but to date there are significant limitations in terms of (1) using still images only, and non-realtime computer support, both of which are not clinically efficient or effective, and (2) often involving magnification endoscopy that is not yet a widespread clinical practice. Deep learning is a branch of artificial intelligence which is a significant advance on traditional machine learning, and with huge computational power, machines can now recognize objects in real time. We sought to apply novel deep learning techniques to optical biopsy for colon polyps.

Aims & Methods: We aimed to evaluate deep learning applied to the classification of colorectal polyps into NICE types 1 and 2, in real-time on unaltered endoscopic videos, for the support of clinically efficient optical biopsy. We used 92 videos of small colorectal polyps (<10 mm) under white light (WL) and narrowband imaging (NBI) (38 NICE type 1, 52 NICE type 2), using Olympus 190 series colonscopes. “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 3-class model representing Types 1, 2, and unsuitable (frames without statistically representative information—blur, bubbles, liquid). The model operated at the individual frame level, without prior segmentation.

For model training purposes, each frame was manually tagged. The final dataset was split into training and validation sets, without overlap. Finally, the analysis was performed separately for NBI and WL frames, allowing for reporting of frame processing time and classification performance.

Results: A total of 33,954 training frames were used, split equally across NBI & WL, and type 1, type 2, & unsuitable classes. We performed a 5-fold cross-validation on the tagged frames for quality control. The trained DCNN model was then used to evaluate the unaltered videos in real-time, with an accuracy for polyp classification of 90% for NBI, and 83% for WL. The confusion matrix on whole-video classification of colorectal polyps gives a sensitivity of 93% and specificity of 85% for NBI. Finally, the processing time of our DCNN model ran at between 25 and 30 frames per second (fps) using a decent gamer-grade GPU (NVIDIA Titan-X) on an unaltered video feed of 60 fps, delivering near-realtime computer support.
Conclusion: To our knowledge, this is the first application of deep learning to the optical biopsy challenge for polyp differentiation into NICE types 1&2 using non-magnification colonoscopy and NBI, specifically in a clinically representative workflow where computer support is provided in realtime on unaltered endoscopic video streams. Although the present investigation was carried on a limited datasets of 92 videos, our deep learning model has shown clinically efficient and relevant performance for optical biopsy, well aligned with PIVI guidelines and the performance of experts. Ongoing work will determine if such a computer support solution could aid in the widespread adoption of a “resect and discard” strategy, and reduce the economic burden of pathological evaluation of benign diminutive colon polyps.

Disclosure of Interest: M.F. Byrne: Chairman of Satis Operations Inc
D.K. Rex: Olympus consulting and research support
N. Chapados: Imagia has commercial interests in artificial intelligence
F. Soudan: Imagia has commercial interests in artificial intelligence
C. Oertel: Imagia has commercial interests in artificial intelligence
M. Linares Perez: research support from Satis Operations Inc
R. Kelly: research support from Satis Operations Inc
F. Chandelier: Shareholder in Cadens Medical Imaging

All other authors have declared no conflicts of interest.

Age, mean (SD), y | 48 (7) | 48 (7) | 50 (17) | 52 (14)
--- | --- | --- | --- | ---
Women, n (%) | 5 (63) | 5 (46) | 19 (54) | 17 (53)
Body mass index, mean (SD), kg/m² | 22.6 (3.6) | 23.3 (4.1) | 22.2 (3.1) | 22.2 (2.8)*
Stoma present, n (%) | 7 (88) | 11 (100) | 10 (29) | 10 (32)*
Colon-in-continuity, n (%) | 1 (13) | 1 (9) | 22 (63) | 24 (77)*
Estimated small bowel length, mean (SD), cm | 128 (98) | 129 (77) | 54 (43) | 73 (56)*
Baseline PS, mean (SD), L/wk | 21.6 (8.1) | 15.9 (10.4) | 11.5 (5.9) | 11.2 (6.4)*
Baseline PS duration, mean (SD), y | 7.2 (7.4) | 8.1 (8.0) | 5.6 (5.3) | 6.1 (5.7)*

*\( n = 31, \) **\( n = 9, \) ***\( n = 32, \) ****\( n = 30. \)