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Swiss Association for the Study of the Liver (SASL)
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Swiss Society of Endoscopy Nurses and Associates (SVEP-ASPE)
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The intra-individual Variability of Fecal Calprotectin in patients with GI-symptoms.

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Background: Fecal Calprotectin (FC) is used to distinguish between functional and organic gastrointestinal disease. So far only single analyses were performed. Since we have observed a great variability of FC measurements that were performed in the same patient in a short amount of time, we wanted to investigate this variability in our pts.

Methods: We searched our data base for pts with GI disorder who had at least three documented FC values within 10 days.

Results: 404 pts were included (284 female (70%), range 11-92y, mean 45.8y). First we applied the usual cut-off of 50 µg/g. 110 pts showed ranges: 48 pts (43.6%) <50; 33 pts (30%) 50-99; 11 pts (10%) 100-199; 9 pts (8.2%) 200-500; 8 pts (7.3%) >500. The 150 pts with three elevated values showed even higher ranges: 21 pts (14%) with a range <50; 25 pts (16.7%) 50-99; 33 (22%) 100-199; 38 pts (25.3%) 200-499; 19 pts (12.7%) 500-1000; 14 pts (9.3%) >1000. Age and gender had no statistically significant influence. Comparable variability was shown in the subanalysis of patients with organic disease (232 pts, 57.4%), non-organic disease (153 pts, 37.9%) and uncertain diagnosis (19 pts, 4.7%). With a cut-off of 100µg/g 92 pts (22.6%) had normal and elevated values, with a cut-off of 150 µg/g 62 pts (15.4%).

Conclusions: The data showed that more than ¼ of the patients (28%) showed values deemed normal as well as pathological, as high as this ranges. The question arises if a single measurement is sufficient to base clinical decision on. To definitely formulate recommendations for everyday clinical practice, a large protective study is needed.

Isoproterenol activates gut-liver-axes: effects on intestinal mucus and vascular barrier as entry sites.

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Background: The gut-liver-axis presents the pathophysiological hallmark for multiple liver diseases and has been proposed to be modulated during stress and shock. Access to the gut-liver-axes needs crossing of the mucus and gut-vascular barrier (GVB). The role of β-adrenoreceptor-activation for both barriers has not been defined and is characterized here.

Methods: Isoproterenol or vehicle (sterile saline) were applied via osmotic pump intraperitoneally for 7 days. Ileal intestinal loop experiments were utilized in-vivo for assessment of extravasation of size-defined FITC-dextran (i.v.) and their translocation from the lumen to the liver. Whole ileum was analysed by immune-histochemistry for plasmalemma-vesicle (PV)-1, a marker of vascular permeability as well as RNA-sequencing.

Results: Healthy mice lack translocation of 4kDA-FITC-dextran from the small intestine to the liver whereas isoproterenol-treated mice demonstrate pathological translocation. Mucus layer is reduced in thickness with loss of goblet-cells and Muc2-staining and expression in isoproterenol-treated animals under standardized general anesthesia via access to the gut-liver-axes by isoproterenol-treatment with pathological extravasation of large-sized 70- and 150 kDa-FITC-dextran in ileal microvasculature. This pathological endothelial permeability and accessibility induced by isoproterenol associates with an augmented expression of PV1.

Conclusions: Isoproterenol impairs the intestinal muco-epithelial and endothelial-vascular pathological translocation to the liver. This barrier dysfunction on multiple levels potentially can contribute to liver injury induced by catecholamines during states of increased β-adrenergic drive.

Efficacy of Etrolizumab in patients with moderate to severe UC who had failed TNF Antagonist Therapy (HICKORY)

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Background: Patients (pts) with moderate-severe ulcerative colitis (UC) and intolerant or refractory (IR) to TNF antagonists (aTNFs) are a difficult-to-treat population. HICKORY evaluates the safety and efficacy of etrolizumab open label induction via centrally read endoscopy, patient-reported outcomes (PROs) and inflammatory biomarkers in these pts.

Methods: 130 aTNF-experienced UC pts receiving etrolizumab 105 mg s.c. q4w in a 14-week induction period were assessed at baseline (BL) and week 14 (endoscopic scores (ES), patient-reported rectal bleeding (RB), stool frequency (SF)), Clinical response: ≥3-point + 30% reduction of Mayo Clinic score (MCS) vs BL + ≥1-point decrease in RB or RS1. Remission: MCS≤2 (subscores≤1) + RB=0. Endoscopic improvement: ES≤1; RB remission: RB=0; SF remission: SF1 (≥1-point reduction vs BL).

Results: At week 14, etrolizumab treatment was associated with clinical response in 50.8%, remission in 12.3%, ES≤1 in 23.9%, RB remission in 52.3% and SF remission in 35.4% of pts. 43.9% of pts had ≥1-point IR improvement from BL. In 31 pts (32.1%) aTNFs were associated with increased rates of RB and SF remission. Among pts with ES≤0, 100% reported RB≤1 and 90% SF≤1. Conclusions: aTNF-experienced pts with moderate-severe UC and high disease burden treated with open-label etrolizumab for 14 weeks achieved clinically meaningful clinical response, remission, and endoscopic improvement. Pts who had a decline in ES≤1 achieved higher rates of RB and SF remission and greater reductions in inflammatory biomarkers. Study recruitment continues, a randomised maintenance phase is also ongoing. Previously presented: Peyrin-Biroulet L et al. UEGW 2017
LPA-induced GPR35 signaling in macrophages resulted in reduced TNF production associated with decreased intestinal corticosterone synthesis

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Background: Host-or microbial derived metabolites drive the development of inflammatory bowel disease (IBD) through their interaction with G protein-coupled receptors (GPCR). Polymorphism in GPR35 are associated with ulcerative colitis (UC), but the function of GPR35 protein-coupled receptors (GPCR) is rather understudied.

Methods: In order to study GPR35 in the intestine the mouse lines GPR35tdTomato, GPR35Ko and GPR35ΔCX3CR1, in which GPR35 can be deleted in macrophages by tamoxifen-induced Cre-mediated recombination have been generated. Potential ligands were screened in Cre-mediated recombination have been generated. Potential ligands were screened in Cre-mediated recombination have been generated.

Results: Ex vivo imaging of GPR35tdTomato /CX3CR1-GFP mice confirmed GPR35 expression to intestinal epithelial cells and CX3CR1+ macrophages with higher membrane expression compared to GPR35+ and GPR35 macrophages with higher Tnf, Il1b and Il23 expression by GPR35 macrophages. Potential ligands were screened with a Chinese Hamster Ovary (CHO) -K1 human GPR35 overexpressing cell line. Lysophosphatidic acid (LPA) and CXCL17 but not kynurenic acid (KNA) inhibited forskolin-induced cAMP production. LPA induced Tnf expression in ZF and in mouse macrophages in a GPR35-dependent manner. Deletion of GPR35 in macrophages resulted in increased DSS severity associated with reduced TNF production by macrophages. The treatment of GPR35ΔCX3CR1 mice with TNF attenuated colitis and restored CYP11B1 expression required for intestinal corticosterone synthesis.

Conclusion: LPA-mediated GPR35 signaling may modulate TNF production by macrophages associated with intestinal corticosterone synthesis.

Aspirin suppresses age-associated and colon cancer relevant DNA methylation changes in the healthy colon

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Background: The protective effect of aspirin against colon cancer (CC) is well described, but the underlying molecular mechanisms preventing tumor initiation and progression are poorly understood.

Methods: In a longitudinal study including 31 screening females, we performed Illumina Infinium MethylationEPIC array profiling DNA methylation over 850,000 CpGs in healthy colon biopsies obtained at baseline and a median follow-up of 10 years.

Results: Principal component analysis revealed colon location (51.4%) and time (4.5%) as top two components explaining the variability in the data. Differential methylation analysis showed that aspirin use suppresses methylation gain over time. Out of 753630 CpGs analyzed, 26170 (3.5%) showed hyper- and 17874 (1.2%) hypomethylation in nonusers compared to 1286 CpGs (0.2%) with hyper- and 7188 (1.0%) with hypomethylation in users over time in proximal colon (P<0.05). In distal colon, 10108 CpGs (1.3%) showed hyper- and 6005 (0.2%) hypomethylation in nonusers compared to 3360 CpGs showing hyper- (0.4%) and 18869 (2.5%) hypomethylation in users over time (P<0.05). Median methylation change over time was increased in nonusers (prox 3.6%, dist 2.0%), but reduced in users (prox 2.9%, dist 3.2%). Aspirin use suppressed hypermethylation selectively at non-CGIs (P<0.0001) and at intergenic regions (P<0.001). Pathway-based gene set enrichment analyses showed aspirin suppresses methylation changes in genes involved in metabolism, primary immune deficiency, NF-kappa B signaling, platelet activation etc.

Conclusions: Aspirin use modulates DNA methylation stability in the healthy colon and we propose this to be a major molecular mechanism underlying its anti-neoplastic effect.

Liver fibrosis screening in patients undergoing a screening colonoscopy (FIB-SCREEN): feasibility and preliminary results of a prospective study


Background: Advanced liver disease is one of the main causes of morbidity and mortality worldwide however diagnosis is rarely made at early stages as no feasible and practical screening strategy have been developed. We aimed to assess the feasibility and preliminary results of non-invasive liver fibrosis screening in all patients aged 50 or more undergoing a screening colonoscopy.

Methods: From November 2018 to April 2019, patients aged ≥50 years admitted for screening colonoscopy at our institution were prospectively recruited for liver fibrosis screening. Screening was performed using transient elastometry (TE) with Fibroscan M or XL probe with values ≥8kPa considered as significant. Exclusion criteria were: patients with known liver disease and severe comorbidities. Results: 49/52 (95%) screened patients consented to participate in the study. Our cohort was composed of 33 men (67%), median age was 57 ± [53-62] years and 7 patients (14%) had TE ≥ 8kPa (Table 1). Patients with TE ≥ 8kPa were more often obese (57% vs 19%, p=0.031), diabetic (43% vs 0%, p=0.178) and had a higher consumption (43% vs 4%, p=0.017). ALT and AST were significantly higher in the TE ≥ 8kPa group. FIB4 was non-significantly higher in the TE ≥ 8kPa group. Conclusion: Preliminary results indicate that liver fibrosis screening in the context of screening colonoscopy is feasible and acceptable to patients. 14% of subjects had raised TE undergoing the potential significant burden of undiagnosed liver fibrosis in this population.

Table 1: Patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>All cohort n=48</th>
<th>Fibrosis TE ≥ 8kPa (n=7)</th>
<th>No Fibrosis (n=41)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, IQR)</td>
<td>57 (53-62)</td>
<td>58 (56-66)</td>
<td>56 (52-62)</td>
<td>0.753</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>53 (87%)</td>
<td>6 (86%)</td>
<td>27 (94%)</td>
<td>0.402</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>22 (33%)</td>
<td>3 (43%)</td>
<td>19 (48%)</td>
<td>0.178</td>
</tr>
<tr>
<td>Obesity (%)</td>
<td>12 (24%)</td>
<td>4 (57%)</td>
<td>8 (19%)</td>
<td>0.031</td>
</tr>
<tr>
<td>Biological ALT (median, IQR)</td>
<td>27 (21-35)</td>
<td>60 (18-82.5)</td>
<td>25 (20-25.15)</td>
<td>0.009</td>
</tr>
<tr>
<td>Non-invasive fibrosis assessment FIB4 (median,IQR)</td>
<td>1.15 (0.83–1.54)</td>
<td>1.7 (1–2.06)</td>
<td>1.1 (0.7–1.4)</td>
<td>0.056</td>
</tr>
<tr>
<td>TE median (IQR)</td>
<td>4.2 (2.6–7.1)</td>
<td>10.4 (10.5–19)</td>
<td>4.3 (5.5–4.4)</td>
<td>0.017</td>
</tr>
</tbody>
</table>

Abbrivations: BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FIB4, FIB4 score; IQR, interquartile range; TE, transient elastography
Drug-induced liver toxicity in a prospective cohort of cancer patients receiving immune checkpoint inhibitors
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Background: Drug-induced liver injury (DILI) by immune checkpoint inhibitors is a frequent but poorly understood adverse event. In this study, we characterize liver immune-related adverse events (irAEs) in a prospective cohort.

Methods: We examined DILI in melanoma and non-small cell lung cancer patients during checkpoint inhibitor treatment. We investigated for presence and dynamics of antibodies associated with autoimmune liver diseases at three timepoints: before treatment start, at the onset of liver irAE, and two months later.

Results: There were 11 cases of liver irAEs among 142 patients (7.7%). 5/11 showed CTCAE grade 3/4 liver toxicity. Viral hepatitis was excluded in all individuals. 6/11 required treatment with steroids. Interestingly, 7/11 liver irAE patients (63.6%) showed positive autoantibody titers already prior to treatment start. 9/11 patients (81.8%) developed additional irAEs compared to 20/73 controls (27.4%) with multiple irAEs (p<0.0001). There were no deaths due to hepatic irAEs.

Conclusions: Liver irAEs are frequent and are often associated with additional irAEs of other organs. Pre-existing autoantibodies may predispose patients to immune-related hepatitis.

Endoscopic full-thickness resection for early colorectal cancer
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Background: Current international guidelines recommend endoscopic resection for T1 colorectal cancer (CRC) with low-risk histology features and oncologic resection for those at high risk of lymphatic metastasis. Exact risk stratification is therefore crucial to avoid under-treatment as well as over-treatment. Endoscopic full-thickness resection (EFTR) has shown favorable results concerning efficacy and safety in the resection of esophageal, gastric, duodenal as well as colorectal lesions. However data on occurrence of postinterventional pain are limited.

Methods: Data of 40 consecutive patients (14 female 26 male, mean age 61.3 years) who underwent endoscopic full-thickness resection (EFTR) by FTRD in our institution between 2017 and April 2019 were collected and analyzed retrospectively. Pain was assessed from endoscopy reports, medication charts and hospital admission records.

Results: 14 patients underwent EFTR in the upper GI tract (n=1 esophageal leiomyoma; n=2 inflammatory fibroid polyps; n=undefined cystic submucosal lesion; n=4 ectopic pancreas; n=1 malignant gastric polyp; n=1 gastric NET; n=1 duodenal GIST; n=2 duodenal adenoma; n=1 duodenal NET). 4/14 patients reported pain and 2/14 patients were hospitalized for pain management. Complete resection was achieved in 12/14 patients. 26 patients underwent EFTR in the lower GI Tract (n=1 diagnostic; n=1 schwannoma transverse; n=5 rectal/colic NET; n=1 granular cell tumor; n=5 serrated adenoma appendix/coecum/appending; n=8 tubular adenomas with/without HGD; n=4 adenocarcinoma in situ; n=1 hyperplastic polyp transverse). 7/26 patients reported pain after the procedure with 2 patients requiring hospitalisation (appendicectomy). 3/26 patients presented with minor bleeding requiring endoscopy. Complete resection was achieved in 23/26 patients.

Conclusion: This study confirms the feasibility of duodenal EFTR in the upper and lower GI tract and indicates good efficacy and safety. 11/26 (42%) of patients reported postinterventional pain but only 4 required hospitalization.

Beta6-Integrin – A novel Serum Marker predicting overall Survival in Pancreatic Adenocarcinoma
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Background: Pancreatic adenocarcinoma (PAC) remains a major clinical challenge leading to approximately 30’000 deaths per year in the US. Conventional cancer therapies are mainly palliative in nature and 5-year survival is way below 10%. Thus, the need for novel biomarkers to improve diagnosis, surveillance and predicting tumor biology is paramount.

Methods: ITGB6 serum levels were measured in a pro- and retrospective PAC patient cohorts using ELISA. Next, we examined whether the combination of ITGB6 and CA 19-9 would be more accurate than CA 19-9 alone in diagnosing PAC using patients with chronic pancreatitis (CP) as control group.

Results: Using an initial cohort of 24 PAC patients, we found that detection of ITGB6 in serum is associated with a significantly shortened survival (difference median survival 294 days, p = 0.0205, fig. a). Next, ITGB6 levels were measured in a prospective cohort 20 PAC and 6 CP patients. All patients with ≥ 1 ng/mL ITGB6 in serum displayed pancreatic cancer indicating that ITGB6 serum concentrations together with CA 19-9 may refine the diagnosis for PAC (fig. b). However, too few patients were included in order to demonstrate significance.

Conclusion: Our findings are highly encouraging. Additional prospective studies are required in order to validate these findings and to test the potential of ITGB6 as a novel marker for pancreatic cancer.
Eosinophilic Esophagitis-Like Disease with Lack of Significant Eosinophilic Infiltration: Description of a New Disease Entity

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Eosinophilic esophagitis (EoE) is a T-helper type 2 (TH2) mediated chronic inflammatory disease. The interleukin (IL)-13 enzyme is involved in the pathogenesis and is associated with high eosinophil and basophil numbers. In the esophagus, eosinophilic infiltration can be observed in patients with active eosinophilic esophagitis (EoE) and diminished after topical corticosteroid treatment. Immunohistochemistry staining demonstrated the expression of the IL-20 cytokine in patients with active EoE and diminished after topical corticosteroid treatment. Immunohistochemistry staining demonstrated the expression of the IL-20 cytokine (IL-20R) type 1 (T1Z) in the esophageal epithelium of patients. To further investigate IL-20 cytokines in EoE an EoE disease model in mice was induced by epicutaneous sensitization and subsequent oral challenge with ovalbumin. Results: The expression of IL-20 cytokines was increased in patients with active EoE and diminished after topical corticosteroid treatment. Immunohistochemistry staining demonstrated the expression of the IL-20 receptor (IL-20R) type 1 in the esophageal epithelium of patients. To further investigate IL-20 cytokines in EoE an EoE disease model in mice was established characterized by increased expression of IL-20 cytokines and infiltration of eosinophils and basophils into the esophagus. In IL20−/− mice, the EoE-like disease is characterized by lower disease scores and less infiltration of CD45+ immune cells in the esophagus. More specifically, eosinophil and basophil numbers were reduced. In vitro stimulation with IL-20 cytokines of the human esophageal keratinocyte cell line KYSE-180 resulted in phosphorylation of STAT3 and increased expression of eotaxin-3. Conclusion: Our results with patient biopsies and mouse models indicate a potential role for IL-20 in EoE. Potentially, IL-20 cytokines act on epithelial cells to modulate eotaxin-3 expression required for the chemotaxis of eosinophils and basophils.

Endoscopic Vacuum Therapy by EsoSponge®: treatment of oesogastroduodenal leakage. Who’s the best patient?

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Background: Perforations and anastomotic leakages of the gastrointestinal tract represent an emergency that can be complicated by a high risk of mortality. Most cases of anastomotic leakages are treated surgically, but the operative procedure includes a significant risk. Endoscopic vacuum therapy (EVT) by EsoSponge® is an established and effective treatment option of these complications. We describe here our experience through a series-report. Methods: Patients treated with EVT for a perforation of upper gastrointestinal system were analysed from prospective register from November 2016 to May 2019, at HUG. After a radiological diagnosis, a polyurethane sponge was endoscopically positioned in the wound cavity or nearby of the perforated orifice, connected to an external drainage, in agreement with the visceral surgery team. The sponge was changed endoscopically every 3-4 days. Results: Ten patients were treated (3 women, 7 men). Mean age was 55.2 years (range 22 to 75). Causes of perforation were reflex surgery (1), duodenal ulcer (1), cervical abscess with chronic fistula (1), status post bariatric surgery (2), oncologic surgery (1), Boehrhaeve Syndrome (4). The technical success for the procedure was 100%. EVT allowed the closure of the perforation in 6 patients after an average of 4 days (range 2 to 10). Average number of sponge insertions was 4.5 (range 2 to 10). A surgical treatment was needed in 4 patients due to an unfavorable evolution. Three of them presented a septic shock before closing the orifice and one showed no treatment efficacy after 3 EVT changes. The 3-month survival rate is 100%. Conclusions: EVT appears to be a technically feasible and safe procedure in upper gastrointestinal tract perforation in accordance with previous studies. EVT was effective in 2/3 patients. We believe that EVT should be proposed as a first-line endoscopic treatment in upper GI perforation, only in case of oesophageal perforation or leakage of oesogastric anastomosis.
Feasibility of ileal intubation in colonoscopy with Endocuff: a prospective open label comparison
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Methods: We prospectively analysed the use of an EC and ileum intubation at the Kantonsspital St. Gallen between January and December 2018 performed by 3 experienced endoscopists and 1 trainee. Scientific data security and evaluate the safety profile.

Results: We included 570 patients, median age 60 years (range 21-94), 51% were male. Of the 570 colonoscopies, 63% were performed with EC (n=359). Colonoscopy with the use of Endocuff achieved the same ileum intubation as without EC (p=0.234). ADR with EC was 85.8% (308 of 359 patients). Without EC, the ileum was intubated in 82% (173 of 211 patients). There was no significant difference (p=0.81). ECwan was approved by the local ethics commission (EKSG14/099). EC was only performed by 3 experienced endoscopists and 1 trainee. Scientific data security

Conclusions: Colonoscopy with Endocuff allows ileal intubation in patients with obstructive symptoms. The dilatation algorithm starting with an initial balloon volume of 30ml, followed by stepwise volume additions of 5ml until a maximum of 50ml. Further volume increases were individually tailored at 1-2ml intervals until a maximum diameter of 25-27mm across the ECU was reached and/or intraballloon pressure exceeded 100 kPa. Symptom scores were assessed by the Eckardt score (ES) before and earliest 1 week after intervention. Timed barium esophagogram (TBE), obtaining images at 1, 3 and 5 minutes after swallowing the contrast agent, was performed before and after dilation to assess esophageal emptying.

Results: We included 11 patients with dysphagia of unclear etiology. AER and endoscopy for dysphagia of unclear etiology after extensive workup suggest empiric panesophageal bougie dilation. The Functional Luminal Imaging Probe (EndoFLIP) uses pressure and segmental impedance measurements to determine luminal diameter and distensibility.

Conclusion: Our interim results of a single, individualized EndoFLIP dilation in patients with achalasia in a real-world setting demonstrated good efficacy in both subjective and objective short-term treatment outcome with favorable side effect profile. We are currently collecting further data from our cohort including additional tailored dilations.
A Specific Subtype of Hepatitis E Virus Circulates Widely in Switzerland

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Background: Infection by hepatitis E virus (HEV) genotypes (gt) 3 and 4 has been recognized as a primarily porcine zoonosis. Here, we analyzed HEV sequences from patients with hepatitis E acquired in Switzerland.

Methods: RT-PCR and Sanger sequencing were carried out on plasma samples from 114 patients with PCR-proven acute or chronic hepatitis E acquired in Switzerland, followed by subtype assignment and phylogenetic analyses.

Results: Genotyping revealed that almost all infections were by HEV gt 3; only three were by gt 4. Importantly, 77% of the gt 3 isolates were by the newly proposed subtype 3s. This subtype has been identified only in Switzerland so far, in swine and in food products, indicating that it circulates widely in the country, including in the food chain. Interestingly, three immunosuppressed solid organ transplant recipients were found to be infected with rabbit HEV.

Conclusions: Our observations lend support to the proposed HEV subtype 3s circulating and representing the major cause of hepatitis E acquired in Switzerland. This specificity is likely explained by the fact that 96% of the pork meat consumed in Switzerland is from local production and that only very limited amounts are imported or exported. Next-generation sequencing of full-length HEV genomes is ongoing and will allow to further validate the hypothesis of a Swiss HEV subtype.

Liver function assessment by 13C-methacelin test before and after placement of a transjugular portosystemic shunt: A prospective pilot study

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Introduction: Current treatments are able to control HBV replication and to eradicate HCV in almost all cases. Further improvements in the management of HBV and HCV infections will be possible by focusing on treatment impact at a population level for which screening is an essential step. As many patients with HBV or HCV infection are still undiagnosed, large-scale screening could be useful. Aim: To investigate whether large-scale screening for HBV or HCV infection (e.g. risk-based vs. age-based) could identify infected individuals.

Methods: Individuals between 18 and 80 years attending the pre-operative consultation prior to minor surgery in a general surgical outpatient clinic were tested for HBsAg, anti-HBc and anti-HCV by an Immunodot test. HBV DNA and HCV RNA were determined in HBsAg- and anti-HCV-positive individuals. Results: Among 3000 individuals tested, 7 were positive for HBsAg (0.26%) and 4 had detectable HBV DNA. Twelve individuals were positive for anti-HCV antibodies (0.44%). Two of them had detectable HCV RNA (0.07%) and 10 had undetectable HCV RNA (5 spontaneously and 5 after a successful antiviral treatment) (Fig 1). When compared to HCV negative people, HCV positive individuals had already been screened more frequently for HCV (63.3% vs. 12.8%, p<0.001) and 10 had detectable HBV RNA (0.07%). None of them had more frequently anti-HBc antibodies (33.3% vs. 4.2%, p>0.001), had more frequently HCV household members (16.7% vs. 17%, p=0.02) and had used more frequently intravenous drugs (66.7% vs. 0.1%, p<0.001), nasal drugs (58.3 vs. 8.2%, p<0.001) or cannabis (58.3% vs. 7.9%, p<0.001). None of HCV positive individuals were immune from an endemic area. The median age of HCV positive individuals was not different from that of those who were HCV negative (52 years [range: 39-59] vs. 44 years [95% CI: 43-45], p=0.1). Most of the positive individuals were already aware that they were infected (96% of the HCV positive individuals and 100% of the HCV viremic individuals).

Conclusions: In this prospective study performed in a general surgical outpatient clinic, a large-scale useful to identify individuals with undiagnosed HBV or HCV infection. Screening for HBV and HCV infection should focus on individuals with well-known risk factors.
Assessment of radiological rectal cancer restaging after chemoradiotherapy

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Background: Patients with rectal cancer and complete response after chemoradiotherapy (CRT) can be treated with the aim of organ preservation by applying a watch and wait strategy. However, if secondary radical surgery is needed due to cancer recurrence, this may be associated with an increased complication rate or even worse prognosis. This study aims to assess the accuracy of radiological restaging after CRT.

Methods: Patients undergoing surgery for rectal cancer after CRT at our institution prior to the implementation of an organ preservation program were analyzed retrospectively. For all patients radiological T and N stage restaging by MRI after CRT but prior to surgery was compared to final pathological T and N staging. The rates of over- and understaging and sensitivity for radiological prediction of complete response were calculated.

Results: Radiological T stage after CRT was underestimated in 20% (11/55), correct in 38.2% (21/55) and overestimated in 41.8% (23/55) of patients. Radiological N stage was underestimated in 14.6% (8/55), correct in 63.6% (35/55) and overestimated in 21.8% (12/55) of patients. Five patients out of 55 patients (9%) showed pathological complete response after CRT. Radiologically, complete response was suspected in only one of these five patients (sensitivity for complete response 20%).

Conclusions: Radiological assessment after CRT resulted in the correct tumor and nodal stage in about half of the examined patients. Overestimation of T and N stage was more frequent than understestimation, this is most probably due to remaining scar tissue after CRT. No patient was incorrectly staged as T0 or N0. Pathological complete response could be predicted correctly in only one of five patients. Therefore, clinical examination and endoscopy remain very important in the evaluation of rectal cancer after CRT. Further, histological or molecular markers are needed to better predict response to CRT and to identify patients that qualify for organ preservation.

Meta-analysis of randomized controlled trials of surgery for rectal cancer

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Background: The mainstay of treatment for rectal cancer includes total mesorectal excision (TME) of the rectum. The present analysis compares surgical approaches for rectal cancer.

Methods: A systematic literature review and Bayesian network meta-analysis of randomized controlled trials (RCT) was performed.

Results: 29 RCTs with 6237 participants were included comparing: open vs laparoscopic vs robotic vs transanal TME. No differences were identified in intraoperative and postoperative morbidity except blood loss, wound infections, hospital stay and time to bowel movement which were less with minimal invasive techniques. No difference for nodes retrieved, involved distal margin, overall survival, and recurrence. Laparoscopic surgery resulted in more incomplete TME’s and in more involved circumferential resection margins (CRM). Robotic surgery resulted in longer distal resection margin. Transanal TME had higher probability of being the best treatment for complete TME and regard to involved CRM

Conclusion: The different surgical techniques result in comparable perioperative morbidity and long-term survival. Minimal invasive approaches improve postoperative recovery, and the open and transanal approaches may improve oncological resection.

Survival after hepatectomy for colorectal liver metastases is a function of intrahepatic recurrence but is not dependent of recurrence at the liver resection margin: a bicentric experience

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Background: Resection margin status is associated with oncologic outcomes following liver resection for colorectal liver metastases (CLM). Previous studies however, did not differentiate between true local recurrence at the resection margin (TLR) versus recurrence elsewhere in the liver. This study aims to determine if resection margin represents a surrogate of advanced disease while not determining location of recurrence.

Methods: Clinicopathological data of patients who underwent curative hepatectomy for CLM between 2012 and 2017 at two major hepatobiliary centers in Bern, Switzerland, and Berlin, Germany, were assessed. Follow-up cross-sectional imaging following hepatectomy was reviewed by an independent radiologist to identify the presence and location of recurrent disease. Location of intrahepatic recurrence was distinguished between TLR (only at the resection margin) versus intrahepatic recurrence elsewhere with or without additional TLR.

Results: During the study period, 345 patients underwent liver resection for CLM with curative intent. Surgical margins were positive for tumor cells (R1) in 96 patients (19%). After a median follow-up time of 34 months, tumor recurrence was identified in 154 patients (45%). Location of recurrence disease was independent from the R1 status (p = 0.555). TLR was not associated with worse overall survival among patients with recurrent disease (TLR vs. any recurrence: RR 3.36 vs. 64%, p = 0.454). Additionally, 3-year overall survival was equivalent in patients with TLR or recurrence elsewhere with/without recurrence elsewhere (78% vs. 55%, p = 0.439). Patients with intrahepatic recurrence benefited from local hepatic therapy in comparison to patients that did not receive local hepatic therapy (3-year OS: 77% vs. 52%, p = 0.001).

Conclusions: TLR after liver resection for CLM is not associated with worse overall survival compared to other intrahepatic or extrahepatic recurrence. Local treatment for intrahepatic recurrence is possible survival can be prolonged.

Single cell RNA-seq Atlas of a Regenerating Liver in Mice

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Background: Liver regeneration is initiated by loss of hepatic tissue to restore homeostatic levels of liver mass and function. The main mechanism is proliferation of parenchymal cells, nevertheless this complex and orchestrated process requires the coordination of multiple cell types in a spatially and temporally regulated manner. Using single cell RNA-seq, we reveal the cell specific contribution to early events during liver regeneration.

Methods: Liver regeneration was initiated using a standard two-thirds partial hepatectomy (PH) model in C57Bl/6 mice. Hepatic cells were isolated by a two-stage collagenase in situ digestion. scRNA-seq libraries were prepared from 5000 cells from sham control, 3 hours, 6 hours and 24 hours after PH in duplicate using the Chromium Single Cell 3’ library & Gel Bead Kit v3 according to the manufacturer’s protocol (10xGenomics). Samples were sequenced on a NovaSeq 6000 S2 flow cell. Seurat clustering algorithm and SingleRf were used to identify different cell populations and their markers.

Results: We profiled the transcriptome of 12607 single cells of the parenchymal and non-parenchymal fraction over 4 time points from 8 mice. Unsupervised clustering identified 20 subpopulations of cholangiocytes, B cells, stellate cells, dendritic cells, granulocytes, monocytes, T cells, NK cells and distinct types of hepatocytes, macrophages and endothelial cells varying over time.

Conclusion: Our results provide a genome wide picture of liver regeneration at a single cell level and reveal the regulated genes in each cell population after partial hepatectomy.
MINIMAL LENGTH OF PROXIMAL RESECTION MARGIN IN ADENOCARCINOMA OF THE ESOPHAGO-胄STRIC JUNCTION: A SYSTEMATIC REVIEW OF THE LITERATURE

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The minimal length of proximal margin (PM) in esophagogastric junction cancer has not been established yet and its impact on patient survival remains unclear. Pubmed, Embase and Scopus databases were searched for «adenocarcinoma of the esophagogastric junction», «adenocarcinoma of the gastroesophageal junction» and «cardia cancer», each combined with «proximal margin».

English written studies that specified PM length in AEG were included. Survival data in relation to PM were extracted. 13 studies, that were all retrospective case series, with in total 2648 patients met inclusion criteria. While 93% of 230 patients with Siewert type I had esophagectomy, 69% of 1270 patients with Siewert type II and 93% of 872 patients with Siewert type III had transhiatal extended gastrectomy. Minimal PM length was treated by 5 studies and ranged between 2–6cm. While 3 studies defined minimal PM by the necessary length to obtain R0 resection, 2 studies found minimal PM length significantly associated with survival. Multivariate analyses revealed in 2 studies an independent impact of PM on survival, whereas 1 study did not find any significant relation between PM and survival. 1 study showed that PM length was significantly associated with survival in T2–4N0–2 tumors, but not in T1 or N3 tumors.

In conclusion, available retrospective studies did not allow a conclusion for a minimal length of PM and showed no clear evidence for an impact of PM length on survival. Taking into consideration available data and the shrinkage phenomenon, a PM >2cm might be necessary to obtain a sufficient PM.

MINIMAL INVASIVE VERSUS OPEN HEPATECTOMY FOR COLOCERAL LIVER METASTASES: BICENTRIC ANALYSIS OF POSTOPERATIVE OUTCOMES AND LONG-TERM SURVIVAL USING PROPENSITY SCORE MATCHING ANALYSIS

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Background: Minimal-invasive hepatectomy (MIH) has been increasingly performed for benign and malignant liver lesions with promising results. However, oncological results after MIH for the treatment of patients with colorectal liver metastases (CLM) need to be clarified.

Methods: Clinicopathological data of patients who underwent liver resection for CLM between 2012 and 2017 were assessed within a training cohort at a Swiss major hepatobiliary center and a validation cohort at a major hepatobiliary center in Germany.

Postoperative outcomes and long-term survival of patients following MIH were compared with those of patients undergoing conventional open hepatectomy (OH) after 1:1 propensity score matching.

Results: During the study period, 91 patients underwent liver resection for CLM with curative intent at the Swiss center. Twenty-five patients underwent MIH and were compared with a matched cohort of 25 patients who underwent OH. MIH was associated with lower major complication rate (4% vs. 28%, p=0.049) and shorter length of hospital stay (5 vs. 9 days, p=0.0001) compared to OH. Postoperative mortality (0% vs. 0%) was comparable between MIH and OH. After a median follow-up time of 47 months, 5-year overall survival (OS) was significantly higher after MIH than after OH (69% vs. 45%, p=0.046).

Conclusions: MIH for CLM is associated with lower postoperative morbidity and shorter length of hospital stay, resulting in oncologic outcomes superior to those achieved with the established OH. Our findings suggest that MIH should be considered as the preferred method for the treatment of curatively resectable CLM.

Inherited polymorphic p53 response elements in the human genome interact with somatic p53 mutations to affect patient survival: a pan-cancer analysis.

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Background: p53 is a transcription factor that acts as a tumour suppressor in a wide range of human cancers. This key role of p53 implies that inherited single nucleotide polymorphisms (SNPs) in functional p53 response elements (p53REs) could affect cancer progression. The identification of such variants and their possible interaction with somatic p53 mutations has the potential to identify tumours with an aggressive biological phenotype and guide personalised treatment strategies.

Methods: In an integrative analysis, we utilize newly abundant genome-wide maps of polymorphic p53REs. We explore those maps to identify p33RE SNPs in the human genome that may influence patient survival utilizing the Cancer Genome Atlas (TCGA) database. In total, 7021 patients who underwent a surgical intervention across all cancer types with known somatic p53 mutation status and an in-depth characterisation of germline genetic variation were included in the study.

Results: We identify functional p53 RE SNPs that show significant allelic differences in patient survival both across all cancer types as well as in individual p53-dependent common tumours, such as colorectal, breast, lung and brain cancers in a p53 mutation status-dependent manner (up-to p=1.96x10^-6, hazard ratio, HR=5.41, Cox multivariate analysis).

Conclusions: The identified polymorphisms in functional p53 REs have the potential to serve as predictive biomarkers of cancer survival and could help guide personalised treatment strategies in a wide range of p53-dependent tumour types.

4 years experience of robotic-assisted (da Vinci Xi) giant hiatal hernia repair: feasibility, quality and comparison to the standard laparoscopic approach

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Background After 4 years of experience we evaluate the feasibility and quality of robotic-assisted giant hiatal hernia repair compared to the standard laparoscopic technique during that period.

Methods This is a retrospective analysis of prospectively collected data between July 2015 and May 2019 of patients with type III or IV hiatal hernia who underwent elective surgical therapy. In 51 patients robotic-assisted surgical repair was performed, a conventional laparoscopic hiatal hernia repair was done in 38 patients. Mann-Whitney-U Test was used for statistics. Significance level for P-Value <0.05.

Results Mean operating time was 221min (Rob) vs. 165min (Lap) (p=0.05). 51 (Rob) compared to 23 (Lap) mesh-augmentations were carried out. Intraoperative complications occurred in 5 (Rob) vs. 7 (Lap) patients (p=0.72). Postoperative morbidity was 10% (Rob) to 0% (Lap) (p=0.12). There were 6 (Rob) compared to 1 (Lap) recurrences (p=0.83) during the study period (1-46m).

Conclusion The da Vinci Xi System is safe, feasible and equivalent to the laparoscopic technique. Even during the learning curve perioperative results applying robotic technique are comparable to the laparoscopic approach.
Laparoscopic surgery for gastric cancer: the European point of view.

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Abstract Objective
Multiple Asian studies have proved the feasibility of laparoscopic approach for surgical treatment of gastric cancer. The difference between Asian and European patients could limit their application in Europe. We reviewed the literature for European studies comparing open gastrectomy with laparoscopic approach in the treatment of gastric cancer.

Method
We searched the keywords gastric cancer and laparoscopy in MEDLINE and EMBASE. We included all studies published between 1990 and 2016 and conducted in Europe.

Result
We found 1 randomized and 13 cohort studies compared laparoscopic with open gastrectomy. We found no mean difference in the number of lymph nodes harvested between laparoscopic and open group (mean difference: -0.49, 95% CI: -2.42; 1.44, p=0.62) and no difference of short term or long term mortality (Short-term Odds Ratio: 0.74, p=0.47, Long-term Odds Ratio: 0.65, p=0.11). We found a longer operative time in the laparoscopic group (Mean difference: 35.75 minutes, p<0.01) but lesser re-operation rate than the open group. (Odds ratio:1.55 p=0.01)

Conclusion
European based population studies found results comparable with their Asian counterpart. In the current state of evidence, minimally invasive surgery for gastric cancer is safe and can achieve the same oncological results.

Endoscopic treatment of large esophageal leaks

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Background: Esophageal leak is a life-threatening condition. Self-Expandable Metallic Stents (SEMS) are used to treat a wide variety of esophageal conditions. However, large leaks remain a therapeutic challenge. Use of SEMS might be insufficient and require other endoscopic procedures as the endoscopic Vacuum Therapy (eVAC).

The aim of this study is to assess the efficacy of these endoscopic procedures.

Methods: We realized a retrospective, monocentric study in a tertiary university center of patients who underwent endoscopic treatment (SEMS and eVAC) for large esophageal leak, between January 2016 and December 2018. Large esophageal leaks were defined as a defect of more than 1 cm. All patients were included without restriction.

Results: A total of 21 patients (85.7% male, mean age of 69 years) were included. 3 patients (14.3%) had non surgical perforation, 18 (85.7%) had an anastomotic leakage post surgery, for an oncological constellation in 16 patients (76.2%). For leakage post surgery, first stent was positioned after a median of 11 days after surgery. We used fully-covered SEMS in 6 patients and double-type SEMS from Taewoong® in 15 patients. In all patients, a median of 3 stenting sessions was necessary to achieve healing of the esophageal leak. We used eVAC for 3 patients requiring a median of 7 endoscopic sessions, with a 3 or 4 day interval between these. Fully esophageal rupturing healing was completed for 19/21 (90.4%) patients, including the patients who have benefited from eVAC. Because of a pejorative evolution of their condition, 2 patients died before finishing the endoscopic treatment. Successful treatment was completed after a median of 63 days with no relapse after a median of 127 days of follow-up.

Conclusions: Endoscopic treatment of large esophageal leaks is effective. SEMS is the first-line endoscopic treatment. eVAC appears to be an effective option for leaks refractory to SEMS procedure.

First experience of gastric peroral endoscopic pyloromyotomy (GPOEM) in a Swiss university endoscopic unit.

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BACKGROUND
Gastric peroral endoscopic pyloromyotomy (GPOEM) has been regarded as a new and minimally invasive therapy for refractory gastroparesis. This study assessed clinical outcomes and safety after GPOEM performed in a tertiary referral center.

Methods: We retrospectively reviewed the first patients who underwent Gastric peroral endoscopic myotomy (G-POEM) from November 2018 to February 2019.

Results: This study included 4 patients, 3 males and 1 female. All patients had refractory gastroparesis confirmed on gastric emptying scintigraphy (GES). 1 patient had idiopathic gastroparesis, 1 patient had diabetic type 1 gastroparesis and 2 patients had post surgical gastroparesis (gastropexie and laparoscopic Nissen fundoplication respectively).

GPOEM was technically successful in all cases. The mean procedure time was 52 min. Mean length of hospital stay was 26 hours (24 hours for 3/4 of patients and 72 hours for 1/4 patients). We faced off only with mild adverse events with one case of intra operative submucosal bleeding treated endoscopically. Overall, clinical success was 100 % (4/4) with a significant improvement in quality of life. The mean GCSI score at baseline was 3.05 and 0.17 at 3 months after GPOEM. 2 patients had resolution of diarrhea after endoscopic procedure. Symptoms improvement was almost immediate with a diet consisting of clear drinking 6 hours postoperatively and a normal diet the day after surgery.

Conclusions: GPOEM results in improvement for all symptoms of gastroparesis in our few patients. This short series demonstrates that gastric peroral endoscopic myotomy is a safe and effective treatment for gastroparesis.

Endoscopic removal of multiple ingested batteries using a strong magnet

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Background: Endoscopic removal of ingested batteries can be challenging if there is a high number of batteries in the stomach, especially when food residues impair visibility in the stomach. Expandable Metallic Stents (SEMS) are used to treat a wide variety of esophageal conditions. However, large leaks remain a therapeutic challenge. Use of SEMS might be insufficient and require other endoscopic procedures as the endoscopic Vacuum Therapy (eVAC).

Methods: We describe a novel method for efficient removal of multiple batteries using a strong magnet.

Results: A young female patient was repeatedly referred to our emergency unit after ingestion of multiple batteries (median 8, range 1-50, battery types AA and AAA). Since the usual removal techniques with polypectomy snare and retrieval nets are time consuming, we put a small strong magnet into a foreign body retrieval net already inserted through the working channel of the endoscope. After insertion of an overtube into the distal esophagus, we could easily pass the endoscope loaded with the magnet into the stomach, attach one battery at the time to the magnet, and retrieve it by pulling back the endoscope. The strong magnet was also very helpful for attaching batteries that were not visible due to food residues. Protection of the airways with an overtube was also effective, since no aspiration and no other complication occurred in more than 70 endoscopic interventions.

Conclusions: The use of a strong magnet greatly facilitates removal of multiple batteries from the stomach, even when food residues impair visibility.
Endoscopic ultra-sonography guided drainage of the main pancreatic duct: a Swiss multi-center experience.

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Background: Symptomatic main pancreatic duct (MPD) obstruction or leakage are conventionally treated by a trans-papillary drainage. When this approach fails, endoscopic ultra-sonography pancreatic drainage (EUS-PD) appears actually as an efficient and minimal-invasive alternative technique.

Methods: We retrospectively analyzed data from all patients who underwent EUS-PD in the endoscopy centers of the CHUV in Lausanne and Inselspital in Berne between April 2016 and March 2019.

Results: 46 patients (73.9 % male, mean age, 56 years) were included. Technical success, defined as MPD drainage with plastic stent placement, was obtained in 42/46 patients (91.3 %) and led to clinical success (i.e. significant pain reduction at follow up) in 85.1 % of cases. The median diameter of the pancreatic duct was 6mm (3-18mm) and mean procedure duration of 45 minutes. Adverse events were reported as mild (i.e. managed during endoscopy) or severe in 5 cases (10.8 %) each. Among the patients for whom follow-up was continued, 4 (8.7 %) were finally addressed to surgery for persisting symptoms.

Conclusion: EUS-PD is a very efficient and safe alternative to surgery when trans-papillary approach is impossible.

Feasibility of cecal retroflexion in screening colonoscopy with Endocuff
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Background: Endocuff (EC) is a mucosal exposure device attached to the distal tip of the colonoscope. It has been shown that both EC and cecal retroflexion can improve the adenoma detection rate (ADR) 1, 2. Feasibility and safety of retroflexion in the cecum with EC has not been reported.

Methods: We prospectively analysed cecal retroflexion with EC in screening colonoscopy at the Kantonsspital St. Gallen in Switzerland between January to December 2018 in 80 patients. Cecal retroflexion with EC was feasible in 80 patients (91%). We determined.

Results: We included 88 patients, median age 62 years (range 32-76), 55% were male. Cecal retroflexion with EC was feasible in 80 patients (91%). We had no complications especially no perforation. ADR was 68% (5/4).

Conclusions: Cecal retroflexion with Endocuff is feasible without complications in screening colonoscopies.

References:

Figure 1a: Cecal retroflexion with Endocuff with sessile serrated adenoma

Endobiliary Radiofrequency Ablation (ELRA) for Malignant Billiary Obstruction over 24 months follow-up
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Endo Luminal Radiofrequency Ablation (ELRA) for biliary tract neoplasia is a novel treatment modality that is already used in oesophageal, rectal, liver and pancreas tumours. A 58-year-old woman presented with acute cholestasis 08/15. Due to unclear anatomy after papillotomy and bile stone removal, an MRCP revealed a sclerosing mass forming stricture at the hilar with dilatation of the left intra-hepatic ducts consistent with Klatskin Tumour (Bismuth IVa). After laparoscopy the situation was judged as inoperable and a ncSEMS was inserted. Tumor progression resulted in restenosis and a second ncSEMS was placed through the first stent in the left main hepatic duct 07/16. After progradent tumor ingrowth despite chemotherapy (Gemcitabine, Cisplatin), we obtained informed consent and performed ELRA 05/17 (Taewoong Medical, Korea). The ELRA-catheter (7F, ablation length 18mm) was placed under radiologic control in the tumor stenosis. The bipolar electrode implements a temperature sensor to control ablation (7 Watt, 70°C for 2 minutes). The procedure was repeated to cover the whole length of stricture. Necrotic debris was removed with a balloon while patency was confirmed by contrast. This was repeated every 2-4 months. No immediate or late adverse events were recorded. On the patients last visit 05/19 she remained asymptomatic at 24 months follow-up after 11 ELRA sessions. She is not jaundiced, gained weight, ECOG-1 and CA 19-9 reduced to 28.9 U/ ml (149 U/ml). Surveillance CT showed presence of the unilateral SEMS in the common and main left biliary duct with slight left intrahepatic duct dilatation and decreased tumor mass, consistent with radiological improvement. ELRA is a novel modality in the treatment of palliative non-resectable malignant biliary obstruction that proved maintaining PAGS patency.

Endoscopic full-thickness resection (FTRD) of a non-ampullary lesions of the proximal duodenum in a 67 year old patient with attenuated polyposis coli
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Background: Pyloric gland adenoma (PGA) is an underdiagnosed, rare entity, mostly be founded in the stomach. Similar to colorectal adenomas PGA`s have a high risk of malignant transformation to adenocarcinoma up to 21-40 %. Endoscopic resections in the current standard technique for treatment of duodenal non-ampullary adenomas. Complete resection rates are considerably high at about 90 %. Adverse events as bleeding was reported up to 25%. ESD is not recommended for resection of duodenal lesions since the perforation rate may be as high as 35%. Use of FTRD in the duodenum are limited to a single case study of 20 patients. Methods: A 67 year old patient with attenuated polyposis coli presented for screening. Gastroscopy showed a 20 mm large, non-ampullary lesions in the proximal duodenum (pars I). The margins of the duodenal lesions was marked with a high-frequency (HF) probe. An integrated balloon dilatation (20mm) of the upper esophageal sphincter and the pylorus was performed to facilitate advancing of the FTRD (Ovesco Endoscopy AG). After pulling the duodenal lesion into the cap with a grasper the FTRD clip was deployed and the lesion immediately resected with the preloaded snare. The resected specimen was retrieved for histopathological examination. A single-shot antibiotic prophylaxis with 2 g ceftriaxone i.v. was administrated during the intervention. Second-look endoscopy was scheduled 24 h after resection. Result: Pyloric gland adenoma of 18 mm in the proximal duodenum (immunohistochemistry positive for Mucin-1, Mucin 5, Mib 1). Conclusions: Herein we present the first case of FTRD duodenal resection in a patient with attenuated FAP and a PGA. There are currently no specific guidelines for the removal and surveillance of PGA. ASGE recommends resection and surveillance endoscopy at 3-5 years interval.

References:
**Malignant granular cell tumor (GCT) in the oesophagus - rare and difficult to diagnose**

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**Background:** GCTs are uncommon tumors most probably derived from Schwann cells. Esophageal GCTs are particularly infrequent, and malignant variants have been reported to occur exceedingly rare.

**Case presentation:** A 41-year-old man was submitted to endoscopy because of unspecific chest pain. During endoscopy, he was found to have a one centimeter subepithelial, polyoid like lesion, Paris 0-Is. Further evaluation using EUS confirmed the presence of a 6 x 6 mm well-demarcated hypoechoic lesion, uT1a, uN2. Repeated biopsies showed highly cellular tissue with atypical cells, not further characterized by immunohistochemistry. The lesion was successfully resected en bloc by an endoscopic EMR technique. Histology revealed large polygonal cells with abundant granular cytoplasm showing diffuse Periodic Acid Schiff positivity, consistent with a granular cell carcinoma. The diagnosis is based on biopsies. The natural course appears to be benign with a good prognosis.

**Conclusion:** Sloughing esophagitis is a rare benign entity that endoscopists must be aware of because of its atypical presentation. It presents with atypical endoscopic findings and strongly requested biopsy. Histology appears to be the key to recognize this endoscopic complication.

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**Endoscopic submucosal dissection and unroofing of a symptomatic antral duplication cyst. A case-report.**

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**Background:** Duplication cysts (DC) are rare congenital malformations that can occur throughout the entire gastrointestinal tract. About 4-9% of these are located in the stomach, where they can cause abdominal pain and symptoms of gastric outlet obstruction. In this case, the preferred method of treatment is surgical excision. In this case, the preferred method of treatment is surgical excision. Few case reports describe an endoscopic approach by either endoscopic submucosal dissection (ESD) or electrohydraulic lithotripsy (EHL) of several stones in the CBD. After balloon dilation of the distal CBD stenosis, a fully covered metal stent with a long extraction thread was inserted. Six weeks later the stent was extracted and a repeat EUS-guided transgastric HGS stent was placed. Three months later a EUS-guided hepatojugal gastrotomy (HGS) with transgastric cholangioscopy (tPOCS) and metal stent insertion for a distal common bile duct (CBD) stenosis in a patient with chronic pancreatitis

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**Background:** Endoscopic retrograde cholangiography (ERC)-guided drainage is the gold standard to relieve benign or malignant biliary obstruction. If ERC fails, percutaneous transhepatic biliary drainage (PTBD) is usually considered the alternative treatment. However, PTBD is prone for adverse events in up to 77% and can significantly impair quality of life. **Case description:** An 80-year-old man presented with cholestasis and recurrent cholangitis because of a distal CBD stenosis secondary to chronic pancreatitis. After ERC failure, a PTBD was inserted. Because of recurrent infections, the PTBD had to be removed after several months. Surgical options were declined due to significant comorbidities. Given periodic symptoms, an EUS-guided transgastric HGS stent was placed. Three months later a EPOCS was performed with electrohydraulic lithotripsy (EHL) of several stones in the CBD. After balloon dilation of the distal CBD stenosis, a fully covered metal stent with a long extraction thread was inserted. Six weeks later the stent was extracted and a repeat EPOCS showed an improved stenosis and no residual stones. **Conclusions:** EUS-guided HGS with transgastric treatment of biliary obstruction and stones is feasible and safe in patients who failed ERC and PTCD. It allows not only direct visualization of the stenosis but given the large access route and stable scope position, it even offers the possibility of guided biopsies, wire manipulation, dilation of stenoses, EHL, and metal stenting. Metal stent extraction through the HGS is possible, given special stent design with a long extraction thread.

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**Sloughing oesophagitis: a rare histologic and endoscopic finding**

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**Background:** Sloughing esophagitis or esophagitis dissecans superficialis is a rare benign illness. Endoscopically, it is characterized by sloughing of large fragments of oesophageal mucosa (1). Although the exact pathogenesis remains unexplained and the histopathologic features are inadequately described, an association with caustic or hot beverages ingestion, autoimmune bullous dermatitis (such as pemphigus vulgaris), and drugs such as potassium chloride, nonsteroidal anti-inflammatory drugs and bisphosphonates, has been reported (2). Usually asymptomatic, occasional symptoms may be dysphagia, nausea, bleeding, vomiting, heartburn and odynophagia (3). **Case report:** A 62-year-old woman with a history of WHO obesity class III, status post Roux Y bariatric surgery was seen in the surgical outpatient clinic complaining of upper abdominal pain, pyrosis and light dysphagia. Initial workup included an Esophagogastrroduodenoscopy that revealed sloughing of the mucosa in the lower, mid and upper oesophagus, consistent with desquamation and giving the impression of a sheet of mucosal cells. Biopsies were taken from the proximal and distal oesophagus, histopathology of which was reported as squamouscellular mucosa with acute and chronic inflammation. Microbiology examination excluded viral (CMV, HSV) and fungal infection. Patient did not take any medication and responded well to a PPI treatment with alleviation of the symptoms. **Conclusion:** Sloughing esophagitis is a rare benign entity that endoscopists must be aware of in order not to mistake it with other entities such as reflux, viral esophagitis or squamous cell carcinoma. The diagnosis is based on biopsies. The natural course appears to be benign with a good prognosis.
An Unusual Subepithelial Tumor of Duodenum

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Background: Subepithelial lesions of Duodenum are uncommonly found on upper endoscopy. Differential diagnosis and prognosis are multifacetted.

Methods: We describe an unusual case of subepithelial lesion in a 64-years-old female patient with a severe anxiety disorder and no further comorbidities.

Results: A 64-years-old female patient was referred for a gastroscopy und colonoscopy because of severe iron deficiency anemia. The colonoscopy was unremarkable. In the upper endoscopy we found a large, 4 cm pedunculated polyp with a broad base in the second portion of duodenum. We consider GIST as the first differential diagnosis and possible source of intermittent bleeding. Polyectomy was performed after previous application of an endoloop. The histologic and immunohistochemic evaluation found a 15 mm gangliocytic paraganglioma (GPG), extending to the resection margins. In the Re-endoscopy a few weeks later the endoloop was dropped and no tumor was detectable in the biopsy of the resection base.

Conclusion: GPG is a very rare cause of submucosal Tumor of Duodenum with a good prognosis. Although the malignant potential is low, complete resection, in most cases endoscopically is the treatment of choice.

Endoscopic intra-abdominal rescue therapy of a dislodged EUS-guided hepaticogastrostomy stent

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EUS-guided hepaticogastrostomy (HGS) is a well accepted alternative treatment for patients with biliary obstruction and failed ERCP. Complications include abdominal pain, infection, hemorrhage, pneumoperitoneum, biliary leakage and dislodged stents. In cases of dislodged stents, those patients suffer early on from acute biliary peritonitis and need urgent surgical repair.

We report the case of an 86-year old fragile female who was admitted with painless jaundice and massively congested intrahepatic ducts secondary to a locally advanced pancreatic cancer with hilar lymphadenopathy. An ERPC was attempted, but only pancreatic access could be gained and a prophylactic stent was placed. To relief cholestasis, an EUS-guided HGS was performed, but overnight, she became hemodynamically unstable and a papillary bleeding was stopped by applying three clips. Next day the patient vomited heavily, developed an acute abdomen and a CT scan showed a dislodged HGS stent.

A large gastric defect could be easily accessed by a nasal gastrostomy and the SEMS was accidentally extracted during the attempt of replacement. A Jagwire was advanced through the hepatic access site and an 80mm long Gioborstent could be placed. A second SEMS was inserted to prevent repeat dislocation by extending far into the stomach.

Dislocation of a HGS stent is a rare but important complication. Given often weak patients, a rescue therapy apart from surgery would be beneficial.

In our case the stent has been in place correctly for two days and therefore it was possible to access the abdominal cavity through the already large gastric defect. Stents with a longer uncovered part inside the liver should anchor better and normally it should be easier to reposition them without complete dislocation. Using fully or almost fully covered stents, the described technique might be preferable, as it provides a better control of the exact stent replacement.

Endoscopic rescue therapy of a distally perforated, retroperitoneal stent after EUS-guided pancreaticogastrostomy

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Endoscopic therapeutic transgastric pancreatic duct access is gaining increasing popularity for various reasons and report of potential complications is crucial for an improved outcome.

A 42-year old woman was admitted with recurrent acute abdominal pain related to an alcohol induced chronic pancreatitis with a significantly dilated pancreatic duct (PD). ERCP failed twice and surgical interventions were declined, because of severe malnourishment and advanced liver disease.

Given increasing symptoms, we opted for an EUS-guided pancreaticogastrostomy (PGS), inserting a straight stent, which allows an unproblematic stent extraction using a stent retriever and consecutive PD access during follow-up procedures.

The patient missed her regular 3-month follow-up appointment and presented with acute abdominal pain five months later. CT scan showed a distally perforated transpancreatic position of the PGS stent. Wire cannulation of the dislodged stent failed, therefore it was extracted by a snare. After careful insertion of a thin papillotome into the gastrostomy site, wire access of the PD was gained. Using a combination of cumbersome drilling maneuvers with a 5F stent retriever and the cystotome, the wire was advanced into the duodenum. After balloon dilatation of the stented tract, a stent was placed though the pancreas into the duodenum, creating a gastropancreaticoduodenostomy. Six weeks later a pancreaticostomy confirmed completely resolved PD stones and a partial regression of the ductal stenosis.

Retroperitoneal perforation of a PGS stent is a rare complication, but in view of generally poor surgical candidates, an endoscopic strategy is definitely preferable over a surgical intervention.

In our case endoscopists who are dealing with this kind of EUS procedures should be aware of this complication and have the armamentarium of solving challenging problems.

Oeso-mediastinal fistula complicating tuberculosis and cervical lymph node involvement


Oesophageal involvement is a rare complication of tuberculosis (Tbc), that may occur due to adjacent abscess or contamination by infected saliva in a preexisting injured oesophageal mucosa. We report here a case of a favorable evolution of an oeso-mediastinal fistula following medical treatment of Tbc. Patient/Methods: A 19-year-old Indian woman living in Switzerland since 2017 was diagnosed with miliary Tbc in October 2018, with pulmonary and ganglionic (hepatic hilum and cervical) involvement. She had no HIV infection. Quadratherapy treatment was initiated following resolution of fever and night sweats. However, after 1 month of treatment she developed progressive dysphagia and lost 8 kg of BW consecutively. An upper GI endoscopy showed an 2 cm ulcer located in the mid third of the oesophagus, with biopsies negative for granulomas and cancer, but positive for Mycobacterium Tbc (PCR).

CT-SCAN revealed a paradoxical increase in size of cervical adenopathy and pneumomediastinum secondary to oeso-mediastinal fistula. A multidisciplinary team discussion considered surgery or endoscopic covered stent, but decision was made to manage the patient conservatively by optimizing antibiotic treatment (Bactrim for 1 month), PPI (omeprazole) and magaldratum (Riopan 4 times daily).

A surgical drainage of cervical adenopathy was also secondarily performed. Results: Dysphagia progressively improved over a 2-month period, and a repeat endoscopy demonstrated a slightly retractile scar with complete mucosal healing of oesophagus and no stenosis. A similar positive evolution was also seen at follow-up imaging. She regained weight and completed the full course for Tbc treatment uneventfully.

Conclusion: This is a rare complication of miliary Tbc, the management of which is poorly codified. Early diagnosis and optimized medical treatment led to symptoms resolution and control of this severe infectious disease.
Rescue EUS-guided gastro-pancreaticogastrostomy after failed transgastric ERP in a patient with obstructive chronic pancreatitis in the pancreatic head

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Background: Endoscopic retrograde pancreatography (ERP) is an effective treatment for pancreatitis. In cases of failed ERP, endoscopic ultrasound-guided pancreaticogastrostomy (EUS-PGS) has recently gained popularity. This transgastric route offers pancreatic duct access for further advanced interventions.

Case description: A 72-year-old male with a past medical history of chronic alcoholic pancreatitis presented with a recurrent episode of acute pancreatitis. An EUS showed a 7mm impacted intraductal stone in the pancreatic head and a leakage of the distal main duct. An EUS-PGS was performed and confirmed the rupture of the pancreatic duct (PD). Given severe abdominal inflammation, only possible PD puncture site was from below the gastric incision. A plastic stent was inserted for three months and the patient rapidly improved. However, given the difficult unstable scope position, a transgastric ERP failed. Due to recurrent symptoms one year later, a repeat EUS-PGS was performed gaining PD access through the gastric body. As the previous PGS-site was still patent, a stent was inserted entering the distal pancreatic duct and exiting through the old puncture site, creating a gastro-pancreatogastrostomy. Currently the patient is symptom free and a transgastric pancreatoscopy with stone therapy is planned in the near future.

Conclusions: EUS-guided PGS with intraductal treatment of main pancreatic duct obstruction or rupture is feasible and safe in patients after failed ERP. To allow transgastric PD access for further interventions, the selection of the initial puncture site is crucial, while the gastric body is preferred.

Endoscopic ultrasound-directed transgastric ERCP (EDGE) in a patient with choledochoolithiasis after Roux-en-Y gastric bypass (RYGB) and inadvertently interposed colon

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Background: Increasing prevalence of obesity led to growing rates of bariatric surgery, including RYGB. Conventional endoscopic retrograde cholangiography (ERC) is rarely successful in these cases given altered anatomy. Current alternatives like balloon enteroscopy-assisted ERC or PTBD are often cumbersome or can cause impaired quality of life and have a significant risk of peri-procedural complications.

Case description: We present a 78-year-old woman with acute cholangitis and a past medical history of a RYGB with cholecystectomy. Endoscopic ultrasound (EUS) showed the residual stomach in close proximity to the efferent small bowel loop. An EUS-guided gastric-jejunostomy was performed by placing a lumen apposing metal stent (LAMS). Nine days later she was admitted with rectal bleeding. During gastroscopy the stent was dislodged and a colon loop was found to be interposed between the small bowel loop and the residual stomach. We inserted two LAMS, one connecting the colon with the residual stomach and the other the small bowel loop with the colon.

Results: A regular ERC with complete stone clearance of the common bile duct was then performed and the two metal stents were removed. Finally, the connection between jejunum and colon was closed by an Over-The-Scope-Clip. Six weeks later a colonoscopy revealed no residual fistula between colon and residual stomach.

Conclusions: EDGE in patients with post-RYGB anatomy is normally an effective and safe treatment modality for performing ERC. However, interventional gastroenterologists must be aware of potential complications and its treatment options.

First experiences with ESD + in a 3 cm rectal polyp. A case study at the Stadtspital Waid, Zurich

Breidert M, Tajasev V, Locher R, Zeitweger M

Abstract

Background

Endoscopic submucosal dissection (ESD) provides an “en bloc” resection of even large laterally spreading mucosal tumors. It seems also suitable for patients at elevated surgical risk. Due to the retrieval of an “en bloc” specimen and because of the low local recurrence rate, ESD seems to be the preferable procedure over standard “piecemeal” resection, especially because of the high rate of early cancers in large rectal polyps.

Methods:

Case study of resection of a rectal polyp about 3 cm in size (pitt pattern III) with ESD + (Aqanife an Coagrasper with AWCo®) in a 48-year-old patient in our clinic. The AWCo® (Additional Working Channel) is an endoscopic system for providing an additional working channel for flexible endoscopes.

Results:

The lesion could be removed with good results after an examination duration of 70 min. Histology revealed complete ablation of a tubulo-villous anenoma with mainly low-grade and focal high-grade dysplasia.

Conclusions:

Dissection of polypoid lesions in the rectum by ESD + is safe. The procedure can be considerably accelerated by more exercise.

Endoscopic control interferes with EndoFLIP measurements

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Background: The functional lumen imaging probe (FLIP) system is an FDA approved tool evaluating the esophagogastric junction (EGJ) dynamically. Even though it has been commercially available since 2009, it is still rarely used due to missing consensus in how to perform and interpret test results. Therefore, we aimed to analyze the influence of endoscopic control on the FLIP measurements.

Methods: In this single center, we reviewed data of 93 patients undergoing EndoFLIP between 2016 and 2018 with and without visual endoscopic control. Indications for EndoFLIP diagnostics were symptoms of esophageal dysmotility. EndoFLIP measurements were performed at the EGJ and distal esophagus using 30ml, 40ml and 50ml distension volumes. All recorded values (distensibility, cross-sectional area (CSA), diameter, balloon pressure) were compared in the different distension volumes between the two measurements using a Wilcoxon Rank Sum test.

Results: There was a significant difference in distensibility, CSA and diameter with index distension volume (40ml) at the EGJ comparing the two measurements: Median CSA was 86.0 mm2 and diameter 12.0 mm (p<0.001) and median distensibility 2.1 mm/mmHg (p<0.001).

Conclusions: Our results show a significant difference in EndoFLIP measurements with and without endoscopic control. This underlines the importance of establishing a consensus on how to technically perform EndoFLIP measurements in order to define normal values and by this, guiding future EndoFLIP diagnostic.
Diaphragm Disease in the Colon ascends ohne Einnahme von nichtsteroidalen Antirheumatika – ein Fallbericht

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Background: Diaphragm Disease des Colon ist eine seltene Erkrankung, bei der membranartige Stenosen im Darm zu Blutungen und Abdominalbeschwerden führen. Sie ist in der Regel mit der Einnahme von nichtsteroidalen Antirheumatika (NSAR) assoziiert.

Methods: Klinischer Fallbericht


The intra-individual Variability of Fecal Calprotectin in healthy individuals

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Background: Fecal Calprotectin (FC) is a marker for intestinal inflammation, which allows the clinician to distinguish between functional and organic intestinal disease, and to monitor chronic inflammatory bowel disease (IBD). So far, there are no studies that analyzed the day to day variability of FC in the intestine as healthy control. Our aim was to determine if intra-individual variability.

Methods: 163 healthy volunteers without gastrointestinal symptoms, colitis related manifestations or intake of NSAID gave three stool samples of the morning bowel movement on three consecutive days. The FC-analysis was made by enzyme-linked immunosorbent essay (ELISA) with a cut-off of 50µg/g by MCL Laboratorien Niederwangen.

Results: Of the 163 volunteers (aged 17-66y, mean 37y, median 32y, f=100), 114 (69.9%) showed FC-values of 50µg/g and lower in all three samples, thus having inconspicuous results throughout. 49 volunteers (30.1%) showed at least one value deemed pathologic. Of these 49, 40 (24.5%) showed both normal and elevated (>50µg/g) values and 9 (5.5%) showed elevated values throughout. By applying a cut-off of 100µg/g, 26 volunteers (15.9%) showed at least one elevated measurement and only 4 (2.5%) had values consistently over 100µg/g.

Conclusions: The presented data show a high variability of FC in a short amount of time in a third of the healthy volunteers. This opens the discussion if repeat measurements of FC would be helpful for optimal decision making. Further investigations in a non-healthy population are recommended.

The data also support the question, if raising the cut-off to 100µg/g would be appropriate to keep the rate of false positive results low without missing relevant disease, as several investigators have recommended already.
Audit of colon polyps’ surveillance programme in daily clinical practice

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**Background:** It is well established that screening colonoscopy reduces colorectal cancer (CRC) mortality. Therefore many countries have surveillance recommendations, as does Switzerland. According to our knowledge there have been no studies that examine the applicability of these recommendations to clinical everyday practice.

**Methods:** The medical history database in our office was searched and the first 109 consecutive pts with polypectomy and at least one follow-up colonoscopy were analyzed. We divided the pts in three risk groups according to the SGG-guidelines: high-risk with a recommended surveillance interval of 5 years, low-risk with 5 years and the no-risk group without additional surveillance.

**Results:** Of 109 pts (f=55, age 18-88y) at index colonoscopy, 24 (22%) had a no-risk finding (small hyperplastic polyps in the rectosigmoid), 20 (18.4%) had a low-risk, and 65 (59.6%) had a high-risk finding. In the no-risk group the mean interval was 5 years (2-7y) for the surveillance colonoscopy, 5 (20.8%) now showed higher risk lesion, of which 4 (16.7%) showed high-risk. In the low-risk group at initial exam, 3 (15%) repeated a low-risk finding and 7 (35%) changed to a higher risk category. In the group of high-risk at initial exam, 26 (40%) had high-risk findings.

**Conclusions:** In this small pilot study we found the suggested control intervals for the low- and high-risk groups to be adequate, since 50% in the low-risk group showed equal or higher risk findings, and 40% in the high-risk group repeated lesions with high risk of developing CRC. Our no-risk group showed a higher risk finding after an average of 5 years in 20.8% of the pts. Therefore the 10 year control strategy for this group should be discussed and explored further in a larger study.

Prospective Study of Risk Score Strategies in the Prediction of Advanced Colorectal Neoplasia at Colonoscopy

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**Introduction:** Current referral pathways in Australia for colorectal cancer (CRC) screening do not differentiate well between low and high-risk populations, and therefore may not be efficiently utilising resources. Whilst multiple CRC risk scoring systems currently exist and are utilised to stratify patients into low and high risk groups for priority of colorectal screening, there remains a need to identify which system has the greatest diagnostic accuracy. Therefore, we prospectively compared three existing CRC-risk score systems in their ability to predict advanced colorectal neoplasia in Australian population; the Asia-Pacific Colorectal Screening (APCS) score; Hong Kong Score (2014); and Imperiale Score (2015).

**Methods:** Patients scheduled for colonoscopy assessment, both with or without gastrointestinal symptoms, were recruited. FOBT positive patients were included, but those who had an examination of the colon, including colorectaloscopy, within the last five years were excluded. Univariate and multivariate logistic regression was applied to identify significant risk factors for advanced neoplasia. For each patient, the 3 different risk scores were applied and the performance of each score in the prediction of advanced neoplasia was compared by examining the area under the curve (AUC) value.

**Results:** A total of 361 patients undergoing colonoscopy (48.2% male, median age 60 years) were prospectively recruited. The prevalence of adenomas was 31.6%, and 10.0% for advanced adenoma including 8 CRC (2.2%). Upon multivariate analysis, age and male sex were found to be significant risk factors (P=0.001, P=0.002). For predicting the prevalence of advanced neoplasia, the APCS score had AUC 0.71 (95%CI 0.63-0.79), Hong Kong Score 0.69 (95%CI 0.61-0.78), and Imperiale Score 0.68 (95%CI 0.59-0.77). Using a non-parametric comparison of the AUCs, there was no statistical significance between each of the scores for both symptomatic and asymptomatic populations (P=0.37 for APCS vs Hong Kong Score; P=0.32 for APCS vs Imperiale Score; P=0.43 for Hong Kong Score vs Imperiale Score).

**Conclusion:** All three scores are equally effective in stratifying the population into low and high risk colorectal neoplasia groups, and may be used to prioritise patients for colorectal screening.

Phytobezoar causing gastric outlet obstruction as a late complication after biliopancreatic diversion with duodenal switch

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**Background:** Bezoars are a known cause for mechanical intestinal obstruction and are more common after previous gastric surgery. The most likely cause of bezoar formation after bariatric surgery is impaired gastric motility. Bezoar formation is recognized as a rare, late complication of gastric bypass surgery. There are only few reports of bezoar formation after sleeve gastrectomy and so far none after biliopancreatic diversion.

**Methods:** We present a case of a patient with a massive dilatation of the gastric sleeve with no other abnormalities. Gastroscopy revealed a large phytobezoar (10 x 5 cm), which was divided into smaller parts and subsequently removed endoscopically. Histologically the bezoar consisted of indigestible plant material.

**Conclusions:** With the increasing number of sleeve gastrectomies, we expect more patients presenting with gastric Bezoars. The preferred treatment is endoscopic removal.

Microbial and Metabolic Profile of Longitudinally Sampled Colorectal Cancer Patients

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**Background:** Many studies characterizing the gut microbiota in context of diseases involve the fecal samples due to the convenient accessibility. However, much less is known about microbiota profile over time at the active site of diseases, specifically at the most distal part of the small bowel which is essential in maintaining the microbiota derived immune and metabolic homeostasis. To investigate the dynamic microbial profile at the ileum and colon, we longitudinally profiled the gut microbiota of patients with ileostomies and colostomies with advantage of re-sampling without adding any distress to host.

**Method:** We deeply characterized ileum and colon microbiota of 72 colorectal cancer (CC), 35 IBD and 42 non-IBD (Control) with ostomies. Additionally, ~20 patients with CC were included into the study to characterize microbial changes before and after stoma surgery until the ostomy was reversed. The microbiota composition of samples was determined by 16S-RNA sequencing and we analysed the same samples for metabolomic differences via quantification of relative metabolite concentrations, carried out with an untargeted mass spectrometer.

**Results:** Disease groups are clustered into three distinct groups mostly characterized by altered bacterial composition and lower diversity in IBD patients. Longitudinal microbiome analysis data shows that there is generally personalized microbiota within individual subjects. The microbial profile in longitudinally sampled CC patients before and after surgery is characterized with an increase of Proteobacteria and Enterobacteriaceae and relative metabolomic changes.

**Conclusion:** The microbial composition of the small bowel microbiota with a deeper resolution in characterization is scarce. This study adds valuable detail of the dynamic composition of the small bowel microbiota without adding any distress to the study participants. It also demonstrates the real dynamic microbiota changes at the specific site over time either in short or long period, such as alpha diversity reduction after surgery.
Diagnosis of Gastric Cancer in the Excluded Stomach after Roux-en-Y Gastric Bypass by Jejunogastronomy
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Background: For patients after bariatric surgery, diagnosis of gastric cancer is a challenge because of the altered gastrointestinal anatomy. This case report demonstrates a novel method to examine the excluded stomach after Roux-en-Y gastric bypass (RYGB) surgery.

Case: A 56-year-old female patient was admitted with upper abdominal pain, nausea and diarrhea. Her past medical history was significant for ethyl-tocic liver cirrhosis and condition after RYGB surgery 16 years ago. Computed tomography scan revealed a liquid-filled excluded stomach with diffuse wall thickening of the gastric antrum and contrast medium uptake, which was suggestive of gastric tumor. The excluded stomach could not be reached by double-balloon enteroscopy. Under endoscopy ultrasound guidance, we created a jejunogastronomy using a Hot AXIXIS stent and electrocautery-enhanced delivery system (Boston Scientific) and installed a 20 mm fully covered and self-expanding lumen-apposing metal stent (LAMS), which allowed biopsies to be taken. Histology confirmed a poorly differentiated ulcerating adenocarcinoma of the stomach with signet cell differentiation.

Discussion: In patients with RYGB, only the pouch of the stomach can be examined endoscopically using conventional oesophago-gastro-duodenoscopy until one reaches the alimentary limb. In addition to the traditional approaches with surgical (laparoscopic) exploration, percutaneous endoscopy by gastrostomy or double-balloon enteroscopy, jejunogastronomy is an effective and safe alternative.
Chenodeoxycholic-acid induced vascular endothelial cell activation: effects on VE-cadherin and endothelial permeability. 1S. Vukovic, 2R. Sfriso, 1M. Sorribas, 2R. Rieben, 1H. West.
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Background: Permeability of the intestinal vascular endothelium (=gut-vascular barrier GVB) controls the exchange of molecules between the blood plasma and the interstitial fluid. The barrier is essential for the observed CDCA-induced hyperpermeability by confocal microscopy. CDCA monolayers were also put in transwell-assays on ThinCert inserts (Ø3 µm pores) and permeation tested by CDCA. However, the effect of bile acids (BA), known to circulate increasingly in liver cirrhosis, on VE-cadherin-expression and the GVB are not known. Therefore, we investigated the effect of CDCA and/or pharmacological FXr-Stimulation on VE-cadherin-expression and endothelial permeability. Methods: Artificial 3D microvessels coated with porcine aortic endothelial cells (PAEC) were exposed to pulsatile flow for 48h and then immune-stained for VE-Cadherin with expression quantified by confocal microscopy. PAEC-monolayers were also put in transwell-assays on ThinCert inserts (Ø3 µm pores) and permeation tested by adding 40 kDa FITC-Dextran (read-out fluorescent tracer in receiver plate). Stimulations were different concentrations of CDCA or fexeramine, a potent FXr-agonist. Results: CDCA dose-dependently increased endothelial permeability in transwell-assays and down-regulated VE-cadherin in 3D microvessels. Fexeramine likely dose-dependently reduced VE-cadherin-expression, however, failed to impact on endothelial permeability. Conclusion: CDCA impacts on VE-cadherin-expression and leads to endothelial hyperpermeability which likely contributes to GVB disruption in cirrhosis. FxR however, does not seem to be essential for the observed CDCA-induced hyperpermeability indicating other signaling pathways playing a role.

Colon Modeling Open Source Tool (CMOST) for modeling of the natural history of colorectal cancer
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Background: Colorectal cancer (CRC) is a leading cause of cancer related mortality. CRC incidence and mortality can be reduced by CRC screening. Colonoscopy is the currently the most powerful CRC screening intervention. However, the efficacy of colonoscopy screening has not been tested in randomized controlled trials and remains unknown. Many open questions regarding colonoscopy screening remain including the best approach to the quality of colonoscopy. Microsimulation models have been advanced to simulate the natural history of CRC and CRC screening but none of the models is publicly available.

Methods: We developed Colon Modeling Open Source Tool (CMOST) as a microsimulation model of the natural history of CRC. CMOST is publicly available and supports the simulation of CRC screening interventions.

Results: Colonoscopy screening at the ages 50, 60 and 70 years reduces the incidence and mortality of CRC by 53% and 61%, respectively. In this setting, approximately 3.5 colonoscopies will be performed for each individual of the screening population and it needs 132 colonoscopies to prevent a CRC case and 25 colonoscopies per life year gained. Colonoscopy screening with a reduced bowel preparation (Aronchick scale ≤3) reduced the effectiveness of the respective screening colonoscopy. However, an immediate repeat colonoscopy had only very limited benefit.

Conclusions: CMOST enables simulation of CRC screening interventions. CMOST can be used to determine the best use of colonoscopy screening. Our calculations suggest a strongly reduced benefit of an immediate repeat of a screening colonoscopy with a poor bowel preparation.
Usefulness of contrast-enhanced ultrasound evaluating focal steatosis in the liver of cystic fibrosis – A case report in a cirrhotic and non-cirrhotic liver – Video Session

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Introduction: Cystic fibrosis (CF) is the most frequent autosomal recessive disorder in European countries. The flip side of improved survival due to increased life expectancy is the higher risk of gastrointestinal and hepatic complications and malignancies related to CF (1,2,3). Up to 40% of patients develop chronic liver disease (focal biliary fibrosis/liver cirrhosis) (2,3). Therefore, liver ultrasound is regularly complemented by hand-having written brochures with information and literature provided by physicians and nurses from the Cantonal Hospital St. Gallen, the University Hospital Zurich and a professional illustrator (only participating in the second cycle). This abstract is the result of two Astellas Pharma AG initiated, organized and financially supported meetings. We expect a high acceptance and use of the illustrations for counseling before and after transplantation. This in turn, might improve safety in deprived patient groups. The lack of radiation exposure in these young patients and the patient’s uncertainty for the patients. The lack of radiation exposure in these young patients and the patient’s uncertainty for the patients. The conclusions drawn from these studies are important as they can guide future research and clinical practice in the field. In conclusion, we propose an interdisciplinary approach to both prevent and treat liver disease in CF patients, which includes early diagnosis, appropriate management, and comprehensive follow-up care.

Methods: Patients with CF and liver disease were evaluated using ultrasound and biopsy. The results were compared to controls, and the effectiveness of different treatment options was assessed. The findings were presented at a national and international conference and published in a peer-reviewed journal. The study was approved by the institutional review board, and all participants provided written informed consent.

Results: Six patients with CF and liver disease were included in the study. Four patients had cirrhosis, and two had mild fibrosis. All patients showed improvement in liver function tests after treatment with ursodeoxycholic acid and low-fat diet. The mean improvement in liver stiffness measurements was 15% at 6 months.

Conclusions: Early identification and targeted therapy for patients with CF and liver disease are crucial for improving outcomes. Further research is needed to identify optimal treatment strategies and monitor long-term outcomes.

Background and Aims: The mesenteric lymphatic network contributes to the transport of fluid and intestinal mucosal-associated immune cells along the gut-liver axis. We hypothesized that Paneth cells, as part of the innate intestinal immune system, regulate the development of lymphatic vessels and affect portal pressure under the control of intestinal bacteria.

Methods: We induced Paneth cell depletion in MatL-expressing mice by injecting three consecutive doses of tamoxifen and performed partial portal vein ligation (PPVL) to induce portal hypertension. After 14 days, intestinal and mesenteric lymphatic vessels were assessed by immunohistochemistry (IHC) using lymphatic vessel endothelial hyaluronan receptor 1 (lyve-1) antibody. The lymphatic vessels were quantified using MetaMorph to calculate pixel ratio. Expression of genes involved in the regulation of lymphatic vessels was evaluated by RT profiler PCR in array in tissue slice. These results were further confirmed by performing quantitative PCR of more specific lymphangiogenic genes.

Conclusion: In conclusion, the intestinal and mesenteric lymphatic vessels’ network were significantly underestimated in this study. This was associated with an attenuated portal hypertension. These findings suggest that Paneth cells not only play an antimicrobial role in the intestine, but also contribute to the regulation of lymphatic vessels and portal pressure.


Quality of life measurement using wrist actigraphy in HCV genotype 1 infected, treatment naïve patients suffering from fatigue and receiving obitalivir, paritaprevir, and ritonavir tablets and dasabuvir tablets (Viekirax®/Exviera®; 3D regimen): The HEMATITE Study

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Background: Physical and mental fatigue is the most common symptom reported by patients with Hepatitis C Virus (HCV), which highly impacts their overall quality of life. This cardinal symptom presents regardless of the stage of liver fibrosis and is difficult to quantify objectively. Similar to other potential reasons for physical and mental fatigue, increasing evidence suggests a direct viral impact on the central nervous system. Data demonstrating a longitudinal change of debilitating physical fatigue are missing.

Methods: HEMATITE is an observational, prospective, open-label, single-arm, Swiss multicentric, real-life study in HCV patients (GT1). The study consists of a Tx preparation phase of 4 weeks (wks), a Tx phase with 3D regimen according to routine clinical practice (12 wks) and a post Tx phase (12 wks) to evaluate Tx response. Fatigue was assessed at every visit using the Fatigue Severity Score (FSS) questionnaire, according to routine clinical care. In addition, physical activity data was collected by providing patients with a wrist-worn activity tracker to be worn for 4 wks before Tx Baseline (BL) and for 4 wks before each visit. Results: 4041 patients reached SR12. The FSS decreased significantly from BL to post Tx week visit 12 (5.9 ± 0.61 vs. 3.3 ± 0.64; p<0.001). The physical activity intensity data analysis could be collected from 9047 out of 4545 (mean ± SD) subjects. Neither the mean activity nor the change of the mean activity between BL and Tx week 12 showed any significance (5.92 ± 0.61 vs. 3.34 ± 0.61 (mean ± SD); p<0.001). The rationale for this observational study is to observe the impact of 3D regimen on physical activity of HCV patients suffering from debilitating fatigue by using wrist actigraphy. CONCLUSIONS: Further research is needed to identify optimal treatment strategies and monitor long-term outcomes.
Early outcome in patients with non-alcoholic fatty liver in comparison with non-alcoholic steatohepatitis undergoing gastric bypass: a propensity score matched analysis
Service of Visceral Surgery, Departments of Surgery, University Hospital of Geneva and medical School, Geneva, Switzerland.

Abstract

Background: Non-alcoholic fatty liver disease (NAFL) is the most common liver disease worldwide. It is characterized by morphological changes of the liver tissue, mainly characterized by accumulation of fat and necroinflammation. The incidence of NAFLD increases dramatically in the last decades. NAFLD is the most common cause of chronic liver disease and the 2nd leading cause of liver transplantation. Pathogenesis of NAFLD is still under debate. NAFLD and NASH patients may benefit from bariatric surgery. NAFLD and NASH are defined as non-alcoholic fatty liver disease (NAFL) and NASH (non-alcoholic steatohepatitis), respectively. NAFL and NASH are the 2nd and 3rd leading causes of liver transplantation in the United States. Postoperative follow-up in patients with NAFL and NASH who underwent RYGB.

Objectives: To evaluate the early outcome in patients with NAFL and NASH who underwent RYGB.

Methods: The study in an institutional review board approved retrospective cohort study of patients with NAFL and NASH who underwent RYGB between 1997 and 2013. Clinical follow up was performed at 12 months after surgery.

Results: Within the entire cohort, at baseline before matching, the NAFL (n=161) and NASH (n=94) groups were comparable in age, body mass index (BMI), ASAT and score and weight loss in the 3 months follow-up period.

Conclusion: Patients with NAFL seem to improve their liver function after gastric bypass and show a lower weight loss in comparison with patients with NASH. Meanwhile, gastric correct seems to be compromised in patients with NAFL after gastric bypass in comparison with NAFL even in well-matched obese patients.

A buyers’ club to improve access to hepatitis C and HIV treatment for vulnerable populations
Vernaz Nathalie1, Calmy Alexandra2, Hurst Samiai2, Jackson Yates2, Negro Francesco2, Perrier Arnaud2, Anne-Claire Bréchet2, Laurent Gelaz2, Wolf Hars2
1Medical Direction, 2Finance Direction, 3HIV Unit, Infectious Disease division, 4Institute for Ethics, 5History, and the Humanities, 6Division of primary care medicine, 7Divisions of Gastroenterology and Hepatology and of Clinical Pathology, University of Bern, 8Division of Hepatology, Geneva University Hospitals, University of Geneva, Switzerland

Background – The estimated prevalence of active hepatitis C virus (HCV) infection in the general Swiss population is 0.4%-0.5%. The prevalent liver disease is high among vulnerable populations such as migrants, intravenous drug users and people living in prison (PLP). Health care systems are struggling to finance costly therapies (such as direct antiviral agent) through public funding for uninsured patients, despite their unprecedented high cure rates.

Methods - A personal importation scheme is based on the legal right of patients to import any drug into Switzerland for personal use. A ‘Buyers’ club’, which is a structure that aims to help patients to import generic medicines safely, was established in October 2016 at University Hospitals of Geneva. To assess the impact of this initiative, we compared the real cost of imported generics with their corresponding Swiss prices. Quality and efficacy were used as outcome parameters.

Results - From October 2016 until April 2019, 7 PLP and 7 migrant patients were treated for HCV. 7 for HIV and 1 HCV/HIV co-infected patient for both viruses. HPLC-UV analysis demonstrate that all generics meet good manufacturing practices. HPLC-UV analysis demonstrate that all generics meet good manufacturing practices. All generics were treated for HCV, 7 for HIV and 1 HCV/HIV co-infected patient for both viruses. HPLC-UV analysis demonstrate that all generics meet good manufacturing practices.

Conclusion: Within the entire cohort, at baseline before matching, the NAFL (n=161) and NASH (n=94) groups were comparable in age, body mass index (BMI), ASAT and score and weight loss in the 3 months follow-up period.

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Evaluation of the prognostic value of histologic parameters in severe alcoholic hepatitis
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(4) Department of Gastroenterology, Hepatopancreatology, and Digestive Oncology, U.C.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium
(5) Department of Gastroenterology and Hepatology, Clinique St Luc, Bouge, Belgium

Background and Aims: Alcohol-related liver disease (ARLD) is a major cause of global mortality and morbidity. AML, who is a structure that aims to help patients to import generic

Aim: To study the prognostic value of AHHS and of Laennec system for survival at 3, 6 and 12 months.

Methods: Liver biopsies of patients with severe AH (Maddrey DF >32) were analyzed independently by 2 pathologists. Fibrosis, neotrophils, binucleated and megamastocytoma were assessed to classify patients into mild, moderate or severe AML. Patients with cirrhosis were also classified according to the Laennec system (4A, 4B and 4C) based on fibrous septa thickness and nodules size.

Results: 55 consecutive patients were included (median age: 54 years [95% CI: 50- 56]), and Maddrey DF: 71 [95% CI: 69-73]) who were treated with corticosteroids. Four patients (8%) were lost to follow-up at 12 months, 24 (44%) died and 1 (2%) underwent liver transplantation. Histologic scoring was available in 53 patients.

Conclusion: AHHS as well as Laennec system could be used to predict survival in patients with severe AH. The severity of fibrosis seems the histologic parameter with the strongest prognostic value.

Robust MAIT cell activation in response to interactions with primary human liver cell subsets
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Background: MAIT cells are a specific form of human innate lymphoid cells that are particularly abundant in human liver, present in significant numbers in all human liver biopsies. MAIT cells are a distinct population of lymphocytes that are present in the liver and are involved in MAIT cell activation or not. When considering Laennec system instead of AHHS, Laennec 4B or 4C was not associated with increased mortality at 1 year (risk ratio: 1.37, 95% CI: 0.85-1.91, p=0.28). When considering Laennec system instead of AHHS, survival rates of patients without cirrhosis or with Laennec 4A were 91% vs. 68% at 3 months (p<0.001), 73% vs. 48% at 12 months (p<0.001). Multivariable analysis adjusted for age and for MELD score, AHHS was not associated with 1-year mortality (risk ratio: 1.37, 95% CI: 0.95-1.87, p=0.01).

Conclusion: AHHS has little added value to predict survival in patients with severe AH. The severity of fibrosis seems the histologic parameter with the strongest prognostic value.

A buyers’ club to improve access to hepatitis C and HIV treatment for vulnerable populations
Vernaz Nathalie1, Calmy Alexandra2, Hurst Samiai2, Jackson Yates2, Negro Francesco2, Perrier Arnaud2, Anne-Claire Bréchet2, Laurent Gelaz2, Wolf Hars2
1Medical Direction, 2Finance Direction, 3HIV Unit, Infectious Disease division, 4Institute for Ethics, 5History, and the Humanities, 6Division of primary care medicine, 7Divisions of Gastroenterology and Hepatology and of Clinical Pathology, University of Bern, 8Division of Hepatology, Geneva University Hospitals, University of Geneva, Switzerland

Background – The estimated prevalence of active hepatitis C virus (HCV) infection in the general Swiss population is 0.4%-0.5%. The prevalence is higher among vulnerable populations such as migrants, intravenous drug users and people living in prison (PLP). Health care systems are struggling to finance costly therapies (such as direct antiviral agent) through public funding for uninsured patients, despite their unprecedented high cure rates.

Methods - A personal importation scheme is based on the legal right of patients to import any drug into Switzerland for personal use. A ‘Buyers’ club’, which is a structure that aims to help patients to import generic medicines safely, was established in October 2016 at University Hospitals of Geneva. To assess the impact of this initiative, we compared the real cost of imported generics with their corresponding Swiss prices. Quality and efficacy were used as outcome parameters.

Results - From October 2016 until April 2019, 7 PLP and 7 migrant patients were treated for HCV. 7 for HIV and 1 HCV/HIV co-infected patient for both viruses. HPLC-UV analysis demonstrate that all generics meet good manufacturing practices. The total costs for the HCV imported generic medicines were CHF 15,525, compared to CHF 477,225 for the corresponding Swiss brand medicines. The HIV imported generic costs were CHF 4,163, compared to CHF 41,624 for the corresponding brand medicines. Two patients with HCV have already terminated their 12-week follow-up and have cleared their infection.

Conclusion: Our personal importation scheme allows to import generics at 4% of the Swiss corresponding costs. This strategy seems highly promising to improve universal access to hepatitis C and HIV medicines to vulnerable populations, such as uninsured patients, with minimal disruption of the conventional, patient-based model of care, and should be expanded to other diseases and settings.
Hepatic gene expression analysis identifies marked differences in acute alcoholic microvesicular steatosis compared to alcoholic steatohepatitis (ASH) 

N.Gossens, L.Rubbia-Brandt, N.Larthier, L. Spade; Hepatic/Gastroenterology, Clinical Pathology, Hepatology, Geneva and Brussels - Acute alcoholic microvesicular steatosis (MIS); alcoholic foamy degeneration; is a potentially severe form of alcoholic liver disease. (SwissMedWeekly 2018: 148(suppl 232): A16).

Pathogenesis of MIS is unclear, and clinical presentation could mimic ASH. Patients/Methods: We studied hepatic gene expression in a subset of 2-fold liver biopsies from patients presenting with MIS (n=7; M/F 3/4; 46 yrs, AlkPhosph (AP) 195 IU/L, triglycerides (TG) 4.23 mmol/L, focal or no liver fibrosis: 5/7) or ASH (n=17; M/F: 8/9; 49 yrs; AP 138 IU/L, TG 1.3 mMol/L, all with cirrhosis). At histology, MIS was defined as > 50% microvesicular steatosis and no inflammation, while ASH included polyinfluenza + macrosteatosis+ ballooned hepatocytes. Liver mRNA was extracted (snap-frozen tissue), followed by microarray hybridization/gene expression analysis. Significant differential expression was defined as > 2-fold differences after correction for false discovery. All fibrosis/cell tissue analysis, the main pathways differentially expressed in MIS compared with ASH are related to cell cycle (upregulated), stellate cell activation, fibrosis and inflammation (downregulated). Other important genes related to lipid metabolism were identified. Table: MIS vs ASH

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<tr>
<th>Function</th>
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<th>Fold change</th>
<th>p value</th>
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<tr>
<td>Cell cycle</td>
<td>CDK2, CDK8</td>
<td>+5.67, +3.6</td>
<td>0.006, 0.002</td>
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<tr>
<td>Inflammation</td>
<td>ALOX15P, CCR2</td>
<td>-3.02, -2.87</td>
<td>0.000, 0.0014</td>
</tr>
<tr>
<td>Lipid metabolism</td>
<td>CD36, PLIN2</td>
<td>+2.66, +4.55</td>
<td>0.005, 0.013</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>FGF</td>
<td>-6.51</td>
<td>0.019</td>
</tr>
<tr>
<td>Detoxification</td>
<td>CYP2E2</td>
<td>+3.56</td>
<td>0.0004</td>
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Conclusions: Multiple genes show significant differential expression in MIS when compared to ASH, involving liver cell repair, lipid metabolism and detoxification process. These observations may help clarify the pathogenesis of MIS (supported by FLAGS)

H11

Loss of Claudin-3 Results in Metabolic Reprogramming and Impaired Regeneration in the Murine Liver

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Background: Tight junctions (TJs) are essential components to maintain the blood biliary barrier in the liver. The proteins that comprise hepatic TJs and their contribution to homeostasis and regeneration remained largely unexplored. Here, we elucidate the cell type specific expression of TJ genes in murine livers, and explore the regulation and functional importance of the transmembrane protein Claudin-3 (CLDN3) in liver regeneration.

Methods: Native liver RNA-seq; tissue RNA-seq. CLDN3 localization was determined by immunofluorescence. CLDN3+ or CLDN3- mice were subjected to 2/3 partial hepatectomy (PH). Proliferative indices were quantified with Ki67 and pHH3. Cell cycle driver gene expression was determined by RT-qPCR. Barrier function was assessed by FACS. Differential gene expression was analyzed with DESeq2. Lipid and bile acid measurements, cytokine expression and immune cell quantifications by FACS. Differential gene expression was analyzed with DESeq2. Lipid and triglyceride levels were quantified with Oil-Red-O.

Results: We quantified the expression TJ genes in native liver tissue. Single cell RNA sequencing revealed that TJ transcripts can be found in hepatocytes and cholangiocytes but also on non-parenchymal cell populations. The TJ gene Cldn3 was regulated following PH. CLDN3+ mice had impaired liver regeneration following PH, which was possibly caused by inefficient baseline energy metabolism.

Conclusions: CLDN3 is among the highest expressed and regulated hepatic tight junction genes in native and proliferating livers. CLDN3 had a zonated expression pattern and a functional role in the maintenance of energy homeostasis and liver regeneration. This suggests that tight junctions of the liver are involved in biological processes that go beyond cell-cell adhesion and barrier formation.

H12

Thrombin generation in patients with liver cirrhosis: modern global hemostasis assays provide new insights into a coagulation state

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Background: Cirrhotic patients are at increased thrombotic risk despite prolonged routine coagulation assays. This has been proven in clinical studies. However, in vitro studies using thrombin generation (TG) showed some discrepancies. This can be explained by high inter-laboratory methodological variability and differences in severity and aetiology of liver cirrhosis. To reach reproducible results and to assess the clinical value of TG assays, larger studies with standardized methods and a prospective follow-up are necessary.

Methods: We report the results for the first 85 patients included in a single-centre prospective study recruiting patients with liver cirrhosis (n=400). We analyzed TG using an automated and standardised assay (ST Genesia, Stago, Asnière, France), including tests with and without thrombomodulin (TM) as activator of the protein C/S (PC/S) system, as well as Thrombodynamics analyser (TD) (Hemacore, Moscow, Russia). A clinical follow-up of 12 months is planned.

Results: We confirm an increased TG with TM in cirrhotic patients compared to healthy subjects. This highlights the reduction of the natural anticoagulants PC/S in these patients. TD shows already without TM an increased and faster propagation of TG at distance of tissue factor compared to healthy subjects. This reflects an increased amplification phase of the coagulation in cirrhosis patients.

Conclusions: We confirm a prothrombotic state in cirrhotic patients due to PC/S deficiency. New insights are: TD shows an increased amplification phase of coagulation in cirrhotic patients, already in the absence of TM; this could be explained by reduced natural anticoagulants, mainly antithrombin. The one-year clinical follow-up should allow to assess the ability of these tests to predict thrombo-haemorrhagic complications.
Out of Africa: Hepatitis C Virus Subtype 4r as Troublemaker

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Background and aim: Direct acting antivirals (DAAs) have revolutionized the management of chronic hepatitis C, with sustained virologic response (SVR) rates > 90%. Here, we characterized patients who did not achieve SVR on DAA-based therapy.

Patients and methods: We conducted an observational retrospective study to characterize the patients treated jointly with a specialized nurse in the Service of Gastroenterology and Hepatology of the CHUV between January 2015 and February 2018.

Results: In the slightly more than three years, 306 patients with chronic hepatitis C were treated with first- or second-generation DAAAs. Of these, 284 (92.8%) achieved SVR and 22 (7.2%) experienced a relapse. SVR rates increased progressively over the years as a result of a declining proportion of patients with advanced liver disease and the introduction of pangenotypic treatment regimens. Significant resistance-associated substitutions were identified in all tested patients who experienced a relapse, indicating a very low rate of non-virological treatment failure. Remarkably, only 27 of the 35 patients infected with HCV genotype 4 achieved SVR (77.1%, p = 0.001 for the comparison with other genotypes). Of the eight genotype 4-infected patients who failed DAA treatment, five were infected with subtype 4r (62.5%), all of them originated from Africa and they harbored NS5A sequence polymorphisms associated with drug resistance already at baseline.

Conclusions: The rate of non-virological treatment failure was very low, likely as a result of close follow-up by a specialized nurse, favoring excellent treatment adherence. Patients infected with HCV subtype 4r were overrepresented among relapsers, as reported recently from other centers. Hence, patients with chronic hepatitis C of genotype 4 originating from Africa may have HCV subtype 4r and a triple DAA regimen may be considered as first-line treatment in the presence subtype 4r.

AXL-expressing immune-homeostatic liver macrophages disappear in progressive cirrhosis

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Background: AXL and MERTK belong to the family of TAM receptor-tyrosine kinases and are phagocytic receptors with distinct patterns of expression. On circulating monocytes in cirrhosis AXL and MERTK dampen innate immune responses, promote phagocytosis and have been associated with infection susceptibility. We sought to assess AXL and MERTK expression in cirrhotic livers related to disease severity.

Methods: Liver biopsies from cirrhotic patients (Child A/n=8, B/n=7, C/n=7) were compared to healthy controls (HC/n=4), chronic liver disease without cirrhosis (n=8), and nodular regenerative hyperplasia (NRH/n=3). AXL and MERTK expression on parenchymal and non-parenchymal cells was assessed in hepatic plates using confocal microscopy on multiplexed immunofluorescence.

Results: AXL+ cells were identified in sinusoids but not in the parenchyma and were predominantly resident macrophages (Kupffer cells, KCs, CD68+). CD68+AXL+ KCs represented the majority (86%) of the entire KC population in HC, but decreased significantly with cirrhosis progression. CD68+MERTK+ KCs were sparse in HC, but increased with progressive cirrhosis. The number of AXL+ KCs negatively correlated with Child-Pugh scores. Numbers of AXL+ KCs were similar in patients with advanced cirrhosis and NRH with portal hypertension.

Conclusions: We newly described AXL expression on the majority of Kupffer cells in healthy liver, which is subsequently lost during progression of cirrhosis and portal hypertension. The data may suggest a role for AXL in hepatic immune homeostasis and firewall function of the liver facilitating clearance of commensal organisms derived from the intestine. In this context, loss of AXL may relate to pathological bacterial translocation in cirrhosis.

Autoimmune Immune-Disorders in HCV patients: Effect of Direct Antiviral Agents - the AIDAA study (SASL 42)

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1Hepatologie, UVM, Inselspital, Bern; 2Epatoentico Ticino, Lugano; 3Fondazione Epatoentico Ticino, Lugano; Klinik für Gastroenterologie/Hepatologie, Kantonsstip. St. Gallen.

Background: Chronic Hepatitis C (CHC) may negatively influence evolution and prognosis of some autoimmune idiopathic disorders (AID). The aim of this study was to investigate the influence of direct antiviral agents (DAA) treatment on AID.

Methods: Patients with HCV and AID treated with DAA in three Swiss medical centers were assessed using self-administered Visual Grading Scale (VGS) and questionnaires assessing the perception of AID activity before, during and after DAA treatment.

Results: We enrolled 23 patients (14 male; mean age 57 years, range 42-80) between 2015 and 2018. 11 (48%) had psoriasis, 8 (35%) rheumatoid arthritis, 3 (13%) Sjögren’s syndrome and 1 (4%) ankylosing spondylitis. Sustained viral response (SVR) was achieved in all cases. Improvement of AID was reported in 8 patients, while 2 reported a worsening. Overall, we observed a trend to improvement in the perception of the severity of AID (mean VGS 4.74 at baseline vs. 3.57 at SVR, p=0.134). In patients with rheumatoid arthritis, mean Patient Activity Scale II (PAS II) decreased from 4.31 to 3.90 (p=0.068). Women were more likely to have an improved perception of their AID on SVR.

Conclusions: Successful treatment of HCV using DAA does not worsen the severity of AID according to patients’ perception. On the opposite, about one third (33%) of patients report a significant improvement of AID symptoms on SVR. Worsening of perceived AID severity occurred only in 2 cases (9%).

ABC4 deficiency associated Copper Overload mimicking Wilson’s disease: a Case report

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Case presentation: A 21-year-old male patient presented with pruritus, fatigue and elevated liver enzymes (Bilirubin 2.3mg/dl, ALT 181 U/L; AST 106 U/L; γ-GT 212 U/L; AP 220 U/L). Comprehensive work-up provided no evidence of viral or autoimmune liver disease; primary biliary cholangitis (PBC) or -sclerosing cholangitis (PSC), 24-hour urinary copper excretion was increased (101 μg/day), though serum copper and coeruloplasmin levels were normal and Kayser-Fleischer rings not detectable. Liver histology showed features of cholangiopathy, bridging fibrosis and an increased hepatic copper content (102 μg/g dry weight). Thus, a diagnosis of probable Wilson’s disease (WD) with a Leipzig score of 3 points was entertained and chelation therapy initiated. However, there was no biochemical response, and sequencing of the Wilson gene (ATP7B) yielded no mutations. Indeed, sequencing of the hepatocarnacular phospholipid transporter ABCB4 revealed two heterozygous nonsense respectively missense mutations: c.139C>T [p.Arg47X] and c.959C>T [p.Ser320Phc]. The patient was diagnosed with progressive familial cholestasis type 3 (PFIC3) and associated copper overload. Ursodeoxycholic acid was started with significant biochemical improvement and stable condition in follow-up.

Discussion: Variable degrees of secondary copper overload have been recognized in common cholestatic diseases e.g. PBC and PSC. However, ABCB4 deficiency with a PFIC3-like phenotype underlying significant hepatic copper deposition with challenging differentiation from WD has only rarely been reported. Sequencing of both ATPB4 and ABCB4 can aid in separating these two entities, as the required therapies are vastly different.
Liver disease following bone marrow transplantation: clinical and biological characteristics of sinusoidal obstruction syndrome (SOS) and graft-versus-host disease (GVH)

Gastroenterology-Hepatology, Oncohematology, Clinical Pathology, HUG.

Patients undergoing bone marrow transplantation (BMT) may suffer from severe liver disease which may impact on survival. The most frequent causes include SOS and GVH, the diagnosis of which remains a challenge due to similarities in liver function tests (LFT) alterations. In this retrospective study, we determined the pattern of LFT changes and time to appearance after BMT, clinical symptoms, and hepatic hemodynamics in patients developing SOS or GVH in a single institution.

Methods: We included all patients who underwent BMT at the HUG (2009-2019) with a histological diagnosis of GVH or SOS. Clinical, biochemical and transjugular liver biopsy data obtained at time of diagnosis were reviewed, as well as patients’ outcome. Results: 16 patients (mean age 38 yrs, 93% male) presented with GVH (n=9), SOS (n=5) or combined lesions (n=1) after a median time of 105 and 165 days after BMT, respectively. Biliary and sinusoidal pressure gradient

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<th>Parameter</th>
<th>SOS</th>
<th>GVH</th>
<th>p value</th>
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<tr>
<td>ALT (IU/L)</td>
<td>104 ± 99</td>
<td>143 ± 128</td>
<td>NS</td>
</tr>
<tr>
<td>AlkPh (IU/L)</td>
<td>117 ± 83</td>
<td>138 ± 103</td>
<td>NS</td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td>239 ± 135</td>
<td>220 ± 170</td>
<td>NS</td>
</tr>
<tr>
<td>Bilirubin (umol/L)</td>
<td>19.5 ± 13.5</td>
<td>31.6 ± 35</td>
<td>NS</td>
</tr>
<tr>
<td>HVPG (mmHg)</td>
<td>13.6 ± 4</td>
<td>5 ± 2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Jaundice</td>
<td>m2 = n1</td>
<td>m2 = NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

An elevated GGT (> 2 ULN) was the most common alteration of LFT. One month after diagnosis and treatment, a marked reduction in LFTs was observed with further degradation in all SOS patients leading to death (n=1). Conclusion: Both GVH and SOS may affect the clinical course after BMT. As clinical symptoms and biochemical alterations poorly discriminate between these 2 entities, liver biopsy and hepatic hemodynamics are essential for a precise diagnosis and to guide therapy.

Preliminary report on the Swiss Autoimmune Hepatitis Cohort Study

Emmanuela Paretì, Ospedale Beata Vergine, Mendrisio; Giacomo M. Cioffi; Fondazione Cardiocentro Ticino; Lugano; Andreas Cerny, Epatocentro Ticino; Lugano; Stefania Casu, Inselspital; Bern; Christiane Sokollik; Inselspital; Bern; Christian Braegger, Universitàts-Kinderhospital; Zurich; David Semela, Kantonsst. Gallen; St. Gallen; Giorgia Mielì-Vergani, King’s College Hospital; London; Diego Vergani, King’s College Hospital; London; Benedetta Terzirollo, Epatocentro Ticino; Lugano and MowatLabs, King’s College Hospital; London.

Background: Autoimmune hepatitis (AIH) is a rare disease affecting children and adults. The Swiss AIH cohort study established in 2017 has the aim of collecting data and samples on AIH. Methods: Inclusion criteria: diagnosis of AIH; Swiss residency. Results: 134 adult, 11 pediatric patients. Adults: 98 female; median age at diagnosis 56 years; 95% white ethnicity. 9 with AIH/primary sclerosing cholangitis overlap; 23 with AIH/primary biliary cholangitis overlap. Median retrospective observation was 52 months, median prospective follow-up 11 months. 72% positive for anti-nuclear antibody, 49% for anti-smooth muscle antibody, of which 40% double positive; 7% for anti-liver (SLA) antigen, 1% for anti-liver kidney microsomal (LKM1) antibody. Initial treatment: 57 received prednisolone of whom 33 received also azathioprine, 10 received budesonide; second-line treatment: mycophenolate mofetil in 15, 6-mercaptopurine in 3, infliximab in 3; 3 had a liver transplantation (LT) after enrolment, none died after enrolment. Pediatric: 5 female, median age at diagnosis 10 years; median retrospective observation 31 months; median prospective follow up 12 months; 3 anti-SLA positive; 3 anti-LKM1 positive. All treated with prednisolone and azathioprine. None underwent LT or died. Conclusion: The Swiss AIH cohort study provides novel information on AIH in Switzerland, raising awareness on the uneven management, and establishes a platform for collaborative national and international research projects.

Preliminary report on the Swiss Primary Biliary Cholangitis Cohort Study

Emmanuela Paretì, Ospedale Beata Vergine, Mendrisio; Giacomo Cioffi, Cardiocentro Ticino, Lugano; Andreas Cerny, Epatocentro Ticino, Lugano; Guido Stirnimann, Inselspital, Bern; Magdalena Filipowicz, Kantonsspital Baselland, Liestal; Joachim Mertens, Universitätsklinikum, Zurich; David Semela, Kantonsst. Gallen, St. Gallen; Adriana Baserga, Fondazione Epatocentro Ticino, Lugano; Stefano Bellentani, Clinica Santa Chiara, Locarno; Benedetta Terzirollo Beretta-Piccoli, Epatocentro Ticino, Lugano, Switzerland and Institute of Liver Studies, MowatLabs, King’s College Hospital, London, UK.

Background and aims: The Swiss Primary Biliary Cholangitis (PBC) cohort study was established in 2017 with the aim of collecting high quality, standardized data and biosamples on PBC in Switzerland. Methods: Inclusion criteria: diagnosis of PBC, or isolated positivity for anti-mitochondrial antibody (AMA) and/or for PBC-specific anti-nuclear antibody (ANA); residency in Switzerland. Results: 172 patients enrolled by March 2019 within 8 centres. 145 female; median age at diagnosis 52 years; 166 white, 4 Asian, 2 black; 25 with PBC/autoimmune hepatitis (AHP) overlap. Three patients required liver transplantation before enrolment, one died 1.5 years after enrollment of liver-unrelated causes. Median retrospective observation was 49 months, median prospective follow-up 12 months; AMA was available in 128, being positive in 91%; 12/16 AMA-negative were positive for PBC-specific ANA; 61 had normal alkaline phosphatase at diagnosis, of whom 26 had a liver biopsy; 22 had histological findings compatible with PBC, 18 at stage Ludwig I-II (5 with overfilling AIH), 4 at stage Ludwig III-IV (1 with concomitant NASH and 1 with previous HCV); 2 had mild unspecified cholestasis, 1 had NASH, 1 had unknown findings. Treatment (available in 114 patients): 110 received ursodeoxycholic acid (UDCA), 1 azathioprine alone, 1 with AIH overlap steroids alone, 2 were not treated; second-line treatments included fibrate in 13 patients, and obeticholic acid in 5 patients. Conclusion: This study provides novel information on PBC in Switzerland, supporting that PBC histological changes are often seen in patients with isolated AMA-positivity, at times with concomitant liver diseases.
The gene signature-MELD score and alcohol consumption determine long-term prognostic value of patients with severe alcoholic hepatitis

Piere Catella1, Eric Tripodi1, Naoto Fujwara5, Nicolas Goossens6, Astrid Marot3,4, David Semenia1
1Dpt of Pathology and Immunology, and 2) Cell Physiology and Metabolism, UNIGE; (3) Dpt of Physiology, UNIL, (2) Division of Gastroenterology, Hepatology and Nutrition, CHUV, University of Geneva, Lausanne, Switzerland; (4) Diagnostics and Therapeutic Center, Lausanne, Switzerland; (5) Dpt of Pathology and Medical Biology, Japon Institute, Sepalle, Switzerland; (6) Dpt of Gastroenterology, Hepatology and Hepatocarcinology, University of Geneva, Geneva, Switzerland.

Background: Accurate prediction of long-term prognosis of patients with severe alcoholic hepatitis (AH) is mandatory to guide therapeutic strategy. The gene signature-MELD score (gs-MELD) score, a combination of a gene signature and the MELD score, has been proposed as a new prognostic tool to evaluate the long-term prognostic value of patients with severe alcoholic hepatitis (SAH) according to the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agree...
A combination of the ACC inhibitor GS-0976 and the nonsteroidal FXR agonist GS-9674 improves hepatic steatosis, biochemistry, and stiffness in patients with nonalcoholic steatohepatitis

Eric Lawitz, Edward Ganeu, Peter Ruane, Robert Herron, Jr., Ziad H. Younossi, Paul Kao, Jie Zhang, Catherine Joo, Jay Chuang, Bryan McGolcan, Chuan Chung, Mani Subramanian, Robert Myers, Ramon Thalib, Michael Mitchell, Varoujan, Marc Helferstein, Mazen Noureddin, Stephen Harrison, Rob Lobitz

Texas Liver Institute, USA; Liver Unit, New Zealand; Ruine Clinical Research, USA; QMeth, Medical Research Unit, SSA, Gladstone, USA; Biostatistics, University of California at San Diego, USA; University of California Berkeley, USA; Cedars-Sinai Medical Center, USA; uPinnacle Diagnostics Research, USA.

Background and aims: Preclinical data suggest that the combination of an ACC inhibitor and FXR agonist is more effective than monotherapy in the treatment of NASH. Here, we describe the combination of these agents, GS-0976 in combination with the nonsteroidal FXR agonist, GS-9674, in patients with NASH.

Method: Twenty patients with NASH diagnosed by a magnetic resonance proton density fat fraction (MR-PDDF) ≥ 10% and liver stiffness ≥ 2.88 kPa by magnetic resonance elastography (MRE), or historical biopsy consistent with NASH and F2-F3 fibrosis were enrolled. Patients received GS-0976 20 mg and GS-9674 30 mg orally once daily for 12 weeks. Data from two cohorts treated with either GS-0976 70 mg or GS-9674 30 mg daily for 12 weeks are provided for comparison. MRI-PDDF and MRE and serum fibrosis markers were centrally read at baseline (BL) and week 12 (W12). Deuterated water was administered to measure hepatic de novo lipogenesis (DNL).

Results: In the combination cohort, 55% had diabetes and the median BMI was 38.7 kg/m2. Compared with BL, significant reductions at W12 in combination-treated patients were observed for PDFF (median: 16.4% vs 9.8%, p = 0.001), MRE-stiffness (3.76 vs 3.43 kPa, p = 0.018), serum TIMP-1 (2.63 vs 2.40 g/L, n = 0.012), PIt-PP (10.6 vs 8.4 g/L, n = 0.003), ALT, and GGT. At W12, a ≥ 30% reduction of PDFF was observed in 19 patients (74%). Compared with monotherapies, combination treatment resulted in greater reductions in hepatic PDFF, ALT, GGT, and hepatic DNL compared with safe and well tolerated with AE rates similar to monotherapies; no patient reported ≥ grade 2 pruritus or discontinued study medications due to AEs.

Conclusion: The combination of GS-0976 and GS-9674 for 12 weeks was safe and led to improvements in hepatic steatosis, liver stiffness, liver biochemistry, and markers of fibrosis in NASH.

Global real-world evidence of sofosbuvir/velpatasvir as a simple, effective regimen for the treatment of chronic hepatitis C patients: Integrated Analysis of 12 clinical practice cohorts

A Phase 3 Study Comparing Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafemafine With Continued TDF Treatment in Virologically Suppressed Patients With Chronic Hepatitis B: Week 48 Efficacy and Safety Results

A Phase 3 Study Comparing Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide With Continued TDF Treatment in Virologically Suppressed Patients With Chronic Hepatitis B: Week 48 Efficacy and Safety Results


1 Uni Degli Studi, Italy; 2 Vait d’Hotein, Switzerland; 3 General Hospital, 4 Severance Hospital, South Korea; 5 Kaohsiung Medical University Taiwan; 6 Kyungpook University South Korea; 7 GI Research Institute, Canada; 8 Chia-Yi Christian Hospital, Taiwan 9 KAAR Centre, 10 Asian Pacific Liver Center, USA; 11 Hahnemann University Hospital, USA; 12 Gilead Sciences; 13 Gilead Switzerland; 14 Silicon Valley Research Unit, USA; 15 Chai-Yi Hospital, 16 King’s College Hospital, UK; 17 Asian Medical Center, Seoul; 18 The Chinese University of Hong Kong.

Background and Aims: TAF, a novel prodrug of tenofovir (TFV), was recently approved for treatment of CHB. We evaluated efficacy and safety in stable, virally-suppressed patients who were switched from TDF to TAF vs. continued TDF for an additional year.

Method: In this Phase 3 study (NCT02979613), CHB patients on TDF for ≥8 weeks with HBV DNA <LLOQ for 12 weeks and <20 IU/mL at screening were randomized (1:1) to TAF 25 mg QD or TDF 300 mg QD, each with matching placebo, and treated for 48 weeks. The primary efficacy analysis was the proportion of patients with HBV DNA ≤20 IU/mL at Week 48 based on the modified US FDA-defined snapshot algorithm, the change in proportion of patients achieving viral elimination. SOF/VEL for 12 weeks is a simple and highly effective regimen that cures HCV patients, irrespective of GT, cirrhosis status, and current/historic IV drug use, with or without resistance to current treatments.

Results: 488 patients were randomized and treated at 42 sites in 8 countries. TAF demonstrated non-inferior efficacy to TDF with a similar rate (0.4%) having HBV DNA ≤20 IU/mL at Week 48, (difference in proportions: 0.0%, 95% CI, -0.9% to +1.3%). TAF treatment resulted in increases in hip and spine bone mineral density (BMD), and decreases in estimated creatinine clearance by Cockcroft-Gault (eGRFC). Markers of bone turnover and renal tubular function were serially assessed.

Conclusion: Viral suppression and complete virological response was maintained in TAF patients, and acceptable renal safety was observed in the 2% of patients with creatinine levels ≥1.5 mg/dL. A significant decrease in albumin levels was observed in patients with chronic hepatitis D, which may be related to a decrease in the major albumin binding site for HBV DNA.

Methods: Data from 12 clinical practice cohorts across North America and EU, representing 7 countries, are included. Adults were treated according to local standards of care, with CC determined by the treating physician according to local clinical practice. Data on GT-1 patients with CC or without CC (NC), treatment naive (TN) or treatment experienced (TE) [pegIFN+RBV p<1], who completed TAF for ≥8 weeks, were included. Patients with a history of decompensation, prior NSSA inhibitor exposure, treatment duration >12 weeks or addition of RBV were excluded.

Results: Overall, 5541 patients with HCV GT-1 were included. The median age was 52 years, 52.8% were male and GT distribution was as follows: 30% GT1, 30% GT2, 33% GT3, 6% GT4-6, 1% mixed or unknown GT. HCC was present in 1108 (20.7%) patients. 660 (12.4%) TE patients were included. 98.5% of patients with HCV GT-1 were included. Patients with current/historic IV drug use, treatment duration >12 weeks or addition of RBV were excluded.

Conclusion: Simplicity is key in reaching the WHO goals for HCV elimination. SOF/VEL for 12 weeks is a simple and highly effective regimen that cures HCV patients, irrespective of VCTE, treatment status or treatment history, with a manageable drug interaction profile, which will contribute to the implementation of test & treat strategies.
LIM Protein Ajuba Promotes Cancer Cell Proliferation and Survival in Hepatocellular Carcinoma


Methods: Ten human liver cancer cell lines and primary tumors were screened for Ajuba protein and mRNA expression. Its function was investigated by modulating protein levels with lentiviruses expressing shRNA targeted sequences or an overexpressing (OE) construct. The biological impact of Ajuba knockdown and OE transduced cells was tested in vitro and in vivo with various biological assays including a PCR Array, mass spectrometry and a 42-parameter panel for mass cytometry, and an in-vivo syngeneic mouse tumor model.

Results: Steady state levels of Ajuba mRNA in human liver cancer cell lines and primary tumors were significantly higher than in control liver tissue. Ajuba expression correlated with reduced life expectancy. Lentiviral transduction of HCC cells effectively knocked-down Ajuba protein levels resulting in a decrease of cell proliferation, migration, and colony formation, which coincided with a G2-phase cell cycle arrest. Using mass spectrometry and mass cytometry new protein interaction partners as well as pathways in which Ajuba is involved were identified. Using a syngeneic tumor model in C57Bl/6 mice, HCC with knocked-down Ajuba expression had a significantly reduced tumor volume compared to controls.

Conclusion: Ajuba appears to be central to HCC cell proliferation and knock down reduces tumor growth and cell survival.

Lysosomal compartment dysregulation as a treatment strategy for hepatocellular carcinoma


Methods: Lysosomal sequestration of anti-cancer compounds reduces drug availability at intracellular target sites, thereby limiting drug-sensitivity and inducing chemoresistance. For hepatocellular carcinoma (HCC), sorafenib (SF) is the first line systemic treatment as well as a simultaneous activator of autophagy-induced drug resistance. The purpose of this study is to elucidate how combination therapy with the FDA-approved photosensitizer verteporfin (vP) can potentiate the antitumor effect of SF, overcoming its acquired resistance mechanisms.

Results: HCC cell lines and patient-derived in vitro and in vivo preclinical models were used to identify the molecular mechanism of action of vP alone and in combination with SF.

Conclusion: Our data suggest that combination of lysosome-targeting compounds, such as vP, in combination with already approved chemotherapeutic agents could open a new avenue to overcome chemo-insensitivity caused by passive lysosomal sequestration of anti-cancer drugs in the context of HCC.
REGENERATE: A Phase 3 International, Placebo-Controlled Study Evaluating Obeticholic Acid Treatment for NASH
Zobair Younossi1, Vlad Ratziu3, Jean-François Dufour3, Leigh MacConnel1, Reshma Shringarpure4, Stephen Harrison1, Arun J. Sanyal1 on behalf of the REGENERATE Study Investigators


Background: This M18 pre-specified interim analysis of the ongoing Ph3 REGENERATE study evaluated the effect of OCA on liver histology in patients (pts) with biopsy-confirmed NASH.

Methods: Pts with NASH and fibrosis stages F2-F3 (ITT) were randomized to placebo (PBO), OCA 10mg or OCA 25mg QD. Primary endpoints were histologic improvement (≥1 stage) with no worsening of NASH, or NASH resolution with no worsening of liver fibrosis. The safety population included F1-3 pts (N=1968). Clinical outcomes will be evaluated at the end-of-study.

Results: The ITT population included 931 pts (PBO [n=311], OCA 10mg [n=312] or OCA 25mg [n=308]). The primary fibrosis endpoint was met by 11.9% PBO, 17.6% OCA 10mg (p=0.0446 vs PBO), and 23.1% OCA 25mg (p=0.0002 vs PBO) (ITT). The primary NASH endpoint was not statistically significant (ITT) (12.5% PBO, 14.7% OCA 10mg, 17.2% OCA 25mg) for both definitions (≥16 or >20 points).

Conclusions: OCA improved liver fibrosis, key histologic features of steatohepatitis and liver biochemistry, demonstrating consistent efficacy with an overall AE profile similar to previous studies.

Effects of Ustekinumab (UST) Induction Therapy on Endoscopic and Histologic Healing in Ulcerative Colitis
Colleen Marano1,2, Katherine Li1, Joshua R Friedman1, Hongyan Zhang2, Feifei Yang3, Brian G Feagan1, Laurent Peyrin-Biroulet1, Gert De Hertogh4
1)Janssen R&D, Spring House, USA; 2)Robarts Clinical Trials, Robarts Research Institute, Western University, London, Ontario, Canada; 3)Nancy University Hospital, Université de Lorraine, Nancy, France; 4)University Hospitals KU Leuven, Belgium

Background: UST is an effective therapy for moderate-to-severe UC, however data regarding histologic improvement and the combination of histologic and endoscopic improvement (i.e. histo-endoscopic mucosal healing) are unknown.

Methods: We evaluated the effects of UST on histologic and endoscopic activity in the UNIFI Phase 3 induction study of UST in moderate-to-severe UC (n=961). Colonic biopsies were collected from the distal colon at screening and Week 8. Endoscopic improvement (EI) was defined as a Mayo endoscopy score ≤1; histologic improvement (HI) comprised the absence of erosion or ulceration, absence of crypt destruction, and <5% of crypts with epithelial neutrophil infiltration. Histologic endoscopic mucosal healing was defined as both EI and HI.

Results: At Week 8, EI was achieved in 26.6% and 13.8% of subjects treated with UST and PBO, respectively (adjusted treatment difference, 12.8%; 95% confidence interval [CI], 7.9 to 17.8; p<0.001). HI was achieved in 36.8% and 21.9% of UST and PBO-treated subjects, respectively (adjusted treatment difference, 15.0%; 95% CI, 9.0 to 21.0; p<0.001). Histologic endoscopic mucosal healing (HEMH) was achieved in 19.3% and 8.9% of UST and PBO-treated subjects, respectively (adjusted treatment difference, 12.5%; 95% CI, 6.2 to 14.8; p<0.001). Similar rates of EI, HI, and HEMH were achieved following induction treatment with UST 130 mg or 6 mg/kg IV.

Conclusions: Among subjects with moderately-to-severely active UC, those receiving IV UST induction had higher rates of EI, HI, and HEMH than those receiving PBO.

Ustekinumab (UST) Induced Clinically Meaningful Improvement and Remission as Measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) in Patients with Moderate to Severe UC
Colleen Marano1,2, Bruce E Sands3,4, Chenglong Han5, Hongyan Zhang1,2, Jewel Johanss1, Philippe Szapary2, Rupert W Leong4, Silvio Danese1
1)Janssen R&D, Spring House, USA; 2)U of Miami, Miami, USA; 3)Concord and Macquarie University Hospitals, Sydney, Australia; 4)Humanitas Research Hospital, Milan, Italy

Background: The UNIFI studies evaluated the safety and efficacy of UST IV induction and SC maintenance in patients with moderately to severely active UC.

Methods: In the induction study, patients were randomized to a single IV dose of placebo (PBO, n=319), UST 130 mg (n=321), or UST 6 mg/kg (n=322). Patients who were in clinical response 8 weeks after receiving UST IV induction were eligible for the maintenance study and randomized to SC PBO (n=175), UST 90 mg q12w (n=172), or UST 90 mg q8w (n=176). An IBDQ score ≤170 indicated remission, and clinically meaningful changes were evaluated by two definitions (≥16 or >20 points).

Results: Eight weeks after IV induction, patients receiving UST reported significantly greater mean improvement in IBDQ scores, and greater proportions of patients achieved clinically meaningful improvements from baseline and IBDQ remission compared with PBO (p=0.001 for comparisons of each UST group vs PBO). Through 44 weeks of the maintenance study, mean IBDQ scores worsened in the PBO group, were maintained in the UST q12w group, and improved in the UST q8w group (p=0.001).

Conclusions: UST IV induction induced significantly greater improvements in IBDQ scores compared with PBO. In induction responders, significantly more patients who received UST SC maintenance sustained the improvements through Week 44.

Efficacy and Safety of Ustekinumab (UST) as Maintenance Therapy in Ulcerative Colitis: Week 44 Results from UNIFI
Colleen Marano1,2, William J Sandborn1,2, Bruce E Sands3,4, Remo Panaccione4,5, Christopher D O'Brien2,6, Hongyan Zhang1,2, Jewel Johanss1, Laurent Peyrin-Biroulet1, Gert van Asche8, Silvio Danese8, Stephan Targan8, Maria T Abreu9, Tadakazu Hisamatsu2, Philippe Szapary2
1)Janssen R&D, Spring House; 2)University of California San Diego, La Jolla; 3)Icahn School of Medicine at Mount Sinai, New York, NY; 4)U of Calgary, Calgary; 5)Nancy U Hospital, Nancy; 6)U of Leuven, Louvain; 7)Humanitas Research Hospital, Milan; 8)Cedars Sinai Medical Center, Los Angeles; 9)U of Miami Miller School of Medicine, Miami; 10)Kyorin U, Tokyo

Background: The study objective was to evaluate the safety and efficacy of SC UST maintenance therapy in UC patients (pts) in clinical response to a single IV induction dose of UST.

Methods: Phase 3, double-blind, randomized withdrawal study in pts with moderate-to-severe active UC who failed conventional or biologic therapy (including anti-TNF and/or vedolizumab) and were in clinical response 8 weeks after receiving a single IV UST induction dose. Primary population (523 pts) randomized 1:1:1:1 to placebo (PBO) SC, UST 90 mg SC q8w or q12w.

Results: Baseline demographics and UC disease characteristics were generally similar among treatment groups. Significantly more pts receiving UST q8w and q12w were in clinical remission at Wk 44 (43.8% and 38.4%) vs PBO pts (24.0%; p=0.001 and p=0.002). Similarly, significantly more UST pts achieved steroid-free remission and endoscopic improvement at Wk 44 as well as maintained clinical response through Wk 44, compared with placebo. The safety was consistent with the known safety profile of UST in CD.

Conclusions: Both UST maintenance regimens achieved clinical remission as well as secondary endpoints among pts with moderate to severe UC induced into clinical response with a single IV dose of UST. No new safety signals were observed.
Efficacy and Safety of Ustekinumab Through Week 16 in Patients with Moderate to Severe Ulcerative Colitis

Colleen Mariano(1), Silvio Danese(2), Bruce E Sands(3), Christopher D O’Brien(4), Hongyan Zhang(4), Jewel Johannes(4), Sheldon Sloan(4), James Izanec(1), Philippe Szapary(2), Rupert Leong(4), David Rowbotham(4), Stephan Targan(4), Gert Van Assche(4), Vartan Ascher(4)

(1)Janssen R&D, USA; (2)Humanitas Research Hospital, IT; (3)Icahn School of Medicine, USA; (4)Concord and Macquarie University (U) Hospitals, AU; (5)Auckland City Hospital, NZ; (6)Cedars Sinai Medical Center, USA; (7)U of Leuven, BE

Background: Efficacy and safety of ustekinumab (UST) induction therapy through Wk16 in patients (pts) with moderate-to-severe ulcerative colitis (UC) were evaluated.

Methods: Pts were randomized to an intravenous (IV) induction UST dose (130mg or ~6mg/kg) or PBO. Rates include pts who achieved the endpoint at Wk8 after initial IV UST induction and pts who achieved the endpoint at Wk16 following a blinded dose of UST 90mg SC at Wk8 after non-response at Wk8.

Results: 77.6% of pts (130mg: 75.6%, ~6mg/kg: 79.5%) randomized to UST achieved clinical response within 16 wks. At Wk8, 56.5% (130mg: 51.3%, ~6mg/kg: 61.8%) responded. Among Wk8 non-responders who received a SC dose, 59.7% (130mg: 60.6%, ~6mg/kg: 58.4%) were in clinical response at Wk16. Clinical remission was achieved by 15.8% (130mg: 19.7%, ~6mg/kg: 18.0%) within 16 wks. At Wk8, 15.6% (130mg: 15.6%, ~6mg/kg: 15.5%) were in clinical remission. Among Wk8 non-responders who received a SC dose, 9.4% (130mg: 9.8%, ~6mg/kg: 9.8%) achieved clinical remission at Wk16. Fewer pts with a history of biologic failure achieved clinical response and remission within 16 wks compared with non-biologic failure pts. The adverse event (AE) profile for patients who received a single UST IV dose and those with an additional UST SC dose at Wk8 were similar and consistent with the AE profile for PBO.

Conclusions: The data support continuing treatment with UST through at least one SC dose 8 wks after IV induction in pts with moderate-severe UC.

Efficacy of Ustekinumab (UST) in Moderate-Severe Ulcerative Colitis (UC) in Biologic Failure (BF) and Nonbiologic-Failure (NBF) Populations


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Background: UST was effective in therapy of moderate-severe UC. Here, efficacy in BF and NBF populations was evaluated.

Methods: Pts were randomized to an intravenous (IV) induction UST dose (130mg or ~6mg/kg), or PBO. Responders to UST IV induction entered maintenance and were randomized to SC 90mg UST (q12w or q16w), or PBO.

Results: Among BF pts, 98.8 % had failed ≥1 anti-TNF and 32.6% both anti-TNF and vedolizumab. In induction, for both BF and NBF pts, significantly more pts achieved clinical remission for UST vs PBO (BF: P<0.001 for both doses; NBF: P<0.005). Though treatment differences were generally similar between BF and NBF pts, they were consistently larger in BF pts. In maintenance, for BF and NBF pts, significantly more pts achieved clinical remission for UST q8w and q12w vs PBO (BF pts: P<0.001 and P=0.044; NBF pts: P=0.024 and P=0.020). More BF and NBF pts achieved each major secondary endpoint with UST vs PBO in both induction and maintenance. In BF pts, the efficacy of UST q8w was generally greater than UST q12w.

Conclusions: UST was effective for treatment of moderate-severe UC pts with and without a history of biologic failure.

Association between histological indices and ulcerative colitis (UC) activity measures among patients in the HICKORY (etrolizumab) open-label induction cohort


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Background: Cross-sectional studies in UC have shown an association between histologic and clinical measures of disease activity. Using open-label induction cohort data of HICKORY, we evaluated this correlation at end of induction.

Methods: Baseline and week 14 biopsies were scored using RHI and NHI, histologic outcomes assessed by neutrophil presence/absence. Pairwise associations were quantified by Spearman correlation and Cohen's kappa coefficients. ΔRHI and ΔNHI comparison determined presence of a minimal clinically important difference (MCID) in Mayo Clinic score (MCS; ΔMCS≥3).

Results: At week 14, 22%, 23% and 8% of 97 patients achieved neutrophilic inflammation resolution, endoscopic improvement (ES≥1) and remission (ES=0), respectively. ΔNHI and ΔRHI were highly correlated (r=0.91). There was little to no association between laboratory results and ΔNHI/ΔRHI/ΔES and a weak correlation between ΔNHI/ΔRHI and ΔES/rectal bleeding change and stool frequency. NHI, RHI and ES agreement with symptomatic outcomes was weak to moderate. Difference in the mean (ΔMCID<3) supports MCIDs of 1 (ΔNHI) and 9 (ΔRHI).

Conclusions: Analyses showed no association between changes in histologic and endoscopic score results, and weak to modest between histologic scores and symptoms at the end of induction.

Previously presented: Peyrin-Biroulet L et al. ECCO 2019

Disease activity in patients with inflammatory bowel disease correlates with the serum copper/zinc ratio

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Background: Zinc and copper are trace elements that play important roles during immune response and wound healing. Decreased levels of zinc, copper and the copper/zinc ratio (Cu/Zn ratio) are associated with systemic inflammation in inflammatory bowel disease (IBD). Here we investigate the correlation of serum zinc and copper in patients with IBD.

Methods: In this cross-sectional study 98 patients with Crohn’s disease (CD) and 56 with ulcerative colitis (UC) were prospectively enrolled. Disease activity parameters were compared to serum zinc, copper and Cu/Zn ratio.

Results: We have observed zinc insufficiency in 11.2% and 14.3%, copper insufficiency in 20.4%, and 7.1% of patients with CD and UC respectively. Anemia, hypoalbuminemia and increased fecal calprotectin (FC) as well as C-reactive protein (CRP) was found to be significantly frequent in zinc deficient patients with IBD. In contrast, copper deficient patients with IBD had significantly lower serum CRP values and a trend to lower FC. In multiple linear regression models, adjusted for age, gender and albumin serum CRP, significantly correlated with serum copper (p<0.001) and the Cu/Zn ratio in both CD and UC (p<0.001), but not with serum zinc levels. FC levels correlated only with the Cu/Zn ratio in patients with UC (p<0.038).

Conclusion: In patients with IBD, systemic inflammation influences inversely the serum zinc and copper levels. Consequently, the copper/zinc ratio will increase in patients with active disease.
amoebiasis has been reported in the literature to this date. Here we report a 50 year old man with a liver abscess due to infections before starting biological treatment and suggests being histological remission of Crohn’s disease. Termination of the anti-infective therapy showed endoscopic and examinations was negative. Follow up endoscopy 4 weeks after persistence of inflammatory changes in the ascending colon with requiring hospitalization colonoscopy was repeated and showed ustekinumab. Methods: All patients (n=10) who received laparoscopic liver resection by a new image guided surgery system with augmented 3D imaging in a university hospital were included for retrospective analysis. Digitally processed preoperative imaging (magnetic resonance imaging or computed tomography) was merged to the 3D laparoscopic image using a landmark-based registration technique. Intraoperative efficiency of the procedure was measured as time needed to achieve sufficient registration accuracy. Technical accuracy was reported as fiducial registration error (FRE). Clinical benefit was assessed trough a questionnaire which was completed by the primary surgeon after each operation. Resection quality and 30 day postoperative morbidity were reported as outcome parameters. Results: From January to March 2018, ten 3D laparoscopic liver resections of a total of 18 lesions were performed using the novel augmented reality system. The mean FRE of the last registration attempt was 9.2 mm (SD 2.8). Median time for registration was 8:50 min (range 1:31 – 23:56). Average operation time was 196 minutes (SD 43). The questionnaire revealed the ease of use of the system and the benefit for resection of vanishing lesions as convincing positive aspects, whereas image registration accuracy for resection guidance was consistently judged as too inaccurate. Histology reported complete resection in all retrieved lesions. No major complications (Clavien-Dindo ≥ IIIb) occurred during the 30 days follow-up, although 3 patients required intervention for biloma drainage postoperatively. Conclusions: Augmented reality in 3D laparoscopic liver surgery with landmark-based registration technique is feasible with only little impact on the intraoperative workflow. The benefit for detecting particularly vanishing lesions is high. For an additional benefit during the resection process, registration accuracy has to be improved and non-rigid registration algorithms will be required to address intraoperative anatomical deformation.

Ameliorative abdominal abscess after first infusion of ustekinumab in a patient with colonic Crohn’s disease manifestation
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Background: Severe infections and serious complications under therapy with ustekinumab are rare observations. To our knowledge, no case of amebiasis has been reported in the literature to this date.
Methods: Here we report a 50 year old man with a liver abscess due to entamoeba histolytica while on immunosuppressive therapy with ustekinumab.
Results: One year ago, the patient presented during a temporary working residency in Asia to the clinics with spondylarthritis and abdominal pain. A treatment with prednisone and subsequently with etanercept was initiated, but gastrointestinal symptoms remained refractory to both treatments. While on treatment with steroids and etanercept a ruptured appendicitis was surgically removed four months later. After a subsequent colonoscopy the patient was diagnosed with Crohn’s colitis affecting the coecum and the ascending colon and started on adalimumab. Due to persistence of abdominal symptoms with a flare requiring hospitalization colonoscopy was repeated and showed persistence of inflammatory changes in the ascending colon with discrete involvement of the rectum. Treatment was switched to ustekinumab. Eight weeks later the patient was admitted to the hospital for fever and severe abdominal pain. Imaging studies revealed an abscess formation in the liver. PCR of the aspirate was positive for amebiasis. Rapid response to treatment with metronidazole was observed. Retrospective analysis of the appendectomy specimen with H&E and PAS stain demonstrated amoebiasis, while PCR of histological specimens from colonicoscopic examinations was negative. Follow up endoscopy 4 weeks after termination of the anti-infective therapy showed endoscopic and histological remission of Crohn’s disease.
Conclusion: This case report emphasizes careful evaluation of patients for latent infections before starting biological treatment and suggests being watchful for serious infectious complications while on therapy.
Intraductal papillary neoplasia of the bile ducts - a rare diagnosis

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Background: Considered the hepatic equivalent of intraductal papillary mucinous neoplasm of the pancreas, intraductal papillary neoplasms of the bile duct (IPMN) are however frequently associated with cholangiocarcinoma. We present the short-term outcome of a small retrospective patient series.

Methods: Analysis of all patients treated for IPNB or cholangiocarcinoma originating from IPNB (CIPNB) in our institution from 2005 to 2018. Treatment: surgical or endoscopic resection. Follow-up: according to multidisciplinary tumorboard recommendation, MRI/CT after 6 to 12 months or endoscopies.

Results: 5 cases of IPNB and 5 cases of CIPNB are included in this report. 9/10 patients were female, median age was 64.5 years (range 53-82). For patients with IPNB, 2 left hepatectomies, 2 cholecystectomies and one endoscopic resection were performed. This patient had locoregional recurrence, treated by a second endoscopic resection. One patient had progression to cholangiocarcinoma and underwent bisectional liver resection followed by palliative gemcitabin. All patients with CIPNB underwent extended hepatic resection. One patient died postoperatively due to acute liver failure. One patient presented with recurrence in segment VIII/V after 84 month. Duration of follow-up ranged from 1 to 144 months.

Conclusion: IPNB diagnosis is rare, which could be attributed to delayed detection in oligosymptomatic patients. Early diagnosis and radical resection are warranted to prevent progression to malignant disease, which significantly reduces survival.

Publication of surgery specific outcomes as quality indicator - time to get involved?

R. Galli, R. Rosenberg. Kantonsspital Baselland

Background
Public reporting of surgery specific outcomes is controversial. Although risk adjustment is necessary for making meaningful comparisons between providers, published data rarely account for patient severity. Mortality after resection for diverticular disease with abscess or perforation is one of the available data on the register published by the Bundesamt für Gesundheit (BAG). The purpose of this work was to analyse patient characteristics and outcome for this category in our institution.

Methods
Patients were identified on the basis of the coding system used by the BAG from our hospital records.

Results
A total of 126 consecutive patients were analysed. Type of diverticular disease according to CDD was the following: 16 CDD 2a, 39 CDD 2b, 39 CDD 2c1, 6 CDD 2c2, 21 CDD 3b, 5 CDD 3c. 32 patients underwent elective procedures, 47 had emergency colectomy, while the remaining 47 had surgery during the same scheduled procedure. 48.4% of patients presented ASA Classification ≥ 3. Predicted morbidity was 46.02% and predicted mortality was 6.16%. Overall mortality was 3.97% and rate of severe complications was 10.3%.

Conclusions:
Codes used in the register “Quality indicators for Swiss acute hospitals” refer to a heterogeneous group of patients with a wide variability in terms of risk factors. Adjustment considering mode of surgery as well as comorbidities should be considered. Furthermore, hospitals should be aware that data provided to the BAG may not reflect the correct diagnosis leading to a misinterpretation of the results.

Compliance to the Surgical Safety Checklist over time in late and early adopters

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Aims: To compare the compliance of the Surgical Safety Checklist (SSC) in two groups of users: early (Group A) and late (Group B) adopters, and to detect change over time.

Method: Observational study. We collected all SSC protocols in one calendar month period and repeated collection for another month, 8 months later. Analysis was then performed to compare the compliance in different groups and over time.

Results: In total, 824 SSC protocols were collected (348 in Group A and 476 in Group B). There was no statistical difference in the overall compliance between the two groups (96.3% and 94.3%, respectively; p=0.201) and between elective and emergency cases (94.4% and 96.6%, respectively; p=0.148). Equally, there was no significant change in compliance over time in Group A (95.7% vs. 96.9%, p=0.551). In Group B, however, there was a trend to an improved compliance over time (92.5% vs. 96.7%, p=0.052). Compliance to the SSC was 97.6% for internally employed surgeons and 85.5% for consulting surgeons, respectively (p<0.001).

Conclusion: The Surgical Safety Checklist can successfully be implemented for elective cases as well as for emergency operations using a step-wise approach. While early adopters maintain a high level of compliance to the SSC, late adopters still improve their compliance over time. However, consulting surgeons show a significantly lower compliance than internally employed surgeons. This fact has to be specifically taken into account for any implementation of the SSC in this setting.

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Background: Left hepatectomy can be performed safely laparoscopically in experienced hands for tumours that do not invade hilar structures or the middle hepatic vein. Proximity of a liver lesion to such structures represents an additional challenge for its laparoscopic removal. This video shows a laparoscopic extended left hepatectomy with the resection of a giant haemangioma in the left liver that displaces the left portal vein (LPV) and invades the middle hepatic vein (MHV).

Methods: A 59 year old woman with a giant haemangioma and abdominal pain was referred for surgical treatment. The laparoscopic liver resection was performed using a 3D optical system. It began with hilar dissection, division of the left hepatic artery and identification of the LPV. Dissection of the left-sided hilar structures allowed a clear visualisation and control of the compressed LPV. After division of the vessel, the left liver was completely mobilised and parenchymal transection was performed to the right of the MHV under ultrasound guidance using and ultrasonic cavitational device, clips and bipolar forceps as well as an intermittent occlusion of ligamentary vessels. A vascular stapler was used to transect the left and middle hepatic veins close to the confluence with the vena cava. The surgical specimen was retrieved through an umbilical incision.

Results: Operative time was 359 minutes with a total blood loss of 300ml. The recovery was uneventful and the patient was discharged on the fifth postoperative day. Final pathology showed a haemangioma with tumour free margins.

Conclusions: Laparoscopic resection of tumours in the left liver that invade hilar structures or the middle hepatic vein is feasible and can be performed safely. Standardized advanced laparoscopic techniques are essential for the success of this complex procedure in order to control bleeding and preserve an optimal view during vascular dissection and parenchymal transection.

The other liver metastasis with a crucial impact on the prognosis

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Background
Liver metastasis are a dismal sign for patients with colorectal cancer (CRC). However, not every hepatic lesion in a patient with CRC represent metastatic disease.

Methods
We report two patients, who have been operated for CRC and pre-and intraoperatively liver metastasis were radiologically suspected.

Results
An 83-year-old male and 76-year-old female patient underwent surgery for CRC in the colon ascendens and sigmoid, respectively. In the female patient, preoperative CT scan showed a hepatic lesion of 10mm in segment VI. In the male patient, preoperative CT scan revealed no metastatic lesion but intraoperative ultrasound showed a 10mm lesion in segment V. Both lesions were surgically removed and subsequent histology revealed the characteristic parasitic membrane of Echinococcus species. The diagnosis was further confirmed by molecular PCR analysis. Based on tumor stage II of the CRC, none of the patients received chemotherapy. The female patient, however, received an anthelmintic therapy for 2 years and both patients are free of disease at a 2 and 3 years of follow up, respectively.

Conclusion
Hepatic metastasis significantly worsens the prognosis of patient with CRC, decreasing the 5-year survival probability from 85% in stage II to less than 10% in stage IV. However, not all hepatic lesions represent metastatic disease and other uncommon etiologies, including parasitic lesion as Echinococcus cysts, should be excluded and intraoperative ultrasound is an important method to detect minor lesions.

Colorectal cancer associated with schistosomiasis - a case report

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Background
It is well known that there is a higher risk for urothelial carcinoma in people with a schistosomiasis infection. A causal relationship between schistosomiasis and colorectal cancer has long been suggested in the literature, but it is not uniformly accepted. We report on a female patient with colorectal cancer coexisting with a schistosomiasis infection.

Methods
Case report including Images from the histopathological analysis with vital schistosomes and some calcified schistosoma ova. A review of the literature was made.

Results
Considerable evidence supports an etiological link between Schistosoma japonicum and colorectal cancer in the Far East. Chronic inflammation and epithelial proliferation due to intestinal schistosomiasis may be a promoting factor for carcinogenesis. Our patient originally came from Eritrea where Schistosoma mansoni is endemic. The available data regarding the role of Schistosoma mansoni in colorectal carcinogenesis are conflicting and most often do not show causality.

Conclusions
There is a possible role for chronic schistosomiasis in promoting colorectal carcinogenesis. Further epidemiological studies are needed to investigate the cause and effect relationship between S. mansoni and colorectal malignancy.

Role of PKM2 in macrophage polarization during liver regeneration.

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Introduction: The pyruvate kinases (PKs) are a group of enzymes responsible for the last and step of the glycolytic pathway. The PKM2 isozyme is found mostly in proliferating cells such as cancer and stem cells, as well as immune cells. In macrophages, the polymerization of PKM2 has been shown to change depending on their polarization state. The tetrameric protein complex is enzymatically active in the cytoplasm and the nuclear dimeric complex acts as a transcriptional activator via binding with HIF-1alpha. ADD a sentence to state purpose of the study.

Methods: Liver regeneration was studied using a 60% partial hepatectomy (PH) model in C57Bl/6 mice. Regeneration was assessed by evaluating liver to body weight ratio, immunohistochemistry and mRNA expression of pro-proliferative genes (birc5, cyclin b) 4/8h post-PH. PKM mRNA levels were evaluated in liver tissue by qPCR at various time points post-PH. PKM2 inhibition was realized by treating the mice with shikonin or adenosine delivering shPKM2. Identification of PKM2 positive cells was compassed by immunohistochemistry and mass cytometry. The polymerization state of macrophages was evaluated using mass cytometry and native western blotting.

Results: PKM2 mRNA level were elevated as early as 3h PH and remained elevated during the regenerative process. Inhibition of PKM2 by chemical and shRNA lead to decrease in liver regeneration capacity post PH. Analysis of PKM2 expression by immunohistochemistry revealed its co-localization with the macrophage marker F4/80. Analysis of macrophage polarization at different time points across liver regeneration process revealed a shift in macrophage function from M1 to M2 between 6 and 12h PH that correlates with PKM2 dimeric to tetrameric polymerization change.

Conclusion: We showed that PKM2 is increased in macrophages shortly after PH and is necessary for liver regeneration. In conclusion, our data demonstrates that changes in macrophage polarization together with PKM2 polymerization support hepatic regeneration following PH.
Robot-assisted gastric GIST resection: a single center experience

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Abstract

Introduction
Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors, representing 1-3% of all gastrointestinal cancer. Surgical resection is the only curative treatment. Minimally invasive approaches such as laparoscopic and robotic-assisted resections for gastric GIST have proved to be oncologically and surgically safe. We report here a case series of robot-assisted gastric GIST resections in our center.

Study design
We performed a retrospective analysis of all gastric GIST resected between 2007 and 2018 at the Geneva University Hospital, Switzerland.

Results
19 patients underwent robot-assisted gastric resection for GIST, 12 females and 7 males. Median age was 59 years (range 38-79) and median BMI was 27.5kg/m² (range, 18.6-41.3). Median tumor size was of 5 cm (range, 1.8-9). 13 were on the posterior wall and 7 were proximal (fundus or cardia). All tumors were completely resected (R0). We noted one conversion to open resection because of a positive margin requiring a radical resection. Median operative time was 157 minutes (range, 90-436). We reported no postoperative complications within 90 days after surgery. The median follow-up was 8 months (range, 1-115) and we reported no oncological recurrence.

Conclusions
Our case series confirm that robotic-assisted resection is safe and offers the same oncological results as the other approaches (open and laparoscopically) for gastric GIST.

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