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Swiss Society of Endoscopy Nurses and Associates (SVEP-ASPE)**  
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### Case report: Resection of a large circumferential rectal adenoma with a novel resection system (EndoRotor)

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**Background:** EndoRotor is a non-thermal, automated mechanical endoscopic resection system designed to remove large areas of mucosal tissue in the GI tract. Suction is applied to aspirate and cut the mucosa in small pieces into a catheter-like device, resulting in a "shaving" resection. The specimens are automatically transported into a collector for histological evaluation.

**Methods:** We present a 63-year-old female suffering from chronic diarrhea. Colonoscopy showed a flat circumferential adenomatous polyp extending over 3-4 cm in the mid part of the rectum. Following perforation of the sigmoid at the initial colonoscopy the patient underwent surgical revision. Due to severe malnutrition and intraoperative difficulties a definitive descendentostoma was created. As the patient was judged unfit for further surgery and the rectal adenoma was by no means amenable to established resection techniques such as EMR or ESD, this was an indication for an EndoRotor resection.

**Results:** Adenoma resection was primarily judged complete. Procedure time was 40 minutes. No major complications, i.e. no bleeding or perforation occurred. Histological workup revealed adenoma without high grade dysplasia. Surveillance endoscopy after 2 months only showed minimal residual adenoma, again treated with EndoRotor resection. Furthermore a clinically irrelevant stenosis at the resection site was noted.

**Conclusion:** The EndoRotor system is an experimental method that appears to be feasible and efficacious in resecting large flat rectal adenomas not amenable to established polypectomy techniques or surgery. The most important limitation relates to completeness of resection; therefore its use is restricted to benign lesions. Histological processing protocols are still under evaluation. Prospective studies will be needed to further evaluate this concept.

### Transoral outlet reduction (TORe) partially reverses weight regain after bariatric Roux-en-Y gastric bypass (RYGB). First clinical experience from a tertiary referral center.

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**Background:** Bariatric surgery is effective in significantly reducing overweight. However the frequent phenomenon of secondary weight gain in the further postoperative course remains a problem. Progressive dilatation of the gastrojejunal anastomosis may contribute to the loss of efficacy of RYGB. Recently a novel endoscopic technique called TORe has been introduced. Full-thickness TORe by an endoscopic suturing system (Overstitch, Apollo Endosurgery, USA) enables the endoscopist to reduce the width of the gastrojejunal anastomosis to a diameter of 8-9 mm. Thereby an adequate sensation of postprandial early satiety may be restored, facilitating consecutive weight loss. We report our first clinical experience with TORe procedures.

**Methods:** Retrospective analysis of 22 consecutive patients suffering from secondary weight gain after bariatric RYGB, treated with full-thickness TORe from 07/2015 through 06/2016. All patients underwent an interdisciplinary evaluation before the intervention.

**Results:** At TORe the mean weight was 98.3 kg (representing a mean secondary weight gain of 18.7 kg). At 1 month post TORe weight loss was 5.8 kg, at 3 months 3.3 kg, at 6 months 4.0 kg and after one year 2.0 kg. One operator-related perforation occurred, which was immediately and successfully closed by an OTSC, otherwise no complications were noted.

**Conclusion:** TORe is effective in at least arresting or partially reversing secondary weight gain after bariatric RYGB, as observed over a follow-up period of 12 months. The procedure appeared to be safe. Further prospective long-term studies are needed to evaluate this technique.

O1

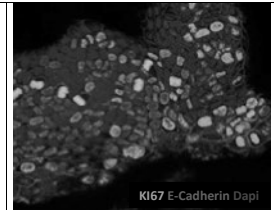
### Gallbladder Derived Stem Cells: A New Chance for Cell Therapy in the Liver

Felix Baier (1), Adrian Keogh (1), Natalia Lugli (2), Thanos Halazonetis (2), Daniel Candinas (1), Deborah Stroka (1)

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**Background** Liver disease related mortality has a growing incidence worldwide. Cell therapy has been proposed as an alternative to overcome the major drawbacks of the current treatment options. We recently reported the Gallbladder as a potent source of adult hepatic stem cells, which can be expanded in the form of organoids. As prerequisite for successful engraftment and function in the recipient livers, we now explore the *in vitro* differentiation potential of these cells towards the hepatocyte lineage.

**Methods** Adult stem cells are isolated from C57BL/6J mouse gallbladders and expanded in Matrigel. Expansion is based on growth factors including Wnt activation and TGF-beta inhibition. Differentiation conditions include epigenetic modulation, Notch inhibition, synthetic Hepatocyte growth factor or Oncostatin M.



**Results** Modification of the organoid culture medium with differentiation promoting factors induced hexagonal cell shapes, multi-nucleation, decreased proliferation, upregulation of hepatocyte lineage markers (HNF4a, Cyp3a11, AFP, Pparg) and downregulation of stem cell markers (CD44, Sox9).

**Conclusions** Our current culture protocol allows a differentiation of the organoids towards a hepatoblast-like state. Ongoing refinements of the differentiation media formulation may allow the formation of committed hepatocyte progenitors in the future. The differentiated cells may then be applied in a mouse model of liver failure.

O2

### Evaluation of Controlled Attenuated Parameter (CAP) for Assessment of Liver Steatosis in an Unselected Population: a Single Center Real Life Experience

Stephan Baumeler<sup>1</sup>, Irina Bergamin<sup>1</sup>, Björn Becker<sup>1</sup>, Wolfram Jochum<sup>2</sup>, Jörg Neuweiler<sup>2</sup>, Rafael Sauter<sup>3</sup>, David Semela<sup>1</sup>

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#### Abstract

**Background & Aims:** Controlled attenuated parameter (CAP) is a new parameter to assess steatosis of the liver, which is obtained together with elastography. Our aim was to assess the performance of CAP in an unselected population with different liver diseases and define cut off values.

**Methods:** Between March 2015 and August 2016, all patients who underwent liver biopsy for any reason were screened to meet the inclusion criteria. The CAP measurement had to be done within the same week as the biopsy and quality standards for CAP measurement were defined. Liver biopsies were classified according to the following degrees of steatosis: S0 <5%; S1 5-33%; S2 34-66%; S3 > 66%. In addition data about fibrosis, inflammatory activity, body mass index (BMI) and liver disease were recorded.

**Results:** 290 patients were screened and 224 (77.2%) were included. 146 (65.2%) were male. Steatosis grades were distributed as follows S0 n=85 (37.9%), S1 n=82 (36.6%), S2 n=33 (14.7%), S3 n=24(10.7%). Mean BMI was 26.8kg/m<sup>2</sup> (SD 5.0), S0 24.9kg/m<sup>2</sup>, for S1 26.5kg/m<sup>2</sup>, S2 27.3kg/m<sup>2</sup> and for S3 32.5kg/m<sup>2</sup>. The steatosis- groups S0 to S3 differed significantly with respect to CAP. The AUC for S0 vs S1-S3 was 0.78, for S0/1 vs S2/3 0.83 and for S0,1,2 vs S3 0.82. Cut-off values for maximal Youden index were 258.5dB/m for S0 vs S1-3, 282.5dB/m for S0/1 vs S2/3 and 307.5dB/m for S0-2 vs S3.

**Conclusions:** CAP shows strong association to steatosis grading. Especially the groups NAFLD/NASH vs other liver diseases and the groups BMI <> 25kg/m<sup>2</sup> showed highly significant different CAP values.

O3

O4



Abstract - Video-Presentation

### Endoscopic removal of foreign bodies

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Gastrointestinal foreign bodies are a recurring challenge for endoscopist and emergency physician. This includes either endoscopically inserted foreign bodies (e.g., ingrown stents) as well as foreign body ingestion in borderline personality or impacted foreign bodies in case of awkward sexual practice. Depending on the localization, size, material and surface condition of the foreign body, this leads to a vital threat to the patient. The removal of the foreign body itself can also lead to injuries and complications itself. For this reason, the technique and the used additional technical devices must be chosen carefully for the best possible outcome.

In this video presentation we show three different foreign bodies and their removal with each technique adapted to the situation.

### VIDEO CASE

**Title: Cholangioscopy of bile duct stenosis: Stone or tumor?**

**Authors:** Bertolini Reto (1), Peter Ueli (1), Schadde Erik (2), Gubler Christoph (1)

**Affiliations:** 1.) Division of Gastroenterology and Hepatology, Kantonsspital Winterthur, Brauerstrasse 15, 8401 Winterthur; 2.) Department of Surgery, Kantonsspital Winterthur, Brauerstrasse 15, 8401 Winterthur

**Duration of the video:** 6-7 min

**Abstract:** We present a cholangioscopy video of a 50-year-old woman who suffered from recurrent right upper pain. In MRI/MRCP, left-sided dilated intrahepatic bile ducts, focal stenosis of the left hepatic duct of unknown reason and left sided portal vein thrombosis were detected. In 18F-FDG PET/CT, a highly metabolic active lesion in the left hepatic lobe without distant metastasis was found. Differential diagnoses were intrahepatic gallstones, parasites or intraductal tumor. She underwent endoscopic retrograde cholangiography (ERC) with sphincterotomy and cholangioscopy. Multiple gallstones with stenosis within the common bile duct up to the left hepatic duct were seen under direct vision. A cholangioscopy-guided electrohydraulic lithotripsy was successfully performed, opening a completely obstructed segmental bile duct. Afterwards the intrahepatic left sided bile ducts could be inspected cholangioscopically, where slight decubital ulceration but no tumor was seen.

05

### Disincentive and motivating factors for colorectal cancer screening in the Swiss population

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**Background:** Colorectal cancer screening (CRCS) has been shown to reduce incidence and cancer-related mortality. Despite this, the acceptance of CRCS remains low for reasons that are largely unexplored. In this study, we explored disincentive and motivating factors for CRCS uptake in the rural and urban Swiss population. **Methods:** We conducted a qualitative study using psychologist-guided focus groups (2 in rural, 2 in urban regions, 7-8 participants each), during which lay people discussed predetermined CRCS-related topics in a semi-structured way. Thirty participants were recruited (14 females, 16 males, 50-74 years of age). The thematic analysis was carried out using ATLAS.ti software. **Results:** We generated the codebook containing 477 codes concerning facts and opinions of participants. The most frequently mentioned disincentive for CRCS was fear (69 out of 339 times disincentive factors were mentioned). Women were more likely to experience generalized fear, while men were more likely to fear various CRCS-associated aspects. The information about CRC incidence and mortality induced fear in many participants. Knowledge about different CRCS possibilities and benefits was a major motivating factor. Ineffective physician-patient communication discouraged screening in women, whilst men cited busy lifestyle as reason for avoiding CRCS. Although confidence in their physician was a motivating factor for CRCS, many participants did not get a recommendation to undergo CRCS. Lack of faith in mainstream medicine diminished participants' interest in CRCS. Participants were more likely to undergo CRCS, if they experienced abdominal complaints. Opinions did not differ between the urban and rural regions. **Conclusions:** Reducing fear of CRCS by emphasizing its benefits and actively recommending CRCS may lead to its better acceptance in at-risk Swiss population. Encouraging the individuals to undergo CRCS in the absence of complaints remains a challenge.

07

06

### Autologous differentiation of liver derived iPSC into hepatocyte-like cells.

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 2. Developmental & Molecular Pathways - Molecular Profiling; Novartis Institute for Biomedical Research, Basel (CH).  
 3. University of Basel – University Hospital Basel; Department of Biomedicine, Cancer Immunotherapy group, Basel (CH).  
 4. University Hospital Basel; Division of Gastroenterology and Hepatology, Basel (CH).

#### Background:

Studying liver diseases is still hampered by the lack of suitable *in vitro* models accurately reflecting liver functions. Besides primary hepatocytes, hepatocyte-like cells (HLCs) differentiated from induced pluripotent stem cells (iPSCs) have emerged as promising models. Nevertheless, incomplete HLC differentiation remains a challenge. It has been suggested that iPSC could carry-on a tissue of origin dependent expression memory, and that the genetic background of the iPSC donor could influence iPSC differentiation into different cell types. Here, we investigated the influence of the tissue of origin on HLC differentiation.

#### Methods:

Human primary liver cells (hPLCs) were expanded from liver needle biopsies and reprogrammed into liver-iPSCs (Li-iPSCs). The pluripotency of iPSCs was then confirmed *in vitro* and *in vivo*.

Li-iPSCs as well as fibroblast derived iPSCs (Fi-iPSCs) were differentiated into HLCs using standard differentiation protocols. Finally, we compared Li-iPSCs and Fi-iPSCs and the HLCs derived from them at the protein, functional and transcriptional level.

#### Results:

We show for the first time that HPLCs can be reprogrammed into Li-iPSCs that allow for the differentiation of HLCs. Profiling analysis showed that Li-iPSCs indeed retain a liver specific transcriptional footprint compared to Fi-iPSCs. Furthermore, the liver-specific gene expression pattern that was lost during the reprogramming of the Li-iPSCs, was partially recovered in Li-HLCs after differentiation. Ultimately we could identify the patient genetic background as the major driver of the gene expression variance in HLCs.

#### Conclusions:

Our results suggest that the tissue of origin for iPSC derivation is not the major determining factor for the HLC phenotype. Thus, Li-HLCs may serve as a tool for personalized medicine, as their transcriptional profile seems to be primarily determined by the patient background.

08

### Exosomal biomarkers to diagnose and monitor pancreatic ductal adenocarcinoma

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<sup>2</sup> Department of Clinical Research, Urology, University of Bern

**Background:** Pancreatic ductal adenocarcinoma (PDAC) is associated with poor prognosis and few therapeutic options. However, much hope is placed in new biomarkers allowing earlier cancer detection and treatment. We developed first a straightforward isolation protocol for plasma exosomes and we evaluated recently discovered exosomal biomarkers for the diagnosis and monitoring of pancreatic cancer.

**Methods:** Plasma samples from PDAC patients were taken before, during and after duodenopancreatectomy and were compared to healthy donors. Exosomes were isolated using size exclusion chromatography, filtered through a 0.22µm filter and ultracentrifuged overnight at 220'000g at 4°C. Size distribution and concentration of microparticles were assessed using NanoSight NS300. Contamination with plasma proteins was assessed using albumin ELISA. PDAC exosomes protein markers glypican-1 (GPC-1) and macrophage migration inhibitory factor (MIF) were assessed by immunoblot.

**Results:** Using the novel protocol, isolation of plasma exosomes was possible with high yield and low plasma proteins contamination. In our data so far, we identified higher concentration of smaller plasma exosomes in patients diagnosed with PDAC compared to healthy controls. In addition, we identified higher levels of GPC-1 and MIF on plasma exosomes of cancer patients compared to healthy controls.

**Conclusion:** After development of an efficient protocol for plasma exosomes isolation, we plan to assess temporal changes of PDAC exosomal markers, including protein markers and miRNAs, before, during and after pancreatic surgery.

O9

### Combined Liver and Lung Transplantation in Geneva University Hospital

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**Background:** Combined liver and lung transplantation is therapeutic option for patients with coexisting lung and liver disease. However, it is performed in few centers and information regarding the management and the outcome with this procedure is limited.

**Methods:** the data of 7 patients who underwent simultaneous liver and lung transplantation in Geneva and Lausanne University Hospitals (Centre Romand Universitaire de Transplantation) from 1999 to 2015 were retrospectively reviewed.

**Results:** Pulmonary indications were cystic fibrosis (n=5), α1 antitrypsin deficiency (n=1) and pulmonary fibrosis (n=1). Liver indications were cystic fibrosis (n=5), α1 antitrypsin deficiency (n=1) and hepatitis C (n=1). At pre-transplantation evaluation, median predicted FEV1 was 24%. Two patients had severe pulmonary hypertension (mean PAP > 50 mm Hg). All patients had cirrhosis and symptomatic portal hypertension. Median (range) donor age was 26 (9-49) years. Median pulmonary and liver cold ischemic time were 4.3 (2-7) and 10.3 (9-12.5) hours, respectively. Early postoperative death occurred at day 14 in one patient because of liver necrosis related to refractory pulmonary hypertension. Another patient died after 9 months because of infection. Median (range) overall survival was 765 (14-4901) days. All patients who had transplantation after year 2000 are still alive.

**Conclusion:** These results suggest that combined liver and lung transplantation is a good therapeutic option if carefully selected patients and donors.

O11

### Treatment of esophageal perforation by Eso-sponge®: first year experience in a Swiss university center.

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**Background:** Esophageal perforation is associated with high mortality and morbidity. Endoscopic vacuum therapy by using polyurethane sponges was first described in 2007 in anastomotic leakages and has become an alternative to self-expanding stent placement or surgery. We describe here our first year experience following the commercialization of the Eso-Sponge® set in Switzerland in April 2016.

**Methods:** We treated three cases between November 2016 and January 2017. The first case, a 71-year-old Child Pugh C cirrhotic male, showed a reflux-induced ulcer perforation of the distal esophagus with right pleural empyema. The second case, a 55-year-old male with chronic alcohol consumption, suffered from a subacute Boerhaave syndrome of the distal esophagus with esophago-pleural fistulisation and left pleural empyema. The third case, a 74-year-old male with known chronic non neoplastic ulcer on long segment Barrett's esophagus (Prague classification C14M14), presented without macroscopic ulcer perforation but with pneumomediastinum and right hydro-pneumothorax. All three cases were treated with Eso-sponge® (changed every 3-5 days; median 4,5) and pleural drainage. **Results:** Total closure of the perforation cavity was achieved in the first case by intracavitary with subsequent intraluminal Eso-sponge® treatment for 44 days in total. The second case required transthoracic esophagectomy with cervical esophagectomy due to persistent sepsis despite 4 days of intracavitary Eso-sponge® treatment and pleural drainage. The last patient resolved pneumomediastinum after 10 days of pre-emptive intraluminal Eso-sponge® treatment. No mortality was observed at follow-up up to 6 months.

**Conclusions:** Eso-sponge® seems an effective and secure treatment option for esophageal perforation, especially in patients at high risk of surgical mortality.

O10

### Efficacy and safety of linaclotide in the treatment of IBS-C from a real-world observational Swiss study

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**Background:** Linaclotide (LIN) has been approved by the BAG for moderate-to-severe IBS-C in adults. This study assessed real-world LIN efficacy and tolerability in Swiss patients (pts).

**Methods:** Data were collected from adults with moderate-to-severe IBS-C at treatment start (LIN 290 µg/d) and ~4 months after start. Pts rated bowel movements (BMs) per week; stool consistency (qualitative); severity of abdominal pain and bloating (11-point scale). Tolerability was assessed by adverse events (AEs) and by the physician (qualitative). **Results:** Data from 52 pts showed mean age: 49 years (range: 19–77); mean BMI: 23 kg/m<sup>2</sup>; 77% (n=40) were female; 60% (n=31) had moderate IBS-C. 60% (n=31) were prescribed LIN due to low efficacy of prior therapy. 94% (n=49) had prior IBS-C therapy; laxatives (79%, n=41) and dietary fibres (69%, n=36) were most frequent. 88% (n=45) had overall improvement in IBS-C symptoms from start to 4 months. BMs per week, severity/frequency of bloating and abdominal pain were improved (Table). Pts had normal stool consistency 10% (n=5) and no abdominal bloating 6% (n=3) at start and 48% (n=24) and 12% (n=6), respectively, at 4 months. 23% of pts (n=12) reported 15 AEs, with diarrhoea the most common (15%, n=8) and 6 pts discontinuing treatment. No AE was serious. Physicians assessed tolerability as excellent/good in 71% of pts. **Conclusions:** LIN was well tolerated and reduced IBS-C symptoms in the majority of pts treated in clinical practice.

Symptom, mean (SD)	Baseline	~Month 4	p value
BMs per week	2.10 (1.39)	4.69 (1.63)	<0.0001
Abdominal pain intensity	5.43 (2.72)	2.53 (2.03)	<0.0001
Bloating intensity	5.75 (2.64)	2.98 (2.24)	<0.0001
Bloating frequency	5.10 (2.09)	2.83 (2.38)	<0.0001

O12

### The Swiss HCV Advisor App - A web-based mobile application to identify suitable treatments with direct antiviral agents for chronic hepatitis C infection

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#### Background and Aims:

With the rapid development of new direct antiviral agents (DAA) for the management of chronic hepatitis C and their complex combinations depending on individual baseline factors and health care policy limitations, it is challenging for practitioners to quickly access up-to-date treatment recommendations during clinical decision making.

Our aim was to develop a clinical decision-oriented, user-friendly and free smartphone application (the Swiss HCV Advisor App) to help clinicians adequately select a specific DAA regimen according to viral characteristics and host parameters in accordance with national guidelines, drug approval status and reimbursement policy as well as recognition of potential interactions and side effects, that runs on web browsers, mobile platforms (iOS, Android) and desktops.

#### Methods:

App development was separated into development of the user interface and the selection algorithms (using the Ionic Framework), and the development of a SQL-Database, which can be easily modified by non-IT-specialists.

After entering viral load and genotype, known NS5a polymorphisms, presence of extrahepatic manifestations, degree of fibrosis, response to a previous interferon-based therapy, patients weight and optional input such as concomitant drug therapy or renal function, the user receives a list of suitable DAA regimens (dose, duration, expected individual response rate based on phase-3-studies, side effects, possible interactions, approval and reimbursement status) including country specific pricing. The Swiss HCV Advisor App was reviewed by the authors of the national guideline and beta tested by members of the Swiss hepatology (SASL) and infectology societies (SSID).

#### Results:

The Swiss HCV Advisor App adequately reflects treatment recommendations provided by the national guideline in individual patients and provides additional information on drug interactions and an appointment calculator. It is available in both the App Store and Google Play Store, and has the capability to use other country- or society-specific databases. Users rated access to treatment information via the Swiss HCV Advisor App faster, more specific and detailed compared to web published guidelines.

#### Conclusions:

Web-based mobile applications have advantages compared to conventional publications due to easy access, allowing individual „shared decision making“. Modern communication technologies such as the Swiss HCV Advisor App support clinical practitioners to adequately select suitable treatment regimens and national societies to provide up-to-date recommendations for the management of chronic hepatitis C.

O13

### gs-MELD score: an integrative transcriptomic and clinical predictor of survival in severe alcoholic hepatitis

O15

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**Background and Aims:** Severe alcoholic hepatitis (AH) confers a high risk of short-term mortality and corticosteroids are the only treatment that reproducibly provide short-term survival benefits. Performance and utility of existing pre-treatment clinical scores is still limited. We aimed to develop a prognostic score of short-term survival, integrating pre-treatment molecular and clinical variables before initiation of corticosteroids.

**Methods:** Gene expression profiles of fixed liver biopsy samples obtained for histological diagnosis of severe AH and clinical variables were assessed in one derivation and two validation cohorts. The primary endpoint was survival without death or liver transplantation at 90 and 180 days after corticosteroids initiation.

**Results:** A prognostic score, integrating a 123-gene signature and the model for end-stage liver disease (gs-MELD score), was defined in the derivation cohort (n=71), and identified poor- and good-prognosis patients at 90 days (event-free survival rates of 32% vs. 76%, respectively, p<0.001) and 180 days (26% vs. 65%, respectively, p<0.001). In validation cohort 1 (n=48), the score similarly discriminated poor- and good-prognosis patients at 90 (43%, [95% CI, 26%-70%] vs. 96% [95% CI, 89%-100%] p<0.001), and 180 days (34% [95% CI, 18%-61%] vs. 84% [95% CI, 72%-100%], p<0.001). The time-dependent area under the ROC curve was 0.86 (95% CI, 0.73-0.99), and 0.83 [95% CI, 0.71-0.96] at 90 and 180 days, respectively, and outperformed other existing clinical scores. Similar results were observed in validation cohort 2 (n=20).

**Conclusions:** The gs-MELD score, incorporating a clinically applicable gene signature test and the MELD score, enables improved pre-treatment survival prediction in severe AH.

### Performance comparison of full-spectrum versus forward-viewing colonoscopy: a randomized controlled trial.

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**Background:** New full-spectrum colonoscopes (FUSE) with 330° angle of view showed a significantly lower adenoma miss-rate. The objective of the present investigator-initiated randomized controlled trial was to assess the utility of this new technique in daily practice.

**Method:** From 3/2015 through 12/2016 patients referred to ambulant colonoscopy were randomly assigned to either a colonoscopy with high definition (HD) FVE Pentax i10 or FUSE instruments. 974 patients were allocated to FUSE and 882 to FVE. All procedures were performed by the first author.

**Results:** There was no significant difference for all baseline characteristics. Adenoma detection rate (ADR) was 51% for all FUSE cases vs 53% in FVE (ns). Mean adenoma per colonoscopy (APC) were 1.1 in FUSE vs 1.2 in FVE (ns). In the whole FUSE group 1.8 polyps per patients were found overall increasing to 1.9 with newer FUSE generation compared to 1.8 in FVE (ns). 84.4 vs 83.7% Polyps were below 5 mm of size and only 3.2 respectively 3.8% bigger than 1 cm. 48% of the extracted FUSE polyps and 50% of the polyps in the FVE group were tubular adenomas, 0.6 vs 1.2% were villous, 17.5% vs 23.6% serrated adenomas (SSA). There was no significant difference in histology. Time to ileum was with the at that time newest FUSE generation 5.0 min (CI 4.7-5.3) compared to 5.5 min (CI 5.2-5.7) with the FVE (p =0.02). Withdrawal time was significantly shorter with FUSE with a time of 15.8 min (CI 15.3-16.3) in FUSE and 19.1 min (CI 16.8-21.4) in FVE (p=0.01). Time for intervention was identical in both groups (3.3 vs 3.4 min). Depending on FUSE generation the overall examination time gain was 3 to 4.1 min (p<0.05).

**Conclusion:** Our RCT with the largest FUSE examined patient cohort in the literature revealed signif. shorter examination time compared to conventional HD colonoscopy with equal adenoma detection rates for both types of instruments 51 vs 53%.

O14

### Palmitoylation Determines the Subcellular Localization of Hepatitis E Virus ORF3 Protein

O16

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**Background:** Hepatitis E virus (HEV) is a positive-strand RNA virus encoding 3 open reading frames (ORF). HEV ORF3 protein, a small, hitherto poorly characterized protein, is involved in viral particle secretion and possibly other functions. We aim to investigate the structure and function of this crucial viral protein.

**Methods:** A panel of ORF3 constructs and the full-length protein expressed by infectious HEV were investigated by confocal laser scanning microscopy and immunoblot using GFP fusion proteins and newly established recombinant antibodies. Posttranslational modifications were probed by site-directed mutagenesis and different biochemical assays.

**Results:** Sequence analyses revealed the presence of an N-terminal cysteine-rich domain in HEV ORF3 which was found to be palmitoylated, as corroborated by <sup>3</sup>H-palmitate labeling, the investigation of cysteine-to-alanine substitution mutants and treatment with 2-bromopalmitate (2-BP). Abrogation of palmitoylation by site-directed mutagenesis or 2-BP treatment relocalized ORF3 protein from the plasma membrane to the cytoplasm and decreased the stability of the protein. The functional consequences of palmitoylation are currently being investigated using infectious HEV clones.

**Conclusions:** HEV ORF3 protein is palmitoylated at conserved N-terminal cysteine residues. This posttranslational modification determines the subcellular localization, stability and likely the function of ORF3 protein. These findings provide new insights into the life cycle of HEV, a major cause of acute hepatitis worldwide.

### LONG-TERM TREATMENT OF EOSINOPHILIC ESOPHAGITIS WITH SWALLOWED TOPICAL CORTICOSTEROIDS: DEVELOPMENT AND EVALUATION OF A THERAPEUTIC CONCEPT

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**BACKGROUND:** Swallowed topical corticosteroids (STC) are efficacious in inducing and presumably maintaining remission in patients with active eosinophilic esophagitis (EoE). Hitherto, it has not been evaluated whether long-lasting remission can be achieved, and whether treatment can be stopped once patients have achieved this remission.

**METHODS:** Since 2007, EoE patients included into a large database at the Swiss EoE Clinics were put on STC as induction/maintenance therapy. Disease activity was assessed on annual basis. In patients, who achieved long-lasting ( $\geq 6$  months) clinical, endoscopic and histological (=deep) remission (DR), treatment was stopped. Data on all patients treated using this therapeutic strategy were analyzed retrospectively.

**RESULTS:** Thirty-three of the 351 patients (9.4%), who were treated with STC, achieved DR. Median age of remitters at disease onset was 32.6 years (IQR 19.1-49.3), and diagnostic delay was 5.4 years (IQR 1.2-11.4). DR was achieved after 89.0 weeks (IQR 64.6-173.8). Female gender was the only independent prognostic factor for achieving DR (OR 2.5, 95% CI 1.2-5.3). Overall, STC were stopped after 104.7 weeks (IQR 65.5-176.6). No mucosal damage was observed upon histological examination. In 27 of the 33 remitters (81.8%), a clinical relapse occurred after a median of 22.4 weeks (95% CI 5.1-39.7). Six remitters (18.2%) did not experience a clinical relapse during a follow-up of 35.1 weeks (IQR 18.3-44.9). So, a total of 1.7% (6/351) were able to discontinue STC in the long term.

**CONCLUSION:** Long-term EoE treatment with STC was well tolerated, but only a minority of patients achieved DR. Female gender is the only prognostic factor for attainment of such remission. After treatment cessation, the majority experienced a clinical relapse.

O17

### Surgical site infections after pancreatic surgery in the era of enhanced recovery protocols

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**Background:** Few data exist on risk factors for surgical site infections (SSI) among patients treated in an enhanced recovery after surgery (ERAS) pathway. This study aimed to assess risk factors for SSI after pancreas surgery in a non-ERAS group and an ERAS cohort.

**Methods:** All pancreas surgeries were prospectively collected from January 2000 to December 2015. Risk factors for SSI were calculated using uni- and multivariable binary logistic regressions in non-ERAS and ERAS patients.

**Results:** Pancreas surgery was performed in 549 patients, among which 144 presented SSI (26%). In the non-ERAS group (n=377), SSI incidence was 27% (99/377), and risk factors for SSI on multivariable analysis were male gender and preoperative biliary stenting. Since 2012, 172 consecutive patients were managed within an ERAS pathway. Forty-five patients (26%) had SSI. On multivariable analysis no risk factor for SSI in the ERAS cohort was found. In the ERAS group, patients with a pathway compliance  $<70\%$  had higher occurrence of SSI (30/45=67% vs. 7/127=6%,  $p<0.001$ ).

**Conclusions:** In the non-ERAS cohort, male gender and preoperative biliary stenting were risk factors for SSI. The introduction of ERAS modified the risk factors without changing the SSI incidence. Male gender and biliary stenting were not found to be risk factors anymore in the ERAS group. In an ERAS pathway, having an overall compliance  $>70\%$  may reduce the SSI rate.

O19

### Coffee accelerates recovery of bowel function after elective colon resection – a randomized controlled trial

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**Background:** Postoperative ileus after colorectal surgery is a frequent problem which significantly prolongs hospital stay and increases perioperative costs. The Aim was to test the effect of standardized coffee intake on postoperative bowel movement after elective colon resection.

**Method:** Between 9/2014 and 12/2016 patients scheduled for elective colon surgery were randomized to receive either coffee (intervention group) or tea (control group). 150 ml of the respective beverage was drunk 3x/d every postoperative day until discharge. The primary endpoint was time to first bowel movement. Secondary endpoints included second bowel movement, use of laxative, insertion of nasogastric tube, length of hospital stay and postoperative complications.

**Results:** A total of 115 patients were randomized: 56 were allocated to the coffee and 59 to the tea group. After coffee intake, the first bowel movement occurred after a median of 65.2h (95% CI: 50.5-79.8) as compared to 74.1h (95% CI: 60.7-87.5) in the control group (intention-to-treat-analysis;  $P=0.008$ ). The hazard for earlier first bowel movement after coffee intake was 1.67 (95% CI: 1.14-2.44;  $P=0.009$ ). Furthermore, 7.1% of the patients in the coffee group experienced the first bowel movement within 24h after surgery as compared to 1.7% in tea group.

**Conclusion:** Coffee intake after elective colon resection leads to a faster recovery of bowel function. Therefore, coffee intake represents a simple and effective strategy to prevent postoperative ileus.

O18

### Impact of venous invasion on short- and long-term outcomes after distal pancreatectomy for cancer

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**Background:** Distal pancreatectomy (DP) represents the treatment of choice for localized malignant tumors of the pancreatic tail. Some evidences suggest that venous invasion (VI) might be an important risk factor for postoperative outcomes. This study aimed to assess and compare overall survival (OS) and recurrence rate (RR) after DP in patients with and without tumoral VI.

**Methods:** All consecutive DP patients from 2000 to 2015 were analyzed. Demographics, perioperative data, and postoperative outcomes were assessed. OS were calculated using Kaplan-Meier curves. Otherwise, standard statistical tests were used.

**Results:** One hundred and five patients had DP during the study period (median age: 63, IQR 49-71). Among these 105 DP patients, 45 presented a malignant tumor (17 women/28 men). Majority of the cancers were ductal adenocarcinomas (32/45, 71%). Among these 45 malignant tumors, histological VI was found in 33 patients (73%). Characteristics and intraoperative data of patients with and without VI were similar. Overall complication rates were 16/33 (48%) in the group with VI and 8/12 (75%) in the group without VI ( $p=0.08$ ). Median length of hospital stay was 13 days in the group with VI and 12 days in the group without VI ( $p=0.94$ ). Median OS and 5-year OS for the group with and without VI were 21 and 16 months ( $p=0.29$ ) and 16% and 20% ( $p=0.29$ ), respectively. RR was 19/33 (58%) for the VI group and 2/12 (17%) for the group without VI ( $p=0.02$ ).

**Conclusions:** VI did neither have an effect on postoperative complications nor on length of hospital stay. OS were similar in case of VI or not. On the contrary, RR was higher in the VI group. This suggests that perioperative treatments focusing on impeding VI could decrease RR.

O20

### Nurse-led self-management support in liver transplantation across two hospitals

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**Background/Aims:** The Cantonal Hospital St. Gallen (SG) closely collaborates with the University Hospital Zurich (ZH) in the provision of care throughout the course of liver transplantation (LT). Both hospitals integrated a master prepared advanced practice nurse (APN) in their interdisciplinary LT-teams. The APNs provide continuity of care and self-management support, which are key components in chronic illness care. We compared the structure and the content provided during the consultations of the nurse-led service.

**Methods:** A descriptive analysis was done on patient demographics, delivery structure and content used during consultations.

**Results:** From 08/2014 until 05/2017, n=40 patients received consultations from APNs, 28 with male gender (70%), mean age in years 59 (range 32-71). Main underlying diagnosis for listing: decompensated cirrhosis (28 (70%)) and HCC (12 (30%)). At time of analysis, 24 patients (60%) had received LT. **Delivery:** Both APN provided 167 consultations, patients received from 1 to 13 consultations (mean 3). **Time point:** 115 consultations (69%) were delivered in SG, mainly before LT 86 (75%), while the APN in ZH provided 52 consultations (31%), most of them after LT (31(60%)). **Duration:** Consultations were shorter in SG compared to ZH (mean 30 vs. 45 minutes). **Provided content during counseling:** The APN in SG provided more content related to pathophysiology of liver cirrhosis, comorbidities and symptom-management (54%), whereas the APN in ZH focused more on health-related behaviour (45%), followed by medication management (11% vs. 26%) and role- and emotional management (35% vs. 29%).

**Conclusions:** The APN collaboration facilitates continuous, nurse-led self-management support. It allows flexible and quick adaptations in the frequency, the duration and the consultation's content tailored to actual patients' needs during the course of LT. This finally enables a seamless transition between the two hospitals.

### Can treatment of activated fibroblasts at the level of fibrosis reduce the development of liver cancers?

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**Background:** Persistent activation of fibroblasts is a key feature of chronic fibrotic diseases. Fibrosis progression is an important prerequisite for the development of carcinoma. The activated phenotype is linked to an increased sensitivity to apoptotic stimuli. This apoptotic priming is induced by an alteration of apoptosis-regulating Bcl-2 proteins. We have demonstrated that CCA-derived activated fibroblasts (AF) are sensitive to navitoclax, a pro-apoptotic inhibitor of anti-apoptotic Bcl-2 proteins, *in vitro*. In addition, in a syngeneic rat model of CCA, navitoclax treatment leads to the depletion of AF and a reduced tumor development. We hypothesize that AF derived from chronic fibrotic diseases share key features of apoptotic priming with cancer-derived AF and can be similarly targeted. Moreover, targeting of AF at the level of fibrosis will reduce the development of liver cancers. **Methods:** Human and mouse fibroblasts were activated *in vitro* with PDGF. Alterations of the Bcl-2 family were assessed with qPCR and Western blot. PDGF-activated fibroblasts were further treated with pro-apoptotic BH3 mimetics specific for Mcl-1, Bcl-2 and Bcl-xL. Induction of apoptosis was examined biochemically by caspase-3/7 activity and morphologically using DAPI staining. For *in vivo* studies, Mdr2<sup>-/-</sup> mice were treated with the selective Bcl-xL inhibitor A-1331852. Liver fibrosis was assessed by Sirius red staining and quantification of hydroxyproline. **Results:** Our data indicate that a) due to a reduction of anti-apoptotic Bcl-2 the survival of AF becomes Bcl-xL-dependent, and b) specific inhibition of Bcl-xL by A-1331852 ameliorates liver fibrosis in Mdr2<sup>-/-</sup> mice. **Conclusions:** Inhibition of Bcl-xL induces apoptosis in AF *in vitro* and reduces fibrosis *in vivo*. This indicates that AF from PSC and CCA can be targeted similarly. We therefore suggest that treatment of AF with Bcl-xL inhibitors at the level of fibrosis may reduce the development of liver cancers.

O21

### Intestinal microbiota significantly alters hepatic expression of energy metabolism genes in mice with acute cholestasis

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**Background:** We were interested in assessing the effects of intestinal microbiota on hepatic gene expression profile and plasma bile acid (BA) composition in basal conditions and in an acute cholestasis.

**Methods:** We induced acute cholestasis in germ free (GF) and altered Schaedler flora colonized (ASF) mice by performing bile duct ligation (BDL) and we performed studies after 5 days. We evaluated gene expression profile in the liver of these mice compared to non-cholestatic control groups using next generation sequencing and pathway analysis. We also measured the plasma concentration of BA by UHPLC-HRMS analysis.

**Results:** We found that acute cholestasis was associated with distinct genes expression patterns mainly involved in the regulation of the immune system, oxidative processes and accumulation of extracellular matrix in both ASF and GF mice. In addition, we observed significant differences related to the hygiene status of the mice in the expression of genes controlling the generation of precursor metabolites, energy metabolism and amino acid metabolic process pathways. In non-cholestatic mice, the absence of microbiota significantly induced or suppressed the expression level of 80 genes involved in organic acid catabolic and fatty acid metabolic processes, leukocyte migration and external side of plasma membrane.

Under basal conditions, there were no significant differences in primary BA concentrations between GF and ASF mice. The concentration of the majority of BA markedly increased after BDL in both groups without remarkable differences according to the hygiene status of the mice.

**Conclusion:** Intestinal microbiota significantly alters hepatic gene expression before and after acute cholestasis. Alterations observed after BDL suggest that microbial-induced differences may impact the course of cholestasis and modulate liver injury.

O23

O22

### The Stimulation of Macrophages with Microbial-Derived Compounds Supports Increased IL-19 Expression in Colitis

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**Background:** Interleukin (IL)-19, a member of the IL-10 cytokine family, that signals through the IL-20 receptor type I (IL-20Rα: IL-20Rβ) is a cytokine with rather unknown function.

**Methods:** To investigate the significance of IL-19 for the development of colitis biopsies of patients with Crohn's disease (CD) and ulcerative colitis (UC) were received from the Swiss IBD cohort study and further studied with a newly generated Il19-tdTomato reporter mouse line. **Results:** The expression of IL-19 is increased in biopsies from UC patients but not CD patients with active disease and is also increased in mice with DSS colitis. As consequence, the development of DSS colitis is attenuated in IL-19-deficient animals. Although gnotobiotic Oligo-MM<sup>12</sup> animals with a defined flora developed DSS colitis, the expression of IL-19 was not induced in Oligo-MM<sup>12</sup> mice. Furthermore, direct activation of macrophages by CD40 ligation caused colitis, but did not induce IL-19 expression indicating that a barrier breach is required for the expression of IL-19. The stimulation of macrophages with Toll-like receptors (TLR) ligands and injection of Lipopolysaccharide (LPS) into mice confirmed *in vitro* and *in vivo* that microbial-derived compounds induced IL-19 expression. Attenuated colitis in IL-19-deficient animals was associated with reduced numbers of monocytes and macrophages in the inflamed lamina propria that produced reduced amounts of IL-6. **Conclusions:** Microbial-derived products induce IL-19 expression by macrophages leading to colitis. The deletion of individual members of the IL-20 cytokine family and individual receptor chains is needed to further dissect the importance of this cytokine family for IBD.

O24



### Nlrp6 expression in activated CD4 T cells is independent of intestinal microbiota

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**Background:** The lack of the inflammasome receptor Nlrp6 leads to microbial dysbiosis and severe inflammation in colitis model, but the mechanisms of its protective effects are not known. We hypothesized that Nlrp6 can regulate the responses of immune cells to protect from colitis. **Methods:** Nlrp6 expression was analyzed in various immune cells isolated from non-treated and wt mice. The ability of naïve wt and Nlrp6-deficient CD4 T cells to differentiate *in vitro* into effector cell types was analyzed by Flow Cytometry. **Results:** The Nlrp6 gene is highly expressed by intestinal epithelial cells, but not in resting immune cells (CD4 and CD8 T cells, B cells, macrophages, dendritic cells and neutrophils). The activation and differentiation of naïve T cells to Th1 effector cells induced the expression of Nlrp6 in CD4 T cells. Nlrp6-deficient CD4 T cells showed impaired ability to differentiate into interferon (IFN) $\gamma$ -producing Th1 cells. The differentiation into Th2, Th17 and Treg cells was not affected in the absence of Nlrp6. Reduced viability was observed in Th1-polarizing conditions when Nlrp6 was absent, but staining for Ki67 indicated that Nlrp6-deficient Th1 cells showed the same proliferation rate as wt cells. **Conclusion:** The inflammasome receptor Nlrp6 is not expressed by naïve CD4 T cells but its expression is induced during Th1 differentiation. Nlrp6 is important for generation and/or survival of INF $\gamma$ -producing Th1 lymphocytes *in vitro*. Cellular differentiation *in vitro* eliminated the possible influences of intestinal microbiota on CD4 T cells indicating that the observed effects of Nlrp6 on CD4 T cells are cell intrinsic and independent of the microbiota.

### Bariatric surgery in patients with hemochromatosis: advantage for proximal gastric bypass over sleeve gastrectomy?

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**Background:** Since bariatric operations lead to reduced iron uptake, there might be a benefit in patients with hereditary hemochromatosis.

**Methods:** Comparison of two cases with hereditary hemochromatosis, which were treated with laparoscopic proximal gastric bypass and laparoscopic sleeve gastrectomy, with the literature.

**Results:** There are five reported cases in literature of patients with hemochromatosis, who received a gastric bypass for weight-loss. In all cases phlebotomies could be stopped and ferritin values remained between 25 and 30  $\mu\text{g/ml}$  after 2-5 years of follow-up. Our patient (48yo male) with the gastric bypass achieved the same result (serum ferritin of 20  $\mu\text{g/ml}$ ) at 37 months follow-up. Serum ferritin levels of the patient (49yo female) with the sleeve gastrectomy were 204  $\mu\text{g/ml}$  at 30 months follow-up and almost within the range of needing further phlebotomies.

**Conclusions:** Bariatric interventions are able to control the iron overload in patients with hemochromatosis. There seems to be an advantage for gastric bypass over sleeve gastrectomy, most likely due to the bypassing of the main location of iron uptake (duodenum and the proximal jejunum).

O25

### Propofol-Sedation in routine endoscopy: case series comparing target controlled infusion vs. nurse administered bolus-concept.

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**Background:** Many studies address safety and effectiveness of non-anesthesiologist propofol sedation (NAPS) for gastrointestinal (GI) endoscopy (1). Target Controlled Infusion (TCI) is a tool for providing optimal sedation regimen and avoiding under- or oversedation (2). The aim of this study is to assess safety and performance of propofol TCI sedation in comparison with nurse-administered bolus-sedation. **Methods:** 45 patients undergoing endoscopy under TCI propofol sedation were consecutively and prospectively included from November 2016 to Mai 2017 and compared to 87 patients retrospectively included that underwent endoscopy with bolus-sedation. Patients were matched for age and endoscopic procedure. We recorded length of time for sedation and endoscopy, dosage of medication and adverse events. **Results:** There was a significant reduction in dose per time of propofol administered in the TCI group, compared to the bolus group ( $8.2 \pm 2.7 \text{ mg/min}$  vs  $9.3 \pm 3.4 \text{ mg/min}$ ;  $p=0.046$ ). The time needed to provide proper sedation level was slightly but statistically significantly lower in the control group ( $5.3 \pm 2.7 \text{ min}$  vs  $7.7 \pm 3.3 \text{ min}$ ;  $p < 0.001$ ). Nonetheless the total endoscopy time was not different. No difference between TCI and bolus-sedation was observed for rate of adverse events. **Conclusion:** This study indicates that sedation using TCI for GI endoscopy reduces the dose of propofol necessary per minute of endoscopy. This may lead to fewer adverse events. However, prospective randomized trials need to confirm this trend.

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O27

O26

### Use of a Novel Ultrasonic Vascular Imaging Technique for the Diagnosis of Focal Nodular Hyperplasia in the Liver - Case Series (Abstract for video sessions)

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**Background:** Diagnostic ultrasound in combination with contrast-enhanced ultrasound (CEUS) has a high accuracy and diagnostic value for focal liver lesions (FLL). Examination of vascular structures and flow dynamics is important in order to differentiate benign from malignant FLL. CEUS enables the diagnosis of focal nodular hyperplasia (FNH) of the liver by visualization of the spoke wheel sign in the arterial phase which is very specific for FNH with the highest diagnostic accuracy especially for FNH < 3 cm in comparison to MRI (EASL CPG 2016). Superb Micro-Vascular Imaging (SMI) is a novel ultrasound Doppler technique with high resolution imaging, minimal motion artefacts and high frame rates. SMI has not been studied in FNH lesions, which have a unique vascular supply that is diagnostic in most cases. Diagnosis is important to avoid unnecessary biopsies and surgical procedures. In contrast to hepatocellular adenoma, the management of FNH is conservative (no risk of malignant transformation/bleeding and no need to stop contraception).

**Methods:** The diagnostic value of SMI technique for diagnosing FNH lesions in comparison to Doppler and CEUS on a Toshiba TM Aplio 500 Platinum<sup>®</sup> ultrasound device was studied. CEUS was performed by using an intravenously injected contrast agent (Sonovue<sup>®</sup>). CEUS was performed according to international guidelines (Claudon M. et 2013). FNH analysis of five patients are demonstrated in a **video case format** using representative still images and recorded video clips.

**Results:** CEUS revealed in all cases FNH with typical early arterial centrifugal spoke-wheel enhancement without washout up to 5 minutes after injection of Sonovue<sup>®</sup>. Correspondingly, we demonstrate excellent visualization of the spoke-wheel-like vessels by SMI without using contrast agent and independently to time response. FNH diagnosis was established by resection/histology (n=2), MRI (n=1) and follow-up 12-18 months (n=2).

**Conclusion:** This is the first European report demonstrating the excellent clinical value of SMI to diagnose typical FNH lesions with spoke-wheel-like vessels. In the presented cases, SMI was able to provide the same diagnostic imaging criteria for FNH as CEUS in the arterial phase. In contrast to SMI, CEUS, CT and MRI require arterial contrast-enhancement, which may be missed due to a short detection period of sometimes only a few seconds. Considering the lack of such a time-specific detection window for SMI imaging, FNH detection by SMI is accurate, less user-dependent and does not require application of a contrast agent.

O28

### Rapid liver hypertrophy after portal vein occlusion correlates with the degree of collateralization between lobes – a study in pigs

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#### Background:

Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS) induces more rapid liver growth than portal vein ligation (PVL). Transection of parenchyma in ALPPS may prevent the formation of collaterals between lobes. The aim of this study was to determine if abrogating the formation of collaterals through parenchymal transection impacted growth rate.

#### Methods

Twelve Yorkshire Landrace pigs were randomized to undergo ALPPS, PVL or "partial ALPPS" by varying degrees of parenchymal transection. Hepatic volume was measured after 7 days. Portal blood flow and pressure were measured. Portal vein collaterals were examined from epoxy casts.

#### Results:

PVL, ALPPS and partial ALPPS led to volume increases of the RLL by 15.5% (range 3-22), 64% (range 45-76), and 32% (range 18-77) respectively with significant differences between PVL and ALPPS/partial ALPPS ( $p < 0.05$ ). In PVL and partial ALPPS, substantial new portal vein collaterals were found. The number of collaterals correlated inversely with the growth rate ( $p = 0.039$ ). Portal vein pressure was elevated in all models after ligation suggesting hyperflow to the portal vein supplied lobe ( $p < 0.05$ ).

#### Conclusion:

These data suggest that liver hypertrophy following PVL is inversely proportional to the development of collaterals. Hypertrophy after ALPPS is likely more rapid due to reduction of collaterals through transection.

O29

### Beta-6-Integrin serves as a novel tumor marker and therapeutic target for colorectal carcinoma

O31

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**Background:** Colorectal cancer (CRC) is the third most common malignancy and one of the leading causes of cancer-related deaths worldwide. The need for novel biomarkers and therapeutic strategies for CRC is obvious and identification of such markers and targets might significantly improve prognosis of CRC patients.  $\beta_6$ -integrin (ITGB6) is a marker for cells undergoing epithelial-to-mesenchymal transition (EMT) and has been associated with many epithelial tumors, such as CRC, lung cancer, breast cancer or pancreatic cancer. ITGB6 serves as a cell surface receptor for matrix proteins, such as fibronectin, and activates matrix degrading enzymes, such as matrix metalloproteinases (MMP) 2 and 9 as well as TGF- $\beta$ . Previous studies identified a possible role for the  $\beta_6$ -integrin (ITGB6) in CRC pathogenesis.

**Methods:** The aim of this study was to investigate whether ITGB6 might serve as a novel serum marker and therapeutic target in CRC patients. We used serum samples of 19 healthy volunteers and 269 CRC patients including 53 patients with metastatic CRC. A follow-up cohort consisted of 19 CRC patients (n = 11 without lymph node metastasis, n = 4 with lymph node metastasis and n = 4 with liver metastasis) serum samples were collected pre-surgery (-3 to -1 days), post-surgery (2 to 6 days) and during follow-up visits (visit 1: 3 to 20 weeks; visit 2: 80 weeks). Wild-type and Itgb6 deficient mice were treated with 0.5–1.0% DSS for 7 days in drinking water followed by a recovery period of 14 days over three cycles. 10 mg azoxymethane (AOM) was administered by i.p. injection six times. ITGB6 serum levels were determined by ELISA.

**Results:** We detected ITGB6 in the serum of CRC patients (range 0–10 ng/ml) and found that a cut-off of  $\geq 2$  ng/mL ITGB6 predicts metastatic disease in 100% of respective patients. An ITGB6 serum level above 2 ng/ml was also associated with a significantly worse prognosis compared to patients with a ITGB6 serum level below 2 ng/mL. By comparing ITGB6 and CEA levels we found that ITGB6 above the cut-off of 2 ng/mL predicts metastatic disease with a higher accuracy as CEA. In a separate follow-up cohort (n = 19), after surgical R0 resection of the colon tumor and concomitant liver metastasis, ITGB6 serum levels declined to zero. Of note, we found that ITGB6 serum levels also declined after removal of the primary tumor in the colon and indicate treatment response to chemotherapy. ITGB6 serum levels rise again when liver metastases were newly diagnosed or tumor progression occurred. In this regard, ITGB6 serum levels were much more reliable as CEA levels. By immunohistochemistry, ITGB6 staining was strongly detectable in the tumor tissue. However, ITGB6 serum levels correlated clearly better with disease course as ITGB6 mRNA or protein levels in tumor tissue. In a colitis-associated colon tumor model, deficiency of Itgb6 protects mice from development of colon tumors in vivo. By endoscopy and histology, we found a significant number of colon tumors in DSS/AOM treated wild-type mice, but no tumors in treated Itgb6 deficient mice.

**Conclusions:** This is the first study showing ITGB6 levels in patients' sera. Our findings provide evidence that ITGB6 can serve as a novel serum biomarker for diagnosis and prognosis of advanced CRC, as a marker for tumor surveillance, relapse and treatment response as well as a therapeutic target for CRC treatment. In summary, our findings suggest that using targeted therapy in patients with high levels of ITGB6 may be a novel treatment option for CRC patients.

O30

### Successful performance of a laparoscopic Pancreatico-duodenectomy (Whipple/Kausch) procedure

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#### Background:

First performed in 1997, laparoscopic PD (Lap PD) has not adopted widely until recently when Lap PD has become the predominant approach in many high volume centers. An international consensus meeting in 2016 recommended cautious introduction of the lap PD in experienced laparoscopic centers. So far, no experience with lap PD has been reported in Switzerland.

#### Methods

Lap PD was introduced in 2017 at Cantonal Hospital Winterthur. Indication, planning, equipment and steps of the procedure are reviewed. Video documentation of the first patient undergoing lap PD is reviewed and the technique is discussed.

#### Results:

A 82 year old woman presented with jaundice and a 2.5 cm cytologically confirmed adenocarcinoma of the pancreatic head. Patient and family were explicitly interested in the laparoscopic approach. The patient was lean (BMI 21), had no history of pancreatitis, radiotherapy, no evidence of metastatic disease and there was no involvement of major vessels. The procedure was performed in supine French position with a 3D camera system using three 12 mm working ports and two 5 mm assistance ports. The specimen was extracted through a 6 cm Pfannenstiel incision and reconstruction was performed using duct-to-mucosa technique, duodenum sparing approach and self-tightening laparoscopic suture material. Blood loss was 120 cc. Recovery was uneventful and the patient could be discharged after 10 days to a rehabilitation hospital. Pathology showed pT2pN2(5/12)cM0L1V1G2R0 status.

#### Conclusion:

Lap PD was performed safely and oncologically adequately in a selected patient. This approach has the potential to be more widely used in selected patients in the future.

### Systematic Analysis of Annual Health-care Costs in Hospitalized Inflammatory Bowel Disease Patients in Switzerland

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**Background and aims:** Real-life data on costs of hospitalized patients with inflammatory bowel disease (IBD) are lacking in Switzerland. We conducted this study to assess costs during a one year follow-up period starting with an index hospitalization and to evaluate the number of re-hospitalizations as well as outpatient consultations in this period.

**Methods:** Based on claims data of the Helsana health insurance group, health care costs (in Swiss Franks [CHF]; 1 CHF = 0.991 US\$) were calculated during a one-year follow-up period starting with an index hospitalization in the time period between January 1<sup>st</sup>, 2013, to December 31<sup>st</sup>, 2014.

**Results:** Out of 213'434 patients with at least one hospitalization in 2013-2014, a total of 296 patients (0.14%) had IBD as main diagnosis (119 UC [40.2%], 177 CD [59.8%], females 169/269 [57.1%]). In comparison with UC patients, CD patients were significantly more frequently treated with biologics (44.6% vs 20.2%,  $p < 0.001$ ) and underwent more frequently a surgical procedure during index hospitalization (28.2% vs. 10.1%,  $p < 0.001$ ). Compared with UC patients, CD patients had significantly higher mean annual costs (29,010CHF vs. 24,020CHF,  $p = 0.044$ ), higher inpatient costs (10,190CHF vs. 9,870CHF,  $p = 0.025$ ), and higher outpatient costs (18,820CHF vs. 14,150CHF,  $p = 0.043$ ). Re-hospitalization rate (33.3% for CD vs. 29.4% for UC) and number of consultations was not different in the follow-up period (median of 21 consultations with physicians for both CD and UC patients).

**Conclusions:** An IBD-related hospitalization including a one-year follow-up in Switzerland generates considerable costs which are higher for CD patients compared to UC patients.

O32

### Impact of diagnostic delay in pediatric Crohn's disease patients compared to adult patients

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**Background and aims:** The length of diagnostic delay in Crohn's disease (CD) is a risk factor for bowel strictures and intestinal surgery. We aimed to assess if diagnostic delay has a similar impact in pediatric CD patients when compared to adult patients.

**Patients and methods:** Retrospective review of data from the Swiss IBD cohort study (SIBDCS). Pediatric patients were diagnosed with CD <18 years of age whereas adult patients were diagnosed with CD >18 years of age. Frequency of CD-related complications were assessed in the long-term follow-up in both groups. Long diagnostic delay was defined as delay >75<sup>th</sup> percentile.

**Results:** From 2006 to 2016, a total of 1,550 patients were included (387 pediatric and 1,163 adult CD patients). Median (IQR) diagnostic delay was 3 (1-9) months for the pediatric and 6 (1-24) for the adult group, respectively. At diagnosis, children presented less complications than adults [any complications: stenosis, perianal fistula, internal fistula, resection surgery, fistula surgery; 14.8% vs. 26.5% for long diagnostic delay ( $p < 0.01$ ) and 11.3% vs. 14.6% for short diagnostic delay ( $p > 0.05$ )]. However, no significant difference could be observed after 15 years of disease evolution regarding stenosis, perianal fistulas and internal fistulas. Adults with long diagnostic delay more frequently underwent fistula and abscess surgery during the first 5 years following diagnosis when compared to pediatric patients.

**Conclusions:** Pediatric CD patients are characterized by shorter diagnostic delay and less complications during the early years after diagnosis when compared to adult CD patients. However, at 15 years of disease evolution the difference with respect to complications does no longer exist when comparing pediatric CD patient to adult CD patients (irrespective of the length of diagnostic delay).

O34

### Efficacy and safety of budesonide orodispersible tablets in active eosinophilic oesophagitis: Results from a randomised, double-blind, placebo-controlled, pivotal, European multicentre trial (EOS-1)

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**Background and aims:** Until now, no approved drug therapy is available for eosinophilic oesophagitis (EoE). We aimed to evaluate in a pivotal Phase 3 trial efficacy and safety of a novel budesonide orodispersible tablet formulation specifically designed for EoE for the induction of clinico-histological remission in adult patients with active EoE.

**Methods:** Eighty-eight patients were randomised to receive 6-weeks double-blind (DB) treatment with either 1 mg budesonide orodispersible tablets (BUL 1mg) twice daily (BID) (n=59) or placebo BID (n=29). Non-responder could receive further 6-week open-label induction (OLI) treatment with BUL 1mg BID. The primary endpoint was the rate of combined clinico-histological remission.

**Results:** BUL 1mg BID was highly statistically superior to placebo in achieving clinico-histological remission (57.6% vs. 0%,  $p < 0.001$ ), histologic remission (93.2% vs. 0%,  $p < 0.001$ ), clinical remission (59.3% vs. 13.8%,  $p < 0.001$ ), and endoscopic remission (61.0% vs. 0%,  $p < 0.001$ ). A prolonged treatment of up to 12 weeks increased the overall cumulative clinico-histological remission rate up to 84.7%. Neither serious adverse events nor clinically relevant changes in the morning serum cortisol levels were observed in any treatment group.

**Conclusions:** A 6-week course of BUL 1mg BID was highly effective and safe in bringing active EoE rapidly in clinical and histological remission, as well as in normalising endoscopic alterations. A prolongation up to 12 weeks brought additional 27% of patients into clinico-histological remission.

O33

### Increasing Imports of Direct-Acting Antivirals (DAAs) via FixHepC Buyers Club and Medical Tourism by Swiss Patients with Chronic Hepatitis C Infection

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**Background:** Due to high costs (average CHF 40'000.-), reimbursement of highly effective direct-acting antivirals (DAAs) against hepatitis C virus (HCV) remains restricted in Switzerland. With few exceptions (i.e. HIV- or HBV-coinfection, selected extrahepatic manifestations), only patients with substantial fibrosis (METAVIR stage  $\geq F2$ ) can be currently treated. Highly motivated HCV patients outside this reimbursement restriction (limitation by Federal Office of Health) are seeking legal and affordable ways to access DAA treatment by buying generic DAAs in low-income countries for a fraction of the regular price (3-4%, i.e. CHF 1'500.-). Our aim is to assess the number of patients, their characteristics and therapy outcomes using this novel treatment option.

**Methods:** Retrospective analysis of characteristics in HCV patients treated in 2015/2016 with generic DAAs (i.e. ordered online via the FixHepC Buyers Club, medical tourism to countries with generic DAAs) in seven Swiss hepatitis outpatient clinics.

**Results:** 84 patients (54% males) aged 15 to 77 years (mean 51 years) were identified. HCV genotype (GT) distribution was GT1 56% (GT1a 24%), GT2 12%, GT3 14% and GT4 18%. Liver fibrosis staging by histology (according METAVIR) and/or liver elastography (Fibroscan<sup>®</sup> mean 5.1 kPa, range 3.3-7.0 kPa) was F0 or F1, except for two patients with cirrhosis (F4). Ledipasvir/sofosbuvir was the dominant treatment choice (52%), followed by velpatasvir/sofosbuvir (30%) and daclatasvir/sofosbuvir (18%). Treatment duration was 8 (5%), 12 (90%) and 24 (5%) weeks, respectively. Most patients ordered DAAs online via FixHepC Buyers Club (54%), whereas the remaining patients bought DAAs in India, Egypt, Morocco or Bangladesh. Treatments were well tolerated; no severe adverse events or treatment failures were reported. Sustained virological response 12 weeks after treatment (SVR12) was available in 27 patients and reached 100%, whereas in 57 patients SVR12 was pending.

**Conclusions:** A growing number of HCV patients not qualifying for reimbursement in Switzerland are using the treatment option of generic DAAs. Drug tolerance and effectiveness seem comparable to original DAAs.

O35

### Hepatocyte transporters expression in chronic liver disease: correlation with fibrosis severity and dynamic gadoteric acid-enhanced (Gd-EOB-DTPA) MRI findings.

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**Background and aim:** In chronic liver disease (CLD), Gd-EOB-DTPA hepatocyte uptake decreases with increasing fibrosis. However, the expression of hepatocyte transporters involved in liver imaging has not been investigated in this condition. We analysed Gd-EOB-DTPA MRI findings and the immunohistochemical expression (IHCE) of hepatocyte transporters at different stages of fibrosis.

**Methods:** Liver biopsies and Gd-EOB-DTPA MRI from 42 patients with suspected liver fibrosis were prospectively collected. Arterial and portal perfusion, hepatocytic uptake rate, sinusoidal backflux, biliary efflux (ml/min/100g for all) and extracellular volume (%) were quantified at imaging after pharmacokinetic modelling. Fibrosis was assessed on liver biopsies according to METAVIR and collagen proportionate area (CPA) automated imaging analysis. The IHCE of OATP2/8, MRP2 and MRP3 was semi-quantitatively scored.

**Results:** Our cohort included 32 men and 10 women with CLD (19 viral etiology, 8 cirrhosis). Increasing fibrosis was associated with: change from portal to arterial perfusion, decrease in hepatocytic Gd-EOB-DTPA uptake, extension of OATP2/8 IHCE from liver zone 3 to the whole lobule, progressively irregular MRP2 IHCE and extension of MRP3 IHCE from liver zone 1 to the whole lobule (p<0.05).

**Conclusions:** Hepatocyte transporters are still present in hepatocytes when liver fibrosis increases. Their modified IHCE might be an adaptive response to intracellular cholestasis. The decrease in Gd-EOB-DTPA uptake by the hepatocytes could reflect a lower interstitial bioavailability of the contrast agent or an altered function of the transporters.

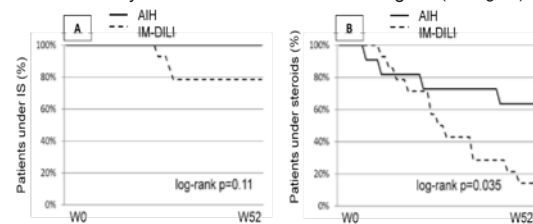
O36

### Discontinuation of immunosuppression in immune mediated drug induced liver injury (IM-DILI) : a case control study

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**Background:** Drug-induced liver injury may present with features similar to autoimmune hepatitis (AIH), a condition named IM-DILI, in which immunosuppressive therapy (IS) is indicated (*Bjornsson Hepatology 2010*). Whether these patients require permanent IS therapy after drug discontinuation is debated. **Aim:** To study the evolution of patients with either classical AIH or IM-DILI after initial decompensation. **Methods:** Retrospective, single centre, case-control study including 29 patients with acute AIH (n=14, 80% female, age 48 yrs) or IM-DILI in which a recent exposition to a potential hepatotoxin was identified (n=15, 71% female, age 57 yrs). Histology, serology and biology was available in all patients. A follow-up (FU) of 12 months included serial values of transaminases and type/dose of IS. **Results:** Demographics/serology/histology were similar between groups at baseline. Causative drugs in IM-DILI patients were: NSAIDs (6); sartans (3); antimicrobials (2); other (4). Transaminases decreased under IS in both groups. Compared to AIH, IM-DILI patients tended to be under less IS and more likely to be weaned of steroids during FU (see figure)



**Conclusion:** These clinically relevant data underline the specificity of IM-DILI in spite of similar initial presentation, and suggest that permanent IS may not be necessary in all patients

O38

### Changes in circulating osteopontin and relationship with serial liver biopsies in the course of alcoholic hepatitis

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**Background:** Liver inflammation is a hallmark of alcoholic hepatitis (AH). Osteopontin (OPN), a multifunctional protein, is involved in neutrophilic infiltration at time of diagnosis (*Morales-Ibanez, Hepatology 2013*) but its evolution over time and relationship with liver tissue changes are not known. **Aim:** Explore serum OPN and liver biopsy changes in AH during a 3-month follow-up.

**Methods:** we included 39 patients with AH derived from 2 previous studies (age 54 yrs, MELD 19.1; Maddrey's DF: 34.3). Liver biopsy was repeated at W4 and W12 in 18 and 21 patients, respectively. Serum OPN, IL-6, white blood cells (WBC) and CCL-20, a leucocyte chemoattractant, were measured. A semi-quantitative score for inflammation (portal and lobular) was applied on biopsies while blinded to patients' data. A group of 9 patients (abstinent alcoholic cirrhosis) served as controls for baseline measures. **Results:** mean  $\pm$  SEM # p< 0.05 vs controls; \*p<0.01 vs wk 0; °p<0.001 vs wk 0

Blood value	Controls (n=9)	AH wk 0 (n=39)	AH wk 4 (n=38)	AH wk12 (n=37)
OPN (pg/ml)	104 $\pm$ 14	377 $\pm$ 47 <sup>#</sup>	225 $\pm$ 35*	159 $\pm$ 24°
CCL-20 (pg/ml)	67 $\pm$ 10	389 $\pm$ 48 <sup>#</sup>	196 $\pm$ 30*	133 $\pm$ 23°
IL-6 (pg/ml)	19 $\pm$ 3	34 $\pm$ 4 <sup>#</sup>	23.4 $\pm$ 3	18.3 $\pm$ 4°
WBC (G/L)	6.1 $\pm$ 1.1	8.1 $\pm$ 0.5 <sup>#</sup>	8.3 $\pm$ 0.6	6.8 $\pm$ 0.4°

On subsequent liver biopsies, at W4, inflammation decreased in 10/18 patients. At W12, all but 2 patients showed a complete resolution of neutrophilic infiltration with persistent mild mononuclear inflammation. Patients with reduced liver inflammation on W4 repeat biopsy demonstrated a more important decrease in serum OPN as compared to those who didn't (515  $\pm$  73 to 222  $\pm$  33, p<0.002 versus 500  $\pm$  139 to 359  $\pm$  63, p=0.47). No such association was observed with CCL-20, WBC or IL-6. **Conclusions:** Circulating OPN, IL-6 and CCL-20 are elevated in AH at hospital admission, with a progressive decrease over time. A decrease in liver inflammation evident at W4 goes in parallel with reduced circulating OPN values. Serum OPN is a promising tool to monitor liver inflammation in patients with AH (**Supported by Foundation for Liver and Gut Studies FLAGS**)

O37

### A Functional Insertion Screen for Hepatitis E Virus

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**Background:** Hepatitis E virus (HEV) infection is the most common cause of acute hepatitis and jaundice in the world. Our current understanding of the molecular virology and pathogenesis of hepatitis E is scarce, especially due to the lack of appropriate functional tools. Our study aims at developing tagged HEV genomes for live cell imaging and as a tool to investigate the viral life cycle.

**Methods:** A selectable subgenomic HEV replicon served as a template for random 15-bp sequence insertion using transposon-based technology. Viable insertions mapped along the replicase sequence were selected in a hepatoblastoma cell line.

**Results:** HEV replicons harboring viable transposon insertions in the Y domain, the hypervariable region (HVR) and the helicase domain of open reading frame 1 have been selected and are currently being further characterised. Functional insertion sites are being used to prepare replicon constructs and full-length viral genomes harboring antibody tags and fluorescent proteins.

**Conclusion:** The development of tagged functional HEV genomes should allow to track viral replication complexes in live cells and should yield new insights into the HEV life cycle.

O39

### Late Hepatitis B Reactivation Following DAA-Based Treatment of Recurrent Hepatitis C in an anti-HBc-Positive Liver Transplant Recipient

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**Background:** Hepatitis B virus (HBV) reactivation has been reported in HBV-hepatitis C virus (HCV) coinfecting patients treated with direct-acting antivirals (DAAs) for chronic hepatitis C (CHC).

**Case presentation:** A 58-year-old male underwent liver transplantation (LT) for end-stage cirrhosis due to CHC of genotype 1a in 2011. At the time of LT, he was positive for anti-HBc alone; HBsAg and HBV DNA were undetectable. The donor was negative for HBsAg, anti-HBc and HBV DNA. Recurrent hepatitis C was treated with pegylated-interferon- $\alpha$ 2a and ribavirin in 2012, followed by a relapse. In 2015, retreatment with ledipasvir/sofosbuvir for 12 weeks resulted in a sustained virological response. Fifty weeks after the end of DAA treatment, routine laboratory examination showed significant transaminase elevation. Diagnostic work-up revealed HBV reactivation, with positive HBsAg and very high serum HBV DNA. Retrospective testing found positive HBV DNA already at 38 but not at 25 weeks post-DAA treatment. Tenofovir was introduced upon documentation of HBV reactivation, with normalisation of liver function tests and negativation of HBV DNA. The patient is now well.

**Conclusions:** This case highlights the complex interactions between HBV and HCV in coinfecting patients and illustrates that HBV reactivation can occur even in low-risk patients and late after DAA-based treatment of CHC. Close and prolonged monitoring of HBV DNA appears to be indicated in this setting, especially in LT recipients.

O40

### Lymph node yield during pancreatic surgery - a distinct view

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**Background:** Pancreatic resection is the only chance for cure for pancreatic cancer patients. The relevance of lymphadenectomy is well established. However, the importance of lymph node (LN) yield is still ill defined given that most guidelines are based on a solitary threshold. We thought to assess the survival impact of LN yield as a continuous measure using advanced statistical modeling.

**Methods:** The population-based National Cancer Data Base from the United States was queried. All resected patients with adenocarcinoma of the pancreas (stage IA-IB) between 2004-2012 were included. First, patients were divided into two groups; LN yield of either 1-19 LNs or more for which multivariable adjusted cox regression was performed to assess overall survival differences. To account that lymph node yield is a continuous measure, jointpoint regression and covariance-balanced propensity score (PS-CB) analyses were performed.

**Results:** A total of 26,241 patients were included, mean age was 65.1 (SD: 11.0) years, 49.3% were female. Mean lymph node yield was 14.8 (SD: 9.3), 19,655 (74.9%) had 1-19 LN and 6,586 (25.1%) had  $\geq 20$  LN retrieved. Over time, resection rate of  $\geq 20$  LN increased from 13% in 2004 to 34.5% in 2012 ( $p_{trend} < 0.001$ ). Jointpoint regression revealed that the likelihood of a positive LN increased with 4.1% per collected LN up to a total of 8 LNs, while it was 0.7% per LN above. Overall 5-year survival was 19.7%. After multivariable adjustment, overall survival for patients with  $\geq 20$  LNs was better compared to their counterparts (HR 0.91, CI: 0.88-0.94,  $p < 0.001$ ). When analyzing the impact of LN yield on a continuous scale using PS-CB methods, survival continues to improve with an increasing number of LNs collected, even when stratified by tumor stage.

**Conclusion:** The current analysis emphasizes the importance of a careful LN dissection given a higher likelihood of a positive LN retrieval with increasing LN yield. Higher number of collected LNs translates directly into a survival benefit across all tumor stages.

O41

### Gut Microbial Changes in Inflammatory Bowel Disease Patients in Response to Biologic Therapy

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**Introduction:** The gut microbiome plays a central role in the pathogenesis and propagation of inflammatory bowel diseases (IBD) such as Crohn's disease (CD) and ulcerative colitis (UC). To determine whether the gut microbiome may predict responses to IBD therapy, we conducted a microbial profiling study of phenotypically well-characterized Swiss IBD patients treated with TNF- $\alpha$  agents and corticosteroids.

**Method:** 941 biopsy samples from 187 CD and 159 UC patients were processed and sequenced using the IonTorrent platform. Data were analyzed using QIIME pipeline and *phyloseq* in R and compared to individual treatment response.

**Results:** There is an overall significant reduction of species richness ( $\alpha$ -diversity) in CD samples and a reduced bacterial diversity ( $\beta$ -diversity) in all IBD patients. When samples are categorized with respect to therapy conditions, there is a significant difference at  $\beta$ -diversity level is observed. Several taxa including *Lachnospira*, *Roseburia*, *Ruminococcaceae*, *Collinsella*, *Sutterella*, *Lachnospiraceae* and *Phascolarctobacterium* are significantly changed among responders to treatments (stronger effect for TNF agents). This remains true when investigated for disease activity.

**Conclusion:** Treatment response to induction therapies such as TNF- $\alpha$  agents and steroids in IBD patients of the Swiss IBD cohort study is associated with several but consistent changes in microbiota composition. These could be identified as possible biomarkers to predict individual response to IBD therapy.

O42

**Treatment Satisfaction of Adult Eosinophilic Esophagitis Patients**

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**Background and aims:** Available treatment options for adult EoE patients include drugs (proton-pump inhibitors [PPI], swallowed topical corticosteroids [STC]), food elimination diets, and esophageal dilation. We aimed to assess EoE patients' satisfaction with different EoE-specific treatment modalities.

**Patients and methods:** Following 3 psychologist-guided focus groups with EoE patients, we created a questionnaire to assess treatment satisfaction with various therapies recalled over a period of 12 months (using the validated "Treatment Satisfaction Questionnaire for Medication" [TSQM], 52 items). The TSQM ranges from 0-100 points with 100 denoting "very satisfied".

**Results:** Patient response rate was 73.5% (108/147). In the last 12 months, 25.0%, 3.7%, 77.8%, 1.9%, 19.4%, and 13.0% were treated with PPI, STC (syrup), STC (powder), STC (spray), diet, and dilation, respectively. When asked about single most important criterion for the choice of therapy, 48.5%, 33.7%, and 11.9%, of patients chose the effect of treatment on symptoms AND esophageal inflammation, the effect of the treatment on the symptoms, and the effect of treatment on esophageal inflammation, respectively, as deciding factor.

Mean TSQM scales	PPI (n=27)	STC (n=84)	Diet (n=21)
Effectiveness	66.7	83.3	77.8
Side-effects	100	100	100
Convenience	88.9	83.3	50
Overall satisfaction	71.4	78.6	78.6
Average score	79.8	84.4	76.6

**Conclusions:** Adult EoE patients consider both effect of medication on symptoms as well as inflammation as most important criteria, when choosing EoE therapy. EoE patients appear to be 'satisfied' with PPI, STC, and dietary therapy.

**Systematic Analysis of Subepithelial Eosinophil Counts Increases Diagnostic Yield in Adults With Eosinophilic Esophagitis**

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**Background and aims:** For technical reasons, the histologic characterization of eosinophilic esophagitis (EoE)-specific alterations is almost exclusively based on those found in the esophageal epithelium, whereas little is known about subepithelial abnormalities. We aimed to systematically assess the nature of subepithelial histologic alterations, analyze their relationship with epithelial histologic findings, endoscopic features, and symptoms, and evaluate the diagnostic impact of subepithelial eosinophil counts in patients with an epithelial peak eosinophil count of <15/hpf.

**Methods:** We prospectively included in this cohort study adult EoE patients who underwent assessment of clinical, endoscopic, and histologic disease activity using scores.

**Results:** We included 200 EoE patients (mean age 43.5±15.7 years, 74% males) with a median peak count of 36 intraepithelial eosinophils/hpf [IQR 14-84]. The following histologic features were identified in the subepithelial layer: eosinophilic infiltration (median peak count of 20 eosinophils/hpf [IQR 10-51]), eosinophil degranulation (43%), fibrosis (82%), and lymphoid follicles (56%). Peak intraepithelial eosinophil counts were higher, identical, and lower when compared to the subepithelial layer in 62.5%, 7%, and 30.5% of patients, respectively. Subepithelial histologic activity correlated with epithelial histologic activity ( $\rho$  0.331,  $p < 0.001$ ), endoscopic severity ( $\rho$  0.208,  $p = 0.003$ ), and symptom severity ( $\rho$  0.179,  $p = 0.011$ ). Forty percent (21/52) of patients with <15 intraepithelial eosinophils/hpf had subepithelial peak counts of  $\geq 15$ /hpf.

**Conclusions:** Systematic assessment of subepithelial eosinophil counts can aid in diagnosing EoE in additional 40% of all patients with epithelial eosinophils <15/hpf.

PG1

**Endoscopic full thickness resection (EFTR) of colorectal neoplasms with the "Full Thickness Resection Device" (FTRD): Clinical experience from two tertiary referral centers in Switzerland.**

PG3

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**Background:** Endoscopic full thickness resection (EFTR) by the "Full Thickness Resection Device" (FTRD), has recently been introduced as a method to allow resection of certain lesions such as adenomatous polyps that would not be resectable by standard polypectomy techniques. We report our clinical experience with FTRD procedures, assessing technical success, completeness of resection (R0 status), rate of histologically proven FTR and safety.

**Patients & Methods:** Retrospective analysis of 33 consecutive patients with colonic polyps treated with FTRD from May 2015 to November 2016.

**Results:** Indications mainly were adenoma recurrence or residual adenoma with nonlifting sign after previous polypectomy. In the 31 cases amenable to EFTR, resection was en bloc and histologically complete (R0) in 87.9% (29/33) of patients. Histologically confirmed complete full thickness resection was achieved in 80.6% (25/31). Three post-procedure bleedings and one perforation were seen.

**Conclusion:** FTRD offers an additional endoscopic approach to treat nonlifting colorectal lesions. EFTR by FTRD appears to be feasible and efficacious in the resection of benign neoplasms of up to 30 mm in diameter and may be an alternative to surgery in selected patients. Given a significant rate of complications, safety is a concern and needs to be assessed in larger prospective studies.

PG2

**Double-balloon enteroscopy-assisted dilatation avoids surgery in majority of patients with small bowel strictures: a systematic review.**

PG4

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**Background:** At present there is a wealth of literature on the value of double balloon enteroscopy (DBE) in the management of small bowel bleeding. However, there is only few data regarding its role in small bowel (SB) strictures. We aimed to evaluate the therapeutic role and safety of DBE in SB strictures and to propose a standard approach to endoscopic balloon dilatation (EBD).

**Methods:** Systematic review of studies involving DBE in patients with SB strictures. Only studies limited to SB strictures were included and those with ileo-colonic strictures were excluded.

**Results:** In total 13 studies were included, in which 311 patients were dilated. The average follow-up time was 31.8 months per patient. The complication rate was 4.8% per patient and 2.6% per dilatation. Surgery was avoided in 80% of patients. After the first dilatation 38% relapsed of which 55% were treated with re-dilatation and the remainder required surgery.

**Conclusion:** DBE-assisted EBD offers safe and effective treatment of SB strictures. Surgery can be avoided in 80% of cases. In our study we propose a flow-chart representing a standard approach to SB strictures.

### Multicentre European Evaluation Of A Novel Technology (Blue Light Imaging) In The Diagnosis Of Small Colorectal Polyps

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**Background:** Fujifilm recently introduced a new technology – Blue Light Imaging (BLI) – which utilises powerful LED technology and short wavelength absorption of haemoglobin with no post processor digital reconstruction to enhance mucosal surface and vessel patterns. We investigated this novel concept concerning diagnostic ability of BLI in the optical diagnosis of diminutive colorectal polyps.

**Methods:** Images from a library of 32 polyps were used. 64 images with equal proportions of high definition white light (HDWL) and BLI were shown to a panel of 6 expert endoscopists (which were blinded to the proportion of adenomas) with experience in using image enhanced endoscopy. They independently classified each of the 64 images as adenoma or hyperplastic using the established NICE classification as no standard BLI classification exists yet. A level of confidence was assigned to each prediction.

**Results:** A total of 384 observations were made with an adenoma prevalence of 59.4%. The table below shows the sensitivity, specificity, NPV and PPV for adenoma detection on HDWL and BLI.

	HDWL	BLI
Sensitivity, % (95% CI)	70.2 (60.9-78.4)%	81.6 (73.2-88.2)%
Specificity, % (95% CI)	96.2 (89.2-99.2)%	96.2 (89.2-99.2)%
NPV, % (95% CI)	68.8 (62.4-74.6)%	78.1 (70.8-84.1)%
PPV, % (95% CI)	96.4 (89.7-98.8)%	96.9 (91.1-98.9)%

The diagnostic accuracy using BLI was significantly higher (109/119, 91.6%) for high confidence predictions compared to 75.6% (59/78) for predictions made with low confidence (p=0.002).

**Conclusion:** We have demonstrated the feasibility of using novel BLI technology in the optical diagnosis of small colorectal polyps. BLI improves the accuracy and sensitivity of endoscopic diagnosis with accuracy rates reaching 92% when high confidence predictions were made. These gains can be maximised by developing a dedicated BLI specific classification system and training module to enable its validation and subsequent application in clinical practice.

PG5

### Mucosal Dendritic Cells and Macrophages Express the G Protein Coupled Receptor 35

PG7

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**Background:** Although variants of the G protein coupled receptor (GPR35) are associated with inflammatory bowel disease (IBD) and primary sclerosing cholangitis, the function of GPR35 in the mucosal immune system is rather unknown.

**Method:** In order to identify the cells that express GPR35 a GPR35-tTomato reporter mouse line was generated. **Results:** *Gpr35* expression increases from the upper to the lower gastrointestinal tract, and the chemokine *Cxcl17*, who is ligand of GPR35, is expressed along the entire gastrointestinal tract. Analysis of purified cell population revealed that intestinal epithelial cells express *Cxcl17*, whereas intestinal epithelial cells, dendritic cells and macrophages express *Gpr35*. In contrast to the small intestine the majority of dendritic cells in the large intestine are CD103-negative dendritic cells, which are characterized by high GPR35 expression in contrast to CD103-positive dendritic cells. During Dextran Sodium Sulfate (DSS) induced colitis, cells with high GPR35 expression infiltrate inflamed lesions. **Conclusion:** Dendritic cells, macrophages and epithelial cells express GPR35 as demonstrated by analysis of a newly generated GPR35-tTomato reporter mouse line. The importance of GPR35 for the homing of mononuclear cells into the intestine will be further studied and may reveal why CD103-negative dendritic cells are preferentially located in the large intestine.

### Development of a Conditional Mouse Line to Study Nutritional Requirements of Monocytes and Macrophages

PG6

### Treatment of a perforated cholecystitis into a congenital liver cyst with EUS-guided liver abscess drainage

PG8

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**Background:** Intestinal mononuclear phagocytes are extending processes into the intestinal lumen and are in direct contact with the chymus, but the importance of constituents of the chymus for appropriate function of mononuclear phagocytes is not known. **Methods:** In order to study nutritional requirements for the appropriate function of phagocytes, we generated a conditional KO mouse, in which mononuclear phagocytes lack CD98hc expression. **Results:** high CD98 expression levels with comparable expression levels in the bone marrow, peripheral blood and mucosal tissues characterize monocyte-derived macrophages and their progenitors. By contrast, embryonic macrophages are characterised by low CD98 expression, but embryonic-derived macrophages, such as Kupffer cells and Langerhans cells acquire CD98 during their development. To study the effect of inflammation on CD98 expression by macrophages, colitis was induced by giving Dextran Sodium Sulfate (DSS) to the drinking water, which did not show significant difference on CD98 expression. Injection of tamoxifen into *Slc3a2<sup>tm1.1Yait</sup> x Cx3cr1<sup>tm2.1(cre/ERT2)litt</sup>* mice silenced CD98 expression by CX3CR1+ monocyte-derived macrophages. **Conclusion:** Monocyte-derived macrophages and their precursors as well as embryonic-derived macrophages with exception of embryonic macrophages have high CD98 expression. The development of a new conditional mouse line allows us to study this molecule in unmanipulated mice and during inflammation.

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**Background:** Interventional radiology-guided percutaneous drainage is the standard therapy of hepatic abscesses followed by the surgical approach. However neither all hepatic abscesses are amenable to this therapy nor are all patients candidates for surgical drainage, mainly due to the relative high complication rate of the aforementioned techniques. EUS-guided liver abscess drainage (EUS-LAD) is an emerging alternative for hepatic abscess drainage in selected patients.

**Case description:** We report the case of a 78 year-old female with a Klatskin type I tumor, who was referred to our hospital due to sepsis caused from a perforated calculous cholecystitis into a congenital liver cyst with consequent development of an intrahepatic abscess. The percutaneous approach was not feasible in the presence of marked ascites. Therefore EUS-LAD was performed transgastrically with placement of a fully covered self-expanding metal stent (SEMS) through the left liver lobe into the abscess cavity.

**Results:** Hemorrhagic purulent content was successfully drained into the stomach. In conjunction with antibiotic therapy the abscess cavity decreased in size and the patient had a prompt and full recovery and was able to receive palliative chemotherapy. There were no procedure related complications.

**Conclusions:** EUS-guided hepatic abscess drainage is a feasible and safe alternative technique. It can provide complete drainage, symptom relief and has a high clinical success rate. Because of a shortened hospital stay and low adverse event rate compared to the percutaneous or surgical approach, EUS-LAD could be considered more often even as a first-line treatment in selected patients.

### Clinical characteristics and treatment outcome of Eosinophilic Gastroenteritis: Analysis of the Swiss Database SEED

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**BACKGROUND:** Eosinophilic gastroenteritis (EGE) is a rare eosinophil-predominant inflammatory process that can involve any part of the gastro-intestinal tract. EGE is a diagnostic challenge for the clinician, little is known about the long-term natural history and treatment strategies including the use of biologics. The purposes of this study were to describe clinical features and natural course of EGE as well as the response to several treatment modalities.

**METHODS:** In this observational single-center study, we retrospectively analyzed clinical features and treatment of 21 patients with confirmed diagnosis of EGE at the Swiss EoE Clinic in Olten, Switzerland. Patients fulfilling the established diagnostic criteria of EGE, in particular 1) recurrent gastrointestinal symptoms, 2) dense eosinophilic infiltrates in biopsies taken from the GI tract or high eosinophil numbers in peritoneal fluid and 3) exclusion of other conditions leading to gastrointestinal eosinophilia, were included in this analysis.

**RESULTS:** In our cohort 62% of the diagnosed patients with EGE were female with a median age at diagnosis of 41 years. The predominant symptoms were abdominal pain (100%), diarrhea (47%), nausea (24%), vomiting (24%) and bloating (23%). Endoscopic alterations were minimal or even absent. In 75% of patients eosinophilic infiltration was seen in more than one segment. For treatment corticosteroids were used in 18/21 (85%), budesonide in 8/21 (38%), proton-pump inhibitors in 7/21 (33%), TNF $\alpha$  inhibitors in 3/21 (14%) and vedolizumab in 4/21 (19%) patients. The majority of patients responded rapidly to treatment with corticosteroids, whereas the TNF $\alpha$  inhibitors showed only minimal benefit. Of note, vedolizumab induced at least a partial remission.

#### CONCLUSIONS:

In this EGE-cohort we found that each segment of the GI-Tract was involved with a predominance of the esophagus and the large intestine. Symptoms were non-specific. The absence of obvious endoscopic abnormalities is suggestive for structured biopsy sampling to prevent misdiagnosis. Corticosteroids were efficient in bringing the disease in remission, whereas TNF $\alpha$  inhibitors were not convincing. Treatment with the integrin blocker Vedolizumab merits further evaluation.

PG9

An unusual cause of severe recurrent gastroenteritis

PG11

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#### Background

An 82 years-old man was hospitalized for the 5<sup>th</sup> time for vomiting, diarrhea and hypotension. A close look at the patient's record showed that his antihypertensive drug (olmesartan) had always been suspended during hospitalization. We did a challenge test with olmesartan. After 1 hour, he suffered from vomiting and diarrhea. C4 complement, C1 esterase inhibitor and tryptase were normal. We retained the diagnosis of visceral angioedema induced by olmesartan.

#### Methods

We searched PubMed, UpToDate and Google Scholar.

#### Results

We found sparse literature about angiotensin II receptor blocker-induced intestinal angioedema. It is better described with angiotensin converting enzyme inhibitors. Diagnostic criteria are: timing with drug intake, typical symptoms and CT images, normal C1 esterase inhibitor and C4 levels and absence of alternative diagnosis.

#### Conclusion

This case report reminds of this rare but potentially severe side effect. Regarding potential drug side effects, careful anamnesis and retrospective medical record study, can be more helpful than repetitive blood sampling and extensive imagery.

### Proximally migrated pancreatic stent extraction assisted by endosonographic-guided pancreaticogastrostomy

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**Background:** Prophylactic pancreatic stents (PS) are increasingly used for patients with difficult endoscopic biliary access. Different transpapillary techniques are available for proximally migrated PS. We describe a novel endosonographic (EUS)-guided transgastric rendez-vous technique (TGRT) in a patient with migrated PS and post-endoscopic retrograde cholangiopancreatography (ERCP) necrotizing pancreatitis.

**Case description:** A 36 year old patient with biliary pancreatitis underwent ERCP with choledochal stenting after transpancreatic septotomy and single pigtail pancreatic stenting. Two month later, multiple transpapillary extraction maneuvers of the accidentally proximally migrated, kinked PS failed. Evolution of pancreatitis and walled of pancreatic necrosis (WOPN) resolved after lumen-apposing metal stent (LAMS)-gastrocystostomy and TGRT with pancreatic duct dilatation followed by transgastric PD plastic stenting. The migrated PS was extracted transpapillary by a dormia basket after further dilatation of PD stenosis one month later.

**Discussion:** PS are increasingly used for post-ERCP pancreatitis prophylaxis and difficult biliary cannulation. Extraction maneuvers of migrated PS can be difficult especially for pigtailed stents and can lead to additional pancreatic damage. WOPN offers new possibilities for TGRT treating the acute inflammation and supporting stent extraction.

PG10

### Cohort Profile: The Swiss Eosinophilic Esophagitis Cohort Study (SEECs)

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**Background and aims:** Eosinophilic Esophagitis (EoE) is diagnosed with increasing incidence and has a current prevalence of 1 in 2,000 persons in Switzerland. The Swiss EoE Cohort Study (SEECs) is part of the Swiss IBD Cohort Study and collects, starting in 2016, longitudinal data on adult patients with eosinophilic esophagitis and proton-pump inhibitor-responsive esophageal eosinophilia (PPI-REE) to better characterize natural history, long-term treatment outcomes, safety aspects, EoE-specific quality of life, and socio-economic impact.

**Patients and methods:** EoE Patients are included using validated instruments for capture of symptoms, EoE-specific quality of life, endoscopic and histologic activity and then followed prospectively once a year. Gastrointestinal biopsies and blood samples are stored at the biobank of Bern University, as well as material from healthy controls and gastro-esophageal reflux disease patients. SEECs is supported by the Swiss National Science Foundation. Approval from the major Swiss IRB's has been granted.

**Results:** As of May 2017, 102 patients with EoE and PPI-REE, 11 with GERD, and 12 esophagus-healthy controls have been included. Recruitment performance is on track with anticipated 70 patients per year with EoE and PPI-REE. Recruitment sites will be increased in 2017 by collaboration with gastroenterologists in private practice. Recruitment of pediatric EoE patients is planned in a second phase.

**Conclusions:** SEECs is on track with respect to patient recruitment targets. Data capture instruments can serve as a model for data acquisition in other countries and thereby foster international collaborations.

PG12



**Adenoma Detection Rates in Colonoscopies at the University Hospital of Basel in 2015**

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**Background:** Training of physicians as gastroenterologists and high quality of patient care is of importance for tertiary centers. **Methods:** In order to investigate whether the adenoma detection rate (ADR) depends on the training level of the examining physician all colonoscopies (n=1707) in 2015 were analyzed in a retrospective observational study for the presence of adenomas at the University Hospital of Basel. **Results:** In 839 out of 1707 colonoscopies (49%) were polyps removed. The ADR over all colonoscopies was 32%. In 25 examinations (2%) the presence of colorectal cancer was detected. Screening colonoscopies (no symptoms of the patients, age between 50 and 70 years, negative family history for colorectal cancers) were carried out in 31 patients. The ADR in screening colonoscopies was 74%. Because of the low case numbers meaningful analysis of the ADR for physicians depending on their training level was not possible. Significant differences between physicians depending on their training levels were not observed over all colonoscopies carried out in Basel for the year 2015. **Conclusion:** Overall, we observed an ADR > 20% in all colonoscopy. Training of assistants did not significantly influence the ADR in our patient group.

PG13

**Endoskopische Behandlung von akuten Blutungen mit einem Over-The-Scope Clip (OTSC)**Alexander Braun, Sarah Peter  
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**Hintergrund:** Der OTSC (Fa. Ovesco) ist ein endoskopisches Clip-System, das zur Behandlung von Blutungen, Fisteln, Hohlorganperforationen und postoperativen Komplikationen verwendet wird. Diese Untersuchung beschreibt das endoskopische Vorgehen zur Behandlung von akuten Blutungen im Gastrointestinal Trakt (GIT) mittels eines OTSC.

**Material und Methoden:** Innerhalb von sechs Jahren (2011 bis 2017) wurden 48 Patienten (Median 75,5 Jahre; 61–92 Jahre; m = 29; w = 18) bei akuter Blutung notfallmässig mit einem OTSC behandelt. Es erfolgten jeweils 34 Behandlungen im oberen – und 14 Behandlungen im unteren GIT. 18 Patienten hatten eine Forrest Ia–Blutung, 22 Patienten hatten eine Forrest Ib–Blutung und 8 Patienten zeigten eine Forrest IIa–Blutung. Für die OTSC–Platzierung wurde eine endoskopische PE-Zange (Boston Scientific) verwendet. Es erfolgten keine weiteren lokalen Therapien. Alle OTSC–Applikationen wurden vom gleichen Untersucher durchgeführt.

**Ergebnisse:** Bei allen 48 Patienten konnte eine erfolgreiche OTSC–Applikation und somit auch eine primäre Hämostase erreicht werden. Keine endoskopische Notfalluntersuchung mit OTSC–Versorgung dauerte länger als 20 Minuten. 26 Patienten (15 Fla, 9 Fib) erhielten eine Follow-up-Endoskopie nach 2 Tagen, wobei sich der Clip in situ zeigte und keine Blutungsstigmata gesehen wurden. Die restlichen 22 Patienten wurden bei klinisch unauffälligem Verlauf nicht unmittelbar nachuntersucht.

**Schlussfolgerungen:** Die Anwendung des OTSC-System in der Notfall-Endoskopie bei akuten Blutungen ist eine sichere und sehr effektive Behandlungsmethode mit primärer Hämostase. Die Anwendung des OTSC-System ist mit einer kurzen Untersuchungszeit verbunden.

PG15

**Effectiveness of Vedolizumab Induction Therapy in IBD Patients**

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**Background:**

Vedolizumab (VDZ) is a new gut selective  $\alpha 4\beta 7$ -integrin-antibody for the treatment of moderate to severe inflammatory bowel disease (IBD). We investigated the effectiveness and safety of VDZ in the treatment of patients with Crohn's Disease (CD) and Ulcerative Colitis (UC).

**Methods:**

All CD and UC patients at the University Hospital Basel (USB), who were treated with VDZ, between March 2015 and March 2016 (n=20) were included in this single center analysis. All patients were initially treated with an induction scheme (VDZ 300mg 0,2,6 weeks) followed by a maintenance treatment (VDZ 300 mg every 8 weeks). Disease activity was assessed with CDAI score and fecal calprotectin ( $\mu\text{g/g}$  stool) for CD patients, as well as partial MAYO score and fecal calprotectin ( $\mu\text{g/g}$  stool) for UC patients. The primary endpoint was clinical remission after 22 weeks of VDZ treatment. Secondary endpoints were to assess change of therapy and safety profile of VDZ.

**Results:**

At week 22, 10/14 UC patients (71.4%) and 2/6 CD patients (33.3%) were in clinical remission according to the MAYO and CDAI score. Whereas only 4/14 UC patients (28.6%) and 1/6 CD patient (16.6%) had FC values <150  $\mu\text{g/g}$ . 6/20 patients (30%) discontinued VDZ therapy until week 22 because of inadequate response, relapse or persistent extra intestinal symptoms.

**Conclusions:**

The intestine-selective  $\alpha 4\beta 7$ -integrin antibody VDZ was effective to induce clinical remission in approximately one third of CD and two third of UC patients. Despite therapy discontinuation in one third of the study population, the results implicate VDZ as an alternative treatment option.

PG14

**Effects of cervical transcutaneous electrical vagus nerve stimulation on esophageal contractility: A pilot trial**

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**Background:** Transcutaneous electrical vagus nerve stimulation (VNS) is applied as therapy for headache and hypertension. Since esophageal motility is controlled by the vagus nerve VNS may have an effect on esophageal contractility.

**Methods:** A pilot trial of VNS was performed in 11 asymptomatic volunteers. Standard esophageal high resolution manometry (ZVU®, Sandhill Scientific, Highlands Ranch, Colorado) was performed with and without VNS (gammaCore®, electroCore, Basking Ridge, NJ) in randomized order. Distal contractile integral (DCI), percentage of intact contractions and integrated relaxation pressure of the lower esophageal sphincter (IRP) were assessed by an investigator blinded to VNS sequence.

**Results:** VNS did not have a significant effect on esophageal contractility (DCI, % intact contractions, IRP). A trend towards higher DCI with VNS was observed in 3 subjects with ineffective esophageal motility (IEM) (Tab. 1). No adverse events occurred.

	n	DCI <sub>mmHg.s.cm</sub> (IQR)		p
		VNS off	VNS on	
Normal motil.	8	1552 (1163-1942)	1595 (1221-2053)	0.42
IEM	3	242 ( 58- 581)	356 ( 120- 789)	0.14
All subjects	11	1301 ( 586-1838)	1388 ( 728-1890)	0.24

**Conclusion:** Transcutaneous VNS had no significant immediate effect on esophageal motility in asymptomatic volunteers. Possible improvement of esophageal hypocontractility by VNS should be investigated in a larger trial.

PG16

### Long term effects after sphincterotomy in patients with suspected functional sphincter disorder: role of Nardi-Test

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Endoscopic sphincterotomy can be considered in patients with suspected functional biliary sphincter disorder, especially in prior sphincter Oddi dysfunction type I and less in type II. However it is not yet well established whether in patients with sphincter dysfunction of pancreatic type an endoscopic sphincterotomy is indicated or not. We selected nine patients, four of them after cholecystectomy, with suspected biliary or pancreatic sphincter dysfunction by applying a Nardi-Test with neostigmine plus morphin-stimulation and sequential MRCP, serum lipase and clinical evaluation (development of typical pain). Seven of them underwent an endoscopic sphincterotomy and they report a great improvement of the symptoms in a follow-up time of up to 2 years after the treatment. Regarding procedure related complications one patient develop post-ERCP pancreatitis, but recovered without long term complications. The two patients with typical symptoms dilated pancreatic duct without stones or other structural abnormalities in a serial MRCP following morphine-neostigmine provocation, who did not undergo an interventional treatment, are still symptomatic.

Conclusion: In patients with suspected functional sphincter Oddi disorder a Nardi-Test could help to select patients that benefit most from an endoscopic sphincterotomy. Larger and randomized trials are needed to proof this convincingly.

PG17

### Impedance planimetry (EndoFLIP®) at the esophago-gastric junction distinguishes neuromuscular disorders from fibrotic lesions in dysphagia patients.

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**Background:** Aim of this study was to evaluate whether neuromuscular or fibrotic etiology of impaired esophago-gastric junction opening (EGJ) can be distinguished by distensibility tests using the EndoFLIP® impedance planimetry device.

**Methods:** EGJ diameter in mm and the distensibility index (DI, cross sectional area/intrabag pressure) in mm<sup>2</sup>/mmHg acquired in 35 dysphagia patients were analyzed retrospectively. Neuromuscular disorders (NM) or fibrotic lesions (F) were diagnosed by endoscopy, HR-manometry and fluoroscopy.

**Results:** NM group patients had achalasia (7), hypertensive lower esophageal sphincter (4) and manometric outflow obstruction (9). F group patients had eosinophilic esophagitis (4), Schatzki-ring (5) and peptic stenosis (6).

	NM (n=20, 4♀)	F (n=15, 1♀)	p-value
Age (yrs)	42.1 ± 19.4	52.9 ± 17.8	n.s.
EGJ Ø 30 ml	6.2 (5.0- 7.9)	7.2 (6.5-10.0)	0.007
EGJ Ø 50 ml	11.6 (8.7-12.7)	9.3 (8.7-10.7)	n.s.
DI 30 ml	1.4 (0.9 - 2.4)	2.3 (1.7 - 3.0)	n.s.
DI 50 ml	2.1 (1.5 - 2.7)	1.3 (0.9 - 1.6)	n.s.
DI 50ml/DI 30 ml	1.4 (1.0 - 2.0)	0.6 (0.5 - 0.9)	0.001

Table 1: Impedance planimetry results

**Conclusion:** In NM patients DI tended to increase with balloon filling volume, whereas a decrease was noted in F patients. The ratio of DI at 50ml to DI at 30 ml with a cut-off at 1.0 can be used as new parameter to distinguish neuromuscular disorders from fibrotic lesions at the EGJ in dysphagia patients.

PG19

### Non-invasive and semi-invasive methods for the diagnosis and clinical surveillance of Eosinophilic Esophagitis (EoE)

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#### Objective

For diagnosis and monitoring of EoE an endoscopic intervention with histological assessment is required. In an exploratory approach we evaluated proteins released by eosinophils and calprotectin for its possible application in EoE disease monitoring. As semi-invasive test approach the Oesotest® was used, initially developed for screening of Barrett's Oesophagus. It is a capsule attached on a string comprising a sponge which is swallowed and then retracted to sample superficial epithelial cells.

#### Methods

In this exploratory study we assessed calprotectin in the stool of 16 patients with active EoE before and after an eight-week treatment with topical steroids. In addition, in 6 patients with active EoE and 5 healthy controls eosinophil-derived proteins including EDN (eosinophil-derived neurotoxin), ECP (eosinophil cationic protein) and CLC (Charcot-Leyden crystal protein) were measured by ELISA in stool samples and string and sponge eluates from the Oesotest®.

#### Results

Calprotectin proved to be increased in stool samples in EoE patients compared to healthy controls (p=0.03). In 11 out of 16 EoE patients decreasing fecal calprotectin values were observed after an eight-week treatment with topical steroids (p=0.019). In the sponge eluates, EDN values were significantly elevated in EoE patients with active disease (p=0.004). CLC levels in the sponge were on average higher in the EoE group (mean ± SD, 300.2 µg/ml ± 320.8 µg/ml) than in the healthy group (mean ± SD, 120.3 µg/ml ± 64.6 µg/ml), but statistical significance was not reached. The other eosinophil-derived proteins and calprotectin were not significantly elevated in EoE patients. Eluates of the string did not show any differences between patients with EoE and unaffected controls.

#### Conclusions

Calprotectin in the stool and EDN in the sponge of the Oesotest® could be potential non-invasive markers for assessment of disease activity in patients with EoE. Whether these proteins are suitable to replace endoscopy in the diagnostic and therapeutic process of EoE remains to be evaluated in larger prospective studies

PG18

### Endoscopic removal of intrahepatic intraductal papillary neoplasm of the left biliary duct (IPNB) via endoscopic ultrasound-based gastro-hepaticostomy (EUS-HGS)

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Intraductal papillary neoplasm of the bile duct (IPNB) are rare biliary tumors in western countries with unknown etiology and current treatment strategies usually involve surgical resection. Here we report the case of a 78 year old female patient initially presenting with painless jaundice and left-sided cholestasis suspicious for cholangiocellular carcinoma due to localized stricture proximal to the separation of the left hepatic bile duct. ERCP with Spy-Glass cholangioscopy revealed an intraluminal sessile polyp and Spy-bite biopsy showed an IPNB with low-grade dysplasia. Due to severe comorbidities with autoimmune myopathy associated with proximal tetraparesis as well as metabolic syndrome, diabetes mellitus and severely reduced physical fitness the patient was considered inoperable. Since the lesion was not removable by transpapillary Spy-glass cholangioscopy, we performed an interventional EUS placing a Hepatico-Gastrostomy (HGS: 60 mm, fully-covered-self-expanding metal stent) in order to get access to the left biliary system. 6 weeks later the stent was removed and utilizing an ultra-slim endoscope a direct cholangioscopy via the HGS was performed. Under direct endoscopic endoluminal visualization the polyp was removed with a 10 mm monopolar snare and remnants ablated with argon-plasma coagulation. Histology revealed an IPNB with low-grade dysplasia without any invasive features excluding malignancy. The patient has been dismissed shortly after the procedure and is doing fine since. Conclusion: EUS-based HGS can be considered a novel alternative approach for interventional removal and/or ablation of biliary intrahepatic left-sided pre-/neoplastic lesions. Especially in inoperable patients or with altered anatomy this new technique offers a wide spectrum of treatment options in different hepatobiliary diseases.

PG20

### Caught on camera: yellow jacket found incidentally during colonoscopy

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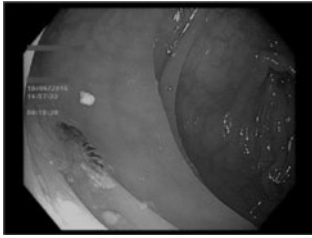
<sup>2</sup>Department of gastroenterology Spital Thun

A 62-year-old healthy woman was referred by her primary physician for colorectal cancer screening. In the family history a grandmother and a cousin died of colon cancer. The patient was asymptomatic.

Bowel preparation was done using 2l of polyethylene glycol the evening prior to screening colonoscopy. The procedure was uncomplicated with no mucosal pathology, however an insect was found in the descending colon.

The patient couldn't remember swallowing a wasp.

Few cases of finding insects in the gastrointestinal tract have been described, most cases in the upper gastrointestinal tract.



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PG21

### Vitamin D status in patients with Inflammatory Bowel Disease in comparison to controls: a cross sectional study.

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#### Abstract

##### Background and aim

Vitamin D plays a main role in the bone metabolism but increasing importance has been shown for chronic immune related diseases. Low vitamin D levels might be associated with disease activity and inflammatory markers in patients with inflammatory bowel disease (IBD). In our study we assess 25-Hydroxy-Vitamin D (25-OH-D3) levels in patients with IBD to controls with Irritable Bowel Syndrome (IBS).

##### Methods

In total 181 patients, 156 with IBD (99 Crohn's Disease (CD) and 57 Ulcerative Colitis (UC)) and 25 in the control group with IBS were included in our prospective cross sectional study. The 25-OH-D3 level in the blood of IBD patients was compared to the control group. Evaluation included clinical data, assessment for inflammatory markers in blood and stool. Disease activity was measured by using Harvey Bradshaw Index (HBI) for CD and Modified Truelove and Witts Severity Index (MTWSI) for UC.

##### Results

In total 58/99 (58.6%) patients with CD and 25/57 (44.6%) with UC had a low 25-OH-D3 level (<50nmol/l). Significantly lower 25-OH-D3 levels were observed for CD patients when compared to IBS controls (p=0.018); whereas no difference was seen for UC. There was a significant inverse correlation between CRP and fecal calprotectin (>100ug/g) for CD (p=0.025), but not for UC patients. Patients with CD showed also an inverse trend between the disease activity (HBI-score) and 25-OH-D3 levels (p=0.074). A seasonal difference for 25-OH-D3 levels in CD was observed in the spring months (april-june), when compared to summer (july-september) as the reference value. No associations were observed for physical activity and disease duration for both CD and UC.

##### Conclusion

A high percentage of patients with IBD showed insufficient 25-OH-D3 levels when compared to controls and suggests careful monitoring for 25-OH-D3 and adequate substitution especially of patients with inflammatory activity.

PG23

### Radiologic, Endoscopic and Functional Patterns in Patients with Symptomatic Gastroesophageal Reflux Disease after Roux-en-Y Gastric Bypass

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#### Background:

Roux-en-Y Gastric Bypass (RYGB) is considered as gold standard in treatment of morbid obesity and Gastroesophageal Reflux Disease (GERD). Resolution of GERD-Symptoms is reported to be around 85-90%. So far, data on evaluation for persistent GERD after RYGB is scarce.

#### Methods:

Prospective data of patients evaluated for persistent GERD with a history of RYGB (01/12-12/15) were reviewed.

#### Results:

Of 47 patients, 44(94%) presented with typical GERD, 18(38%) with obstructive, 8(17%) with pulmonary symptoms and 21 (45%) with pain. Interval post-RYGB was a median 3.8y(min 0.8-max 12.6), median age 26.2y(19.1-65.3). Median total weight loss was 34.4% (14.2-56.7).

Gastro-gastric fistulae were seen in 2(4%) and hiatal hernias in 25 patients(53%); gastric pouches too large in 5(11%). 12(26%) had esophagitis >LA grade B. pH-manometry was performed in 44 patients(94%): 8 had aperistalsis(18%), 9(19%) ineffective esophageal motility, 26(55%) hypotensive LES; 27(61%) increased esophageal acid exposure and 30(68%) increased number of reflux episodes, of which 21(70%) had positive symptom association.

#### Conclusions:

The evaluation for persistent GERD after RYGB revealed a high percentage of hiatal hernias, hypotensive LES and other severe esophageal motility disorders. These findings might have an influence on hiatal hernia closure concomitant to RYGB and the role of pH-manometry in the preoperative bariatric assessment.

PG22

### Endoscopic submucosal dissection and endoscopic mucosal resection for treatment of high grade dysplasia and adenocarcinoma in Barrett's esophagus: a case series.

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**Background:** Superficial adenocarcinoma and high grade dysplasia with visible lesions in Barrett's esophagus (BE) should be resected either by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) according to international guidelines. We report our preliminary experience of esophageal ESD and EMR over a one year period.

**Methods:** From July 2016 to February 2017, ten patients: median age 65 years [50-82], suffering of high grade dysplasia lesions or superficial adenocarcinoma developed on BE were consecutively treated by EMR or ESD. For lesions ≤ 15 mm, EMR was performed and ESD for lesions > 15 mm. All ESDs were performed by one experienced endoscopist (VL). The first control endoscopy was performed at 3 months, when R0 resection was achieved.

**Results:** Seven ESDs were performed with the tunnel technique using a DualKnife, all were en bloc and R0. Median lesion size was 4 cm [2.6 - 6.3], median intervention time was 40 min [37-100]. Three EMR were performed by cap technique with two monobloc resections. All of them were R0 as well. The depth of invasion according to the Paris classification of superficial neoplastic lesions was for ESD: 1x m2, 1x m3, 3x sm1, 2x sm2 and for EMR: 2x m2 and 1x sm1. The two patients with sm2 and lymphatic invasion and one patient with a squamous compound inside the resection required esophagectomy. No major peri and postprocedural complications were observed. Mean hospital stay was 2.5 days [2-4].

**Conclusions:** Esophageal ESD is a safe technique if performed by experienced endoscopists. With a high rate of R0 resection, ESD appears to be the first choice treatment for resection of superficial BE neoplasia (high grade dysplasia and adenocarcinoma) larger than 15 mm.

PG24

### Comparison of two bowel preparations for colonoscopy Moviprep and Citrafleet in daily practice

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**Background:** The success of any colonoscopy depends upon the quality of bowel preparation. Low volume preps (Moviprep with 2 l, CitraFleet with twice 0.15 l) are increasingly used. The scope of our study was to evaluate possible differences between the two products and the type of application (e.g. same day or split dosing) in routine gastroenterology.

**Methods:** From February 2015 through December 2016 we tested two types of bowel preparation (CitraFleet and Moviprep) in two different ways of application as split (1<sup>st</sup> Dose 8 pm the day before; 2<sup>nd</sup> Dose 4-6 hours before colonoscopy) or same day dosing (1<sup>st</sup> Dose 8 am the day of colonoscopy; 2<sup>nd</sup> Dose 4 hours before colonoscopy) in a typical colon carcinoma screening population of a private practice. We compared 450 randomly assigned CitraFleet cases with 1111 patients taking Moviprep. The efficacy of the two regimens was judged according to Boston bowel preparation scale (BBPS).

**Results:** The BBPS Score (best score of 9) for Moviprep was 7.2, for CitraFleet 7.1 (p=0.03). The Scores for the right colon were 2.3 for CitraFleet and 2.3 for Moviprep, for the transverse colon 2.3 vs 2.4 respectively and 2.4 vs 2.4 for the left colon. The two groups slightly differed in average age (61 years for CitraFleet vs 66 years for Moviprep) and in gender (42% males vs 51%) - with identical BMI (mean 25). The effect of gender, age and obesity on quality of preparation was negligible (R<sup>2</sup> < 1%). Split dose or same day dosing did not significantly differ with 7.2 vs 7.2.

**Conclusion:** Our data revealed no clinically relevant difference neither for split or same day dosing nor for the two preps used, especially not in what concerns cleaning of the right colon.

PG25

### Bouveret's syndrome - case series

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**Background:** Bouveret's syndrome is a rare complication resulting from gallstone disease due to biliodigestive fistula with gastric outlet obstruction. There are no well established recommendations for this rare condition. We describe our experience with endoscopic treatment options and propose a structured approach.

**Methods/Results:** 6 cases in 3 Swiss hospitals from 2016-2017

Pat. N°	Sex	Age (at intervent.)	Location	Procedure	Pre-intervent. CT scan
1	Female	83	Duodenum	Direct stone extraction	Yes
2	Female	93	Duodenum	EHL with partial lithotripsy and reconstitution of transit	No
3	Female	92	Duodenum	Direct stone extraction	No
4	Female	80	Duodenum	EHL with partial lithotripsy, laparoscopic gastrostomy	Yes
5	Male	83	Duodenum	EHL with complete lithotripsy, spontaneous passage	Yes
6	Male	70	Sigmoid	EHL with complete lithotripsy, spontaneous passage	No

Electrohydraulic Lithotripsy (EHL)

**Conclusion:** In 4 of 6 cases we achieved a complete endoscopic stone removal. We propose a pre- interventional CT scan as necessary basis for treatment decision. Surgery should be considered as first line treatment. For an endoscopic approach it is substantial to know if the gallstone has completely migrated to the GI-tract or is still fixed to the fistula. In case of complete migration to the GI-tract direct extraction can be tried; otherwise lithotripsy is indicated.

PG27

### Lumen-Apposing Metal Stents for Drainage of Pancreatic Fluid Collections: Experience From Two Non-University Centers in Switzerland

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**BACKGROUND:** Pancreatic pseudocysts (PP) and walled-off pancreatic necrosis (WOPN) are common complications of acute and chronic pancreatitis. Lumen-apposing metal stents (LAMS) are a promising option in the management of pancreatic fluid collections. **METHODS:** We evaluated all patients having undergone EUS-guided drainage of PP or WOPN using LAMS at two non-university centers retrospectively. Outcome was classified into complete resolution (CR) (size <2cm), partial resolution (PR) and non-improvement (NI). **RESULTS:** Fifteen patients underwent EUS-guided drainage with LAMS between December 2015 and December 2016 (median age 55.5y [range 38.7-71.5], median BMI 26.9kg/m<sup>2</sup> [range 15.2-34.0], median size of pancreatic fluid collection 7.0cm [range 3-12], median hospital stay 11d [range 2-40], median follow-up 27.0 weeks [range 6.3-57.0]). Five patients were females (33.3%). Ten patients underwent drainage for WOPN (66.7%), 5 patients for PP (33.3%). Pancreatitis was caused by alcohol (7/15, 46.7%), or impacted gallstones (6/15, 40.0%). Two cases were idiopathic (2/15, 13.3%). Technical success rate was 93.3% (14/15). In 1 patient, immediate dislocation of LAMS resulted in gastric perforation, which could not be completely closed by an over the scope clip and required surgery. Post-interventional, procedure-related complications were reported in 2 cases (13.3%): stent-induced arrosion of a posterior cystic wall vessel led to upper gastrointestinal bleeding and stent removal at day 7 in 1 case, while another patient showed mild aggravation of pancreatitis at day 6. Nine of the 15 patients needed additional direct endoscopic necrosectomy (6 with 1, 2 with 2 and 1 with 4 interventions). In all of the 14 patients with technical success, LAMS was removed after a median of 53 days (range 8-161). Ten of these 14 patients showed complete resolution (71.4%), while in 4 patients at least partial resolution of fluid collection was reported (28.6%). **CONCLUSION:** Endoscopic drainage of PP and WOPN using LAMS has a high technical success rate and seems to be effective for treatment of pancreatic fluid collection.

PG26

**Safety of glecaprevir/pibrentasvir in adults with chronic genotype 1-6 hepatitis C virus infection: an integrated analysis**

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**Background and Aims:** The direct-acting antivirals (DAAs) glecaprevir (an NS3/4 protease inhibitor identified by AbbVie and Enanta) and pibrentasvir (an NS5A inhibitor) were developed as a combination regimen (G/P) to treat adults with chronic hepatitis C virus (HCV) infection due to genotypes (GTs) 1-6 with compensated liver disease. In a large registrational program, G/P achieved sustained virologic response rates of ≥95% and low rates of virologic failures in most populations evaluated across all major GTs. We report the integrated safety results from patients enrolled in phase 2 or 3 studies. **Methods:** Key inclusion criteria from 8 multicenter, phase 2 or 3 clinical trials included in this analysis were age ≥18 years, compensated liver disease, and treatment-naïve or treatment-experienced status. Exclusion criteria were hepatitis B virus co-infection and creatinine clearance <50 mL/min. Patients received G/P 300/120 mg once daily for 8, 12, or 16 weeks. Adverse events (AEs) and laboratory abnormalities were monitored. **Results:** Of the 2265 patients in the analysis, 288 (12.7%) had compensated cirrhosis, while 1977 (87.3%) did not have cirrhosis. AEs occurring in ≥10% of subjects were headache and fatigue (Table). Most AEs were mild (65.9%), and the frequency and severity of AEs were similar in subjects with cirrhosis and subjects without cirrhosis. Frequency of grade ≥3 AEs, AEs leading to discontinuation of study drug, and serious AEs were 2.9%, 0.4%, and 2.1%, respectively. Grade ≥3 laboratory abnormalities were infrequent (≤0.4%). No cases consistent with drug-induced liver injury occurred.

Table: AEs

Event	Overall, n (%), N=2265
DAA-related AEs	
Any	929 (41.0)
Serious AE	1 (<0.1)
AE grade ≥3	4 (0.2)
AE leading to discontinuation of study drug	3 (0.1)
Most frequent AEs (≥10%)	
Headache	410 (18.1)
Fatigue	330 (14.6)

**Conclusions:** In patients with HCV GT1-6 infection, G/P was well tolerated in subjects with compensated liver disease, with mostly mild AEs, low rates of serious AEs and treatment discontinuation. On-treatment laboratory abnormalities were rare, and patterns and rates of AEs were similar in subjects with and those without compensated cirrhosis. G/P was not associated with drug-induced liver injury.

PH1

**OCA Treatment in Patients with PBC and Cirrhosis**

PH3

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**Background:** Obeticholic acid (OCA) is a selective FXR agonist developed for treatment of primary biliary cholangitis (PBC). POISE was a randomized, double-blind, placebo-controlled, Phase 3 study of OCA in patients with PBC. This analysis assessed the efficacy of OCA in patients with cirrhosis.

**Methods:** Patients were randomized to Placebo (PBO) (n=73), OCA 5-10 mg (n=70) or OCA 10 mg (n=73). Patients were considered to have cirrhosis if they met one of the following criteria: biopsy-proven cirrhosis, transient elastography of ≥16.9 kPa, or history of cirrhosis. The primary composite endpoint was ALP <1.67x ULN with ≥15% reduction in ALP and BILI ≤ULN after 12 months.

**Results:** Cirrhosis was present in ~17% of patients in POISE: PBO, n=13; OCA 5-10 mg, n=13; OCA 10 mg, n=10. At Month 12, 54% (p<0.05) of patients in the OCA 5-10 mg group and 40% (p=0.06) in the OCA 10 mg group met the primary composite endpoint compared to 8% of PBO patients with cirrhosis. Patients in both OCA groups had significant changes in ALP (p<0.01) and BILI (p<0.05) compared to PBO at Month 12.

**Conclusion:** No additional safety concerns due to OCA were observed in the cirrhosis subgroup, and OCA treatment resulted in significant improvements in biochemical markers associated with disease progression. These results suggest that OCA may play a beneficial role in preservation of the functional capacity of residual liver tissue in cirrhotic patients.

**High SVR Rates with 8 and 12 Weeks of Pangenotypic Glecaprevir/Pibrentasvir: Integrated Efficacy and Safety Analysis of Genotype 1-6 Patients without Cirrhosis**

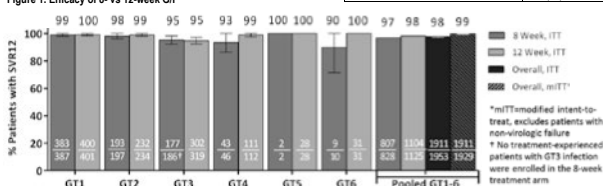
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**Background:** The pangenotypic direct-acting antivirals (DAAs) glecaprevir and pibrentasvir, comprise the interferon (IFN)- and ribavirin (RBV)-free regimen G/P. In seven phase 2/3 clinical trials, G/P achieved SVR12 rates of 92-100% across all six major HCV genotypes (GTs). Here we present an integrated analysis from these studies on the efficacy of 8 and 12 weeks of G/P treatment in non-cirrhotic patients with GT1-6 infection. **Methods:** Data were pooled from the phase 2 SURVEYOR-1 and -II, and phase 3 EXPEDITION-4 and ENDURANCE 1,2,3 and 4 studies. Patients with chronic HCV GT 1,2,3,4,5 or 6 infection without cirrhosis received G/P without RBV for either 8 or 12 weeks. Patients were either treatment-naïve or treatment-experienced with IFN-based or sofosbuvir (SOF)-based regimens. Patients experienced with a DAA other than SOF were excluded. Efficacy was evaluated as the rate of sustained virologic response (HCV RNA <lower limit of quantification) 12 weeks after the end of treatment (SVR12). Safety was assessed in all patients. **Results:** In total, 1981 patients without cirrhosis were enrolled and 1975 received study drug. Select baseline characteristics are shown in Table 1. SVR12 rates by treatment duration and genotype, excluding 22 patients that were treated for 16 weeks, are shown in Figure 1. In the intent-to-treat population (ITT), 1911/1953 (98%) patients achieved SVR12, with similar rates of 97% and 98% in patients treated for 8 and 12 weeks, respectively. Across all genotypes, there were 4 breakthroughs (0.2%), 14 relapses (0.7%) and 11 discontinuations (0.6%). G/P was well-tolerated; discontinuations due to adverse events, DAA-related serious adverse events and grade 3 or higher laboratory abnormalities were rare.

**Conclusions:** The G/P regimen yielded high SVR12 rates across all genotypes, regardless of prior treatment or treatment duration. The results from this integrated analysis suggest that the G/P regimen could provide an effective 8-week IFN- and RBV-free treatment option for patients with HCV GT1-6 infection without cirrhosis.

Table 1. Baseline Characteristics		G/P, N=1975
Male, n (%)		1053 (53)
White race, n (%)		1575 (80)
Age, median (range), years		53 (19-84)
BMI, median (range), kg/m <sup>2</sup>		25.5 (17.3-65.7)
Treatment-naïve, n (%)		1458 (74)
HCV RNA, median (range) log <sub>10</sub> IU/mL		6.2 (0.7-8)
Fibrosis Stage, n (%)		
F0-F1		1591 (81)
F2		153 (8)
F3		227 (11)

Figure 1. Efficacy of 8- vs 12-week G/P



PH2

**FXR/TGR5 Dual Agonist INT-767 Reduces NAS & Fibrosis & Improves Plasma & Hepatic Lipid Profiles in the AMLN Mouse Model of Diet-induced & Biopsy-confirmed NASH**

PH4

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**Background:** The nuclear FXR & membrane TGR5 receptors are regulators of metabolism, inflammation & fibrosis in chronic liver diseases including NASH. We evaluated the therapeutic potential of the dual FXR/TGR5 agonist INT-767 in a dietary model of NASH displaying features observed clinically on NAS, fibrosis stage, metabolic & transcriptomic profiles.

**Methods:** *Lep<sup>ob/ob</sup>* mice were fed the AMLN diet or standard chow. At week 12, livers were biopsied & mice with a steatosis score of 3 & F2-F3 fibrosis stage were randomized (n=10/grp) to receive either vehicle (0.5% CMC) or INT-767 (3 or 10 mg/kg) for 8 weeks. Primary endpoints included a blinded histological assessment for components of NAS, fibrosis stage, & IHC for Col1a1 & LAMB2.

**Results:** INT-767 (10 mg/kg) improved liver fibrosis score by 1 stage from 2.7±0.1 to 1.6±0.2; p<0.001. Total NAS & each component were reduced (total from 6.2±0.2 to 3.0±0.4; steatosis 3.0±0.2 to 1.8±0.2; inflammation 2.3±0.1 to 1.0±0.1; ballooning 0.9±0.1 to 0.2±0.1; all p<0.001) to levels observed in *Lep<sup>ob/ob</sup>* chow controls (all NS). Col1a1 & LAMB2 were reduced by 44% & 30%, respectively (10 mg/kg; both p<0.05).

**Conclusion:** INT-767 alleviated key hallmarks of NASH in mice with diet-induced and biopsy-confirmed disease as reflected by reduction in NAS, liver fibrosis stage & fibrogenic IHC markers, as well as an overall improvement in their metabolic phenotype.

### Investigating the Role of Tetraspanins CD63 and CD151 in the Hepatitis E Virus Life Cycle

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**Background:** Hepatitis E virus (HEV) is a positive-strand RNA virus encoding 3 open reading frames (ORF). ORF1 encodes the viral replicase, ORF2 the viral capsid and ORF3 a small protein involved in virion secretion. Recent data indicates that virus egress involves the exosomal pathway. A published yeast two-hybrid screen identified tetraspanins CD63 and CD151, known exosomal factors, as interactors of ORF3 protein. Our study aims at validating CD63 and CD151 as interacting partners of ORF3 protein and at defining their roles in the HEV life cycle.

**Methods:** The subcellular localization of CD63 and CD151 as well as viral proteins was investigated by confocal laser scanning microscopy. Replicon and full-length constructs were used to investigate HEV entry, RNA replication and virus production following siRNA- or CRISPR/Cas9-mediated knockdown of CD63 and CD151.

**Results:** Immunofluorescence analyses revealed that CD151 co-localized with HEV ORF3 and CD63 partially co-localized with HEV ORF2 protein in cells producing infectious virus. Furthermore, CD151 re-localized to bile canalicular-like structures together with ORF3 protein. In addition, functional analyses revealed a participation of CD151 in HEV entry. However, neither CD63 nor CD151 were found to be involved in HEV RNA replication. Efforts to decipher a potential role of CD63 and/or CD151 in virus production are ongoing.

**Conclusions:** Our results demonstrate that CD151 co-localizes with HEV ORF3 protein in cells producing HEV. This work shall yield new insights into the function of viral proteins and virus-host interactions required for productive HEV infection.

PH5

### Epidemiology and Treatment of Hepatitis C Virus Infection in a Hospital-Based Population in Eastern Switzerland

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**Background/Aims:** Chronic hepatitis C virus (HCV) infection has an estimated prevalence of 0.7% in Switzerland. Half of the 40'000 infected persons have not been diagnosed yet and only a minority of patients has been cured so far. In order to reach the WHO goal of HCV elimination by the year 2030, improved understanding of the national epidemiology is crucial. Therefore, the aim of our study was to investigate the epidemiology and treatment status of HCV infected patients in Eastern Switzerland (cantons SG, AR, AI) covering 600'000 inhabitants, representing almost 10% of the Swiss population.

**Methods:** This single center study was conducted by retrospective analysis of electronic medical records between January 1<sup>st</sup> 2004 and December 31<sup>st</sup> 2016 of all patients with a positive anti-HCV screening test (acute or chronic HCV infection) presenting at the cantonal hospital of St. Gallen KSSG covering the cantons SG, AR and AI. Data of identified patients was compared with the reported and estimated prevalence of the Federal Office of Public Health (FOPH).

**Results:** In total, 1374 anti-HCV positive patients were identified at our hospital center. These identified patients represent only 34% of the FOPH estimated (n=4040) and 62% of the FOPH reported (n=2218) cases for our region. 1298 (94%) of the identified 1374 patients were HCV-RNA tested and 1184 (86%) were HCV-RNA positive. Mean age of these patients was 53 years (17-94) and 893 (65%) were male. The major identified risk factor for HCV transmission was a history of intravenous drug use (in 739, 54%) while for 459 (33%) no risk factor could be identified. 205 (15%) were coinfecting with HIV, 391 (28%) with hepatitis B virus. Liver fibrosis stage was assessed in 1194 (87%): F0-F1 in 512 (43%), F2-F3 in 408 (34%) and F4 in 274 (23%). In 660 (48%) patients, HCV treatment was initiated leading to definitive cure (sustained virological response (SVR)) in 525 (38%). A total of 49 cases of hepatocellular carcinoma were diagnosed and 13 liver transplants were performed as a consequence of chronic HCV infection.

**Conclusions:** Only a minority of the presumed HCV patients are already diagnosed and treated in Eastern Switzerland. While new treatment regimens with highly effective anti-virals show excellent cure rates, diagnosis rates and treatment numbers have to increase significantly in order to meet the 2030 WHO HCV elimination goal.

PH7

### Comparison of human NAFLD and animal models using hepatic whole-genome transcriptomic meta-analysis

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**Background and Aims:** Numerous mouse models of non-alcoholic fatty liver disease (NAFLD) exist but none recapitulates the entire phenotype of this complex disease. We performed an unbiased whole-genome transcriptomic meta-analysis to identify animal models most closely related to human NASH and especially advanced fibrosis in NAFLD.

**Methods:** We assessed human hepatic transcriptome profiles and 7 mouse models of NAFLD (early, late and overall high-fat [HF], choline- and folate-deficient [CFD], methionine and choline deficient [MCD], HF, high-cholesterol, high-cholelate [CL] and HF high-sucrose [HSHF] diets. We compared the animal and human hepatic transcriptome by gene expression meta-analysis, principal component analysis and hierarchical clustering. Overlap of molecular pathways was analyzed by gene set enrichment analysis (GSEA).

**Results:** We identified 10 studies comparing human NASH versus healthy controls, including 128 NASH subjects and 134 healthy controls. 123 genes were differentially expressed in either of the human meta-analyses (FDR < 0.05 and beta > 1.0) of which 71 genes (58%) were differentially expressed in at least one animal model. Despite marked heterogeneity in molecular pathway induction, our approach indicated that some diets reproduced key pathways induced in human NASH or NAFLD fibrosis, for example fatty acid metabolism was suppressed in NAFLD fibrosis, similar in CFD, CL or MCD diets but induced in NASH subjects, similar to HSHF and HF diets (Figure 1).

**Conclusions:** Although no animal model perfectly recapitulates the complex

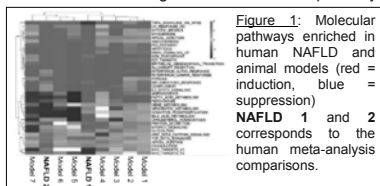


Figure 1: Molecular pathways enriched in human NAFLD and animal models (red = induction, blue = suppression) NAFLD 1 and 2 corresponds to the human meta-analysis comparisons.

PH6

### How to Eliminate Hepatitis C in Eastern Switzerland – A Model-Based Scenario

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**Background:** Direct-acting antiviral drugs (DAA) have revolutionized hepatitis C virus (HCV) treatment and made an elimination of HCV possible. The Swiss hepatitis strategy aims for an elimination of chronic HCV infection by the year 2030 with a reduction of chronic HCV cases by >90%.

**Methods:** A previously described HCV disease burden model (Razavi H et al. *J Viral Hepat*, 2014) was used to develop an elimination scenario to achieve the Swiss hepatitis strategy goals in Eastern Switzerland (cantons SG, AR, AI, population of 600'000). Our real-life hospital data with 1374 HCV-positive patients and current prevalence data from the federal office of public health (FOPH) with 4040 HCV patients with a steady-state scenario were used for comparison and validation of the model.

**Results:** Under the steady-state scenario with a constant treatment rate, an insufficient decrease in HCV-related morbidity and mortality is predicted for 2030 compared to 2015: reduction of mortality by 57%, reduction of liver cancer by 53% until 2030. In this steady-state scenario, chronic HCV infections will decrease by 62% until 2030. By retaining the current hepatitis C detection rate of 90 patients/year, 85% of all infected patients could be detected by 2030. By increasing the HCV treatment rate (from currently 107 treatments/year in 2015 to 230/year in 2017-2020 and 195/year in 2020-2030), morbidity and mortality could be reduced by the targeted 90% in 2030. This translates into treating 1130 patients with chronic HCV between 2015 and 2030 in Eastern Switzerland in order to achieve the Swiss hepatitis strategy goals. With the current treatment restriction (FOPH limitation with  $\geq$ F2 fibrosis), these goals cannot be achieved due to a theoretical lack of eligible patients for HCV treatment after the year 2025.

**Conclusions:** Elimination of chronic HCV infection in Eastern Switzerland by 2030 is possible, but not with the currently restricted treatment access. Higher treatment and diagnosis rates are necessary to meet the 90% elimination goal.

PH8

### Verteporfin potentiates the anti-tumor effect of Sorafenib by inhibiting hepatocellular carcinoma progression through interfering with the autophagic flux

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Hepatocellular carcinoma (HCC) is one of the most common malignant cancers worldwide and unfortunately, diagnosis often occurs at an advanced stage. Sorafenib (SF) is the only FDA-approved systemic treatment for advanced HCC with limited success and substantial side-effects. It has been shown that HCC exhibits an increased autophagic flux, often correlated to a high resistance to hypoxia, starving conditions and multi-drug resistance development. Here we study the effect of the photosensitizer Verteporfin (VP) on HCC growth in a preclinical model without prior light activation, focusing particularly on its mechanism of action either alone or in combination with SF. Our data suggest that VP markedly reduces tumor growth in a subcutaneous HCC xenograft mouse model, potentiating the effectiveness of SF, by decreasing tumor cell proliferation (Ki67) and impairing tumor angiogenesis (CD31). We found that Verteporfin inhibits Huh7 and HepG2 cell proliferation, interfering with cell-cycle progression by enhancing apoptosis (flow cytometry) and down-regulating the expression of pro-proliferative and differentiation genes (q-PCR). Combining VP with SF led not only to a synergistic (Huh7) and additive (HepG2) reduction of HCC cell line proliferation, but also to an increased inhibition of angiogenesis (tube formation assay). Furthermore VP co-localizes within lysosomes, increasing their number and altering their shape and size (enlargement). Immunoblot analysis showed that VP interferes with the early-stage of the autophagic flux, impairing SF-induced autophagy, which can be activated as a cellular adaptive response mechanism. VP was able to decrease the formation of newly forming autophagosomes (LC3-I), inducing an accumulation of high-molecular weight complexes of proteins (HMW-p62), which finally leads to a proteotoxic effect. Taken together, these findings suggest that VP, without prior light activation, acts as an early-stage autophagy inhibitor, significantly potentiating the anti-tumor effect of SF in a HCC preclinical model. Treatment of HCC with VP (+/-SF) may be a novel therapeutic strategy for patients with advanced, otherwise inoperable HCC.

### The impact of preoperative investigations on the management of bariatric patients; results of a cohort of more than 1200 cases

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**Background:** Despite the increasing use of bariatric surgery as the most effective treatment of morbid obesity, there is still no consensus on its pre-operative diagnostic work-up. The aim of this study is to identify the impact of the endoscopic and radiological findings before performing bariatric surgery and to evaluate their influence in the therapeutic approach.

**Methods:** Retrospective analysis of prospectively collected data of 1225 consecutive patients who underwent laparoscopic Roux-Y gastric bypass (n = 834) or sleeve gastrectomy (n = 391) at our institution. An abdominal ultrasound was performed in 1188 patients, 1190 patients underwent upper GI endoscopy, 1178 patients underwent upper GI series and 610 patients underwent esophageal manometry.

**Results:** Gallstones were detected in 222 (18.1%) patients and a synchronous cholecystectomy was performed in 220 (18.0%) patients. The upper GI series indicated hiatal hernias in 325 (27.6%) patients. The most common findings of the upper GI endoscopy were Type-C gastritis (224 patients, 18.8%), reflux esophagitis (229 patients, 19.2%), H. pylori-positive gastritis (158, 13.3%) and hiatal hernia (55 patients, 4.6%). Additionally, we detected one Barrett's high-grade dysplasia, two Barrett's carcinomas and one stomach cancer in asymptomatic patients who were due to have a sleeve gastrectomy. Esophageal motility disorders were detected in 104 (17.0%) individuals who underwent esophageal manometry.

**Conclusions:** Abdominal sonography and upper GI endoscopy are mandatory before bariatric surgery as they reveal findings which influence the therapeutic approach. Upper GI series and esophageal manometry help to define patients not suitable for sleeve gastrectomy.

PS1

### Laparoscopic Versus Open Intraoperative Onlay Mesh Incisional Hernia Repair

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#### Background

Intraoperative onlay mesh repair (IPOM) of incisional hernia can be performed by open and laparoscopic approach. The aim of this observational study was to assess long-term incidence of hernia recurrence of open versus laparoscopic IPOM.

#### Methods

All patients who underwent IPOM for incisional hernia in one institution between September 2004 and September 2015 were analysed. The primary outcome measure was the incidence of hernia recurrence, secondary outcome measures include operation time, length of hospital stay, frequency of complications, surgical site infections, reoperations, chronic pain, and localisation of hernia recurrence.

#### Results

Of a total of 553 patients with incisional hernia repair, 326 (59%) underwent laparoscopic and 227 (41%) open IPOM. Recurrence rate was 20% after laparoscopic and 19% after open repair (p=0.660). Compared to open surgery, patients undergoing laparoscopic IPOM had significantly shorter operation times (mean 147 ± SD 68 vs. 199 ± 101 min., p=0.001) and hospital stay (6 ± 3 vs. 10 ± 8 days, p=0.001), reduced complications (9% vs. 25%, p=0.008) and fewer surgical site infections (1% vs. 23%, p<0.001). The primary site of hernia recurrence for both methods was in the midline between xyphoid process and umbilicus.

#### Conclusions

Laparoscopic IPOM is associated with shorter hospital stay, fewer surgical site infections and reduced complications. The incidence and localisation of long-term hernia recurrence after incisional hernia is not different between open and laparoscopic IPOM.

PS3

PS2

### Outcomes of 66 consecutive transanal total mesorectal excisions for low rectal cancer

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#### Background

Transanal total mesorectal excision (taTME) is an alternative to conventional mesorectal excision owing to its reported ability to achieve clear distal and circumferential resection margin in low rectal cancers.

#### Methods

Consecutive patients treated at a single centre by taTME were included in a prospective cohort study. Perioperative and short-term oncologic outcomes were measured along regular clinic visits and the results were reported as median and interquartile range (IQR).

#### Results

66 patients with a low rectal cancer (median 7cm to anal verge, IQR 6-8) underwent a taTME between Feb 2013 and Mai 2017. Age and body mass index were 65.5 years (IQR 56.25-76) and 26kg/m<sup>2</sup> (IQR 21.8-29.4). 48 (72%) patients had neoadjuvant radiochemotherapy. Median surgery time was 359.5 minutes (IQR 312.5-422.75), including an ileostomy in all patients. Dissection of the mesorectum was good (95% Quirke 3) and all distal and circumferential margins were clear. Median T stage was 3 (IQR 2-3). 17 patients had lymphnode metastases for a median number of retrieved nodes of 24 (IQR 18-34). Cumulative 30-day morbidity amounted to 28.7% major complications (Dindo Clavien III-V), including 7 anastomotic leaks (10%) and 30% minor complications (Dindo Clavien I-II). Median length of hospital stay was 12 days (IQR 9-15.75).

#### Conclusion

Transanal total mesorectal excision allows good surgical and oncologic quality to the expenses of a reasonable surgery time and morbidity.

PS4

### Incidence and prognosis of lymph node metastases in patients with limb soft tissue sarcoma

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**Background:** Soft tissue sarcomas (STS) remain a disease with poor prognosis. Moreover, STS are difficult to treat and mutilating operations are often necessary. In the late 1980s, a new approach was developed: isolated limb perfusion (ILP). The present study aimed to assess incidence and impact on patient survival based on lymph node metastasis

**Methods:** Retrospective study of 57 consecutive patients treated by ILP for limb STS with simultaneous radical lymph node dissection in our tertiary referral center between 1992 and 2014.

**Results:** Median age was 62 years (19-87) and 30 patients were male (53%). Lymph node involvement was observed in 13 patients (N1, 23%), regarded as metastatic spreading in 4 angiosarcomas, 3 epithelioid sarcomas, 2 leiomyosarcomas, 2 undifferentiated sarcomas and 2 synovial sarcomas. For the N0 patient group, median survival was 73.9 months (CI 95 % 41.9-105.9) compared to 15.1 months (CI 95 % 7.4-22.6) in case of metastatic lymph node (p=0.002). The median disease-free survival was 33,0 months (CI 95% 12,5-53,5) in N0 group and 8,0 months (CI 95% 4,0-11,9) in N1 (p=0.006).

**Conclusions:** Lymph node metastases of STS seemed to have a negative impact on both overall and disease-free survival. Radical lymph node dissection should be included systematically in ILP procedures and possibly into selected sarcoma surgery to have more precise diagnosis with possible positive impact on outcome to be further investigated.

PS5

### Pure laparoscopic liver hanging maneuver for right hepatectomy – a video

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**Background:** The liver-hanging maneuver for right hepatectomy is a widely used technique in open liver resection. In laparoscopic liver resections it is not used routinely. Since blind dissection between the anterior surface of the inferior vena cava and the liver is required, injury of the vena cava is feared.

**Methods:** After dissection of the right pedicle a bottom-up dissection on the anterior surface of the inferior vena cava is performed, followed by a cautious dissection between the right and middle hepatic vein. By introducing the Goldfinger retractor between the hepatic veins the passage on top of the inferior vena cava can be completed. To apply the hanging maneuver a Foley catheter is placed from between the hepatic veins and set in proximity of the inferior vena cava in direction of the porta hepatis in an up-to-down technique. For visualization the EndoEYE flex 3D videoscope (Olympus Switzerland) is used, a camera with up to 100 degrees of articulation in all directions.

**Results:** From January to December 2016, five patients underwent pure laparoscopic right hepatectomy. In four of them we performed the laparoscopic liver-hanging maneuver successfully. The median time for the maneuver was 101 minutes (range 72 – 138 min; learning curve). During the preparation and passage no bleeding has occurred.

**Conclusion:** In conclusion, pure laparoscopic liver hanging maneuver is feasible and safe. A 3-D videoscope with a bendable tip helps to perform the dissection between the liver and the inferior vena cava under permanent view. The hanging maneuver is therefore applicable in laparoscopic liver surgery and helps to reduce the risk of bleeding and air embolism. The Foley catheter positioned between the right and middle hepatic vein serves as guiding element during the parenchymal transection.

PS7

### The purinergic receptor P2X1 is required during immune mediated liver injury

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#### Background

During liver injury, extracellular ATP is released and binds to specific P2 receptors that modulate a variety of immune cells. Screening revealed that pharmacological inhibition of P2X1 is critical for the secretion of the hepatoprotective cytokine IL-22. In the current study, we assessed if immune mediated liver injury depends on P2X1.

#### Methods

Expression of P2X1 was assessed by PCR and western blotting. In a model of immune mediated hepatitis, Concanavalin A was injected intravenously at a dose of 15 mg/kg in P2X1 null and C57Bl/6 mice. Liver injury was assessed with ALT levels and histology. Liver tissue was used for ELISA and Western Blot after protein extraction.

#### Results

The P2X1 receptor is specifically and highly expressed on inflammatory and immune cells including B-, T-, NK- and NKT-cells of the liver but not on hepatocytes. Liver injury and cytokine levels were significantly decreased in P2X1 null compared to C57Bl/6 mice. As a marker of reduced apoptosis, expression of PARP/c-PARP was decreased in P2X1 null compared to C57Bl/6 mice.

#### Conclusion

The purinergic receptor P2X1 is only expressed on immune cells but not on hepatocytes and is required for immune mediated liver injury. P2X1 thereby represents an unidirectional modulator between the hepatic immune cells and hepatocytes.

PS6

### Bacterial Translocation impairs Liver Regeneration after two third Partial Hepatectomy

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**Background:** The liver plays a pivotal role in anti-bacterial defense against gut bacteria. We hypothesized that during major surgery the liver clears translocated bacteria. Therefore it was first assessed if bacterial translocation occurs during partial hepatectomy and second if insufficient clearance of bacteria impact on liver regeneration.

**Methods:** Two third partial hepatectomy in an aseptic manner was performed in colonized C57Bl/6 and Rag 2<sup>-/-</sup> γc<sup>-/-</sup> (lacking, T, B, NK cells) mice. Translocation was assessed by the measurement of colony forming units (CFU) and bacterial rRNA in mesenteric lymph nodes, liver, spleen, and lungs after 24 hours. Liver regeneration was assessed using qPCR of liver regeneration genes.

**Results:** Translocation was observed at low rates in wild type mice in mesenteric lymph nodes. In immune deficient RAG 2<sup>-/-</sup> γc<sup>-/-</sup> mice translocation was observed in mesenteric lymph nodes, liver, spleen and lungs. Sequencing of CFUs revealed mainly Enterobacter cloacae in liver tissue, a typical intestinal bacterium. Liver regeneration was impaired in Rag 2<sup>-/-</sup> γc<sup>-/-</sup> after 24 hours reflected by an increase in CDKN1a.

**Conclusion:** Bacterial translocation is observed in low levels in wild type mice but was significantly increased in immune deficient mice. Bacterial translocation is associated with impaired liver regeneration.

PS8



### Porcine islets of Langerhans: Multifocal transplantation might improve transplantation outcomes

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Although the transplantation of porcine islets of Langerhans (PLI) seems a promising treatment modality for type 1 diabetes, the success of xenotransplantation has, thus far, been disappointing. A better understanding of the characteristics of transplant-destined islets is clearly needed. We studied the influence of islet cell equivalent (IEQ) number, the effect of microencapsulation, and the role of glucose in culture media on the insulin secretory ability of PLI. We also assessed the functionality of cells prior to transplantation by correlating islet cell vitality and stimulatory/secretory potential. IEQ number was negatively correlated with insulin secretion per islet, and we found that insulin secretion of a single cell could be up to 7000% higher than that of grouped cells. Microencapsulation had no effect on insulin secretion or secretion profiles of PLI, whilst the insulin secretion rates of PLI cultured in hyperglycemic media was approximately 3.3 fold higher than that of PLI cultured in low glucose media. We found no correlation between the amount of insulin that a cell could secrete and its vitality. Our results suggest that *in vivo* insulin secretion is regulated by means of negative feedback following "cross-talk" between PLI. Therefore we propose multifocal transplantation of PLI for improved transplantation outcomes.

### Immunosuppression and Echinococcus multilocularis infection: The influence of a weakened immunostatus on disease incidence

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#### Background

The incidence of alveolar echinococcosis (AE) increased in the three last decades. The aim of this study was to identify a potential clinical association of immunosuppression and incidence of AE.

#### Methods

Retrospective analysis of the database from the University Hospital of Bern containing all patients that were diagnosed with AE since 1971, including patients' characteristics and immunosuppressive therapy.

#### Results

A total of 130 AE patients were analysed. Within this cohort a total of 6 patients were immunosuppressed (1x HIV, 2x TNF inhibitors, 1x corticosteroids, 2x kidney transplantation). Onset of AE was within 4 years after onset of TNF inhibitors. Diagnostic serology was positive in all cases.

#### Conclusion

There is an apparent indication that the use of TNF inhibitors associates with the onset of AE. This is supported by experimental findings, in which it has been shown that TNF contributes to a Th1-oriented resistance status in murine AE.

PS9

### Tight Cell Junction Control of Liver Regeneration

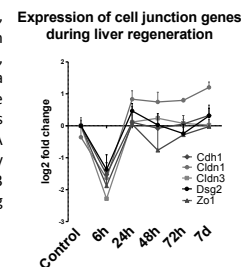
Felix Baier, Giulio Loforese, Ramesh Kudira, Fadi Jebbawi, Daniel Candinas, Guido Beldi, Deborah Stroka

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**Background** Failure to regenerate after surgical resection is a major cause of death in advanced liver diseases. To improve the clinical outcome after intervention, it is crucial to first understand the basic mechanisms which initiate and regulate liver regeneration. Within this project, we studied tight junction proteins as potential triggers of the regenerative process.

**Methods** Liver regeneration was induced using a mouse <sup>2</sup>/<sub>3</sub> partial hepatectomy model. Expression of junctional proteins was measured on the mRNA and protein level. Hepatic proliferation and junctional subcellular proliferation was analyzed using immunofluorescent staining.

**Results** 6 hours after partial hepatectomy, we observed a significant downregulation of the mRNA expression of Cldn1, Cldn3, Cdh1, Dsg2 and Zo1 followed by a restoration or slight upregulation above the initial levels. CLDN3 Protein levels coincided with the observed mRNA expression. Immunofluorescent histology revealed a focal accumulation of CLDN3 within the nucleus of proliferating hepatocytes.



**Conclusions:** We found that the mRNA of proteins composing adherence- and tight junctions are regulated during the early phases of liver regeneration. Nuclear trans-localization of CLDN3 might be indicative for a potential role on hepatic proliferation, which will be studied further with the phenotypic analysis of CLDN3 deficient mice. A potential involvement of cytokines on regulation of junctional proteins is under investigation.

PS10

### LIM Protein Ajuba Promotes Cancer Cell Proliferation and Survival in Hepatocellular Carcinoma

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**Background:** The Lim domain protein Ajuba is a structural protein with a role in the maintenance of cell junctions, cell migration, differentiation and proliferation. We are investigating the role of Ajuba in hepatocellular carcinoma (HCC) and hypothesized that Ajuba expression is increased in HCC cells and that loss of Ajuba has a biological impact on HCC cell growth and survival. **Methods:** Ajuba mRNA and protein expression were examined in mouse liver cancer cell lines BNL and RIL-175 and were compared to quiescent mouse liver tissue. Human liver cancer cell lines (HepG2, Hep3B, HLE, HLF, skHep1, Hepkk1, Huh7) were compared to primary human hepatocytes. The biological function of Ajuba was investigated using lentiviruses expressing shRNA sequences targeting Ajuba. Biological and functional assays were then performed with transduced cells *in vitro* and *in vivo*. **Results:** Steady state levels of Ajuba mRNA were significantly higher in mouse and human cancer cell lines compared to quiescent mouse liver tissue and isolated primary human hepatocytes. ShRNA expressing lentiviruses effectively knocked-down Ajuba protein and resulted in a decreased ability of the cells to migrate and to form colonies. In addition, Ajuba knockdown increased sensitivity to radiation-induced cell damage. *In vivo* injection of transduced cells show a significantly reduced tumor volume for shAjuba compared to the control RIL-175 using a syngeneic tumor model in C57BL/6 mice. **Conclusion:** Our results suggest that Ajuba is highly expressed in proliferating cells and may have a crucial role in cell proliferation and survival. Also *in vivo* experiments showed that Ajuba knock down has a direct effect on tumor volume. We now aim to define the mechanistic role of Ajuba in cell proliferation and survival in HCC.

PS12

#### Direct and indirect hepatoprotective mechanism of CBLB502 a TLR5 Agonist

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**Background:** CBLB502 is a peptide synthesized from bacterial flagellin and is an agonist of toll-like receptor 5 (TLR5) showing protective properties in various model. Here we investigated its potential hepatoprotective effect and mechanism of action.

**Methods:** A mouse model of partial liver I/R was used to assess the hepatoprotective effect of CBLB502 against acute liver injury and assessed by serum ALT/AST levels and tissue myeloperoxidase activity. Hepatic NF- $\kappa$ B and Stat3 signaling was evaluated by western blot and q PCR. Serum cytokine were measure by cytokine bead array.

**Results:** Preliminary data show that in mice treated with 0.2 mg/kg<sup>-1</sup> CBLB502 i.p., there is a beneficial influence on clinical symptoms of hepatic ischemia reperfusion injury by reducing ALT/AST and (myeloperoxidase activity. Direct protective mechanism, was shown by induction of NF- $\kappa$ B signaling in hepatocytes and liver as well as downstream cytoprotective genes. In parallel, TLR5 induced cytokine response was access showing increased in various serum cytokines and IL-22 level was the most striking (2 $\mu$ g/ml). IL-22 produced by cells found in colon and MLN was shown to activate Stat3 signaling in hepatocyte thus inducing hepatoprtecton through an indirect mechanism.

**Conclusions:** I/R injury associated with hepatic resections and liver transplantation remains a serious complication in clinical practice. Hepatic damage could potentially be diminished by prior activation of an innate immune response targeting TLR5.

PS13

#### Macrophages regulate outcome of sepsis via connexin 43 dependent ATP release

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**Background:** During sepsis, ATP is released into the extracellular space to modulate immune responses via specific purinergic receptors present on immune cells. Screening ATP release mechanisms by using hemichannel blockers revealed active ATP release from primary macrophages via hemichannel connexin 43 (cx43). We aim here to identify mechanisms of endotoxemia elicited ATP release and their impact on innate immune responses during sepsis.

**Methods:** ATP release was assessed in vitro and in vivo using a luciferin-luciferase assay. Cx43 was blocked using Gap27, a specific cx43 inhibitor. To model sepsis in rodents, caecal ligation and puncture (CLP) was performed. Conditional KO cx43<sup>fl/fl</sup> lysozyme 2<sup>cre/cre</sup> mice were developed to assess the impact of cx43 in macrophages. Liver, lung, spleen, and peritoneal fluid immune cells expressing cx43 were characterized (IHC, FACS). Cytokine levels (ELISA), gene expression (qPCR) and protein expression (immunoblot) were assessed.

**Results:** We identified cx43 expression in primary macrophages upon LPS stimulation in vitro and in hepatic macrophages following CLP in vivo. Macrophages were identified to release ATP in response to TLR 4 and 2 agonists, which was abrogated by pharmacological inhibition of cx43 by Gap27. Blocking of cx43 during CLP prolonged survival and was associated with lower bacterial load (CFU/ml) in the blood and peritoneal fluid. Cx43 blocking modulated the immune answer leading to decreased systemic and local levels of inflammatory cytokines (TNF, IL1, IL6) and chemokines (CCL2). Results obtained with Gap27 were confirmed in our conditional cx43 KO mice (6).

**Conclusion:** Systemic pharmacological inhibition as well as macrophage specific deletion of cx43 improves survival after sepsis. This effect was associated with decreased systemic inflammation and reduced bacterial load.

PS15

#### Intraabdominal hypertension leads to systemic ATP release

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**Background:** Intra-abdominal hypertension (IAH) is defined as a pressure of more than 12 mmHg in the peritoneal cavity. It is a serious complication in critically ill patients, leading to compartment syndrome, multi-organ failure and high mortality. No well-defined treatment strategy is known so far.

**Methods:** Intra-abdominal pressure (IP) was increased by injecting Ringer-lactate intra-peritoneally in pig. IP was monitored using an intra-vesical catheter. Vascular flows in the portal vein, hepatic artery and right kidney artery were monitored using ultrasound Doppler flow probes placed prior to IP increase. Blood was harvested from carotis communis artery in CTAD tubes (citrate, theophylline, adenosine, dipyridamole) immediately after reaching pressure threshold. Samples were processed directly and ATP was quantified using a luciferin-luciferase assay.

**Results:** We identified increased ATP levels in the plasma of pigs with increased IP. A dose-dependent effect was observed with higher plasma ATP levels for each increase of IP and maximal ATP levels reached at 35-40 mmHg IP. No correlation between ATP levels and vascular flows in portal vein and hepatic artery was observed. However, we observed a negative correlation between vascular flow in the right kidney artery and systemic ATP levels.

**Conclusion:** We identified ATP release consecutive to the increase of intra-abdominal pressure in a pig model. ATP release was pressure dependent and was correlated with kidney artery flow. This observation could lead to the identification of a new potential target in the management of IAH.

PS14

#### Is there a role for surgery for neuroendocrine tumors of the esophagus – a contemporary view from NCDB

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**Background:** Neuroendocrine tumors (NET) of the esophagus are extremely rare, aggressive, and have a poor prognosis. Given the rarity of the disease, treatment guidelines are ill defined and mainly based on evidence from case reports and seeking analogy among similar disease sites. We felt that a study using the population-based National Cancer Database (NCDB) had the potential to provide highest level of evidence for guiding therapy.

**Methods:** NCDB was reviewed for histologically confirmed stage I-III, primary esophageal NETs from 2006 to 2013. Patients were grouped whether or not they underwent a primary tumor resection. Univariate and multivariable adjusted Cox regression analyses were used to assess survival differences between the two groups.

**Results:** Over the study period, a total of 175 patients were identified. Mean age was 66.0 (SD: 12.1) years and 117 (66.9%) patients were male. Most patients (n=120, 68.8%) had a G3/4 tumor while 87 (49.7%) patients had stage III disease. Oncological esophageal resection was performed in 49 (28%) cases. 34.7% and 53.1% of the resected patients did not have chemo- or radiotherapy, respectively, while it was 24.6% for the not resected patients for both treatments. 2-year survival rates were higher in the operated group (55.8%), compared to 32.6% in the non-surgical group (p<0.001). The survival benefit hold true even after multivariable adjustment (HR: 0.23, CI: 0.14-0.39, p<0.001).

**Conclusion:** Multi-modality treatment including surgery is associated with better overall survival compared to chemo/(radio)-therapy alone. Additional research is needed to further define patients who benefit from esophagectomy including definition of appropriate treatment sequence.

PS16

### Checkpoint blockade modulates the immune response in hepatic Alveolar echinococcosis infection

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#### Author information

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#### Background

Alveolar echinococcosis (AE) is a chronic liver disease, which is caused by *Echinococcus multilocularis*. Infection with this parasite is associated with hepatic lesions that cannot be curatively treated by pharmacotherapy alone. Not all patients exposed to the parasite develop the disease and therefore the parasite potentially exhibits opportunistic properties. Currently little is known about immune mediated mechanisms that are associated with the infection or clearance of the parasite.

In this studies, we are exploring the fraction and function of hepatic immune cells in AE infected mice. Moreover we investigated how the programmed cell death (PD-1)/ PD ligand (PD-Ls) pathway regulates the immune responses using surface markers and modulating the pathway by inhibition PD-L1 and PD1 pharmacologically and genetically.

#### Methods

Wild type (wt) and PD-1 knock out (KO) mice were infected with AE at day 0 using two different infection strategies: oral (representing acute infection) and IP (representing chronic infection) infection. Lesions count and weight in the infected liver was measured at day 30 post infection. The expression of PD-1 on Treg, T<sub>H</sub>17 cells, NK, NKT and innate lymphocytes cells was assessed using flow cytometry technology.

#### Results

In vivo, AE was associated with decreased fractions of hepatic CD4 T and CD4 Treg cells but increased activation of hepatic CD4 T, CD4 Treg and CD8 T cells that potentially lead to exhaustion. Expression of PD1 was significantly increased in CD4 Treg and CD8 T cells. Deletion of PD1 in PD1-KO mice and pharmacological blockade of PD-L1 was associated with significantly decreased numbers of hepatic lesions compared to wt mice after both oral and IP infection. Excessive activation of hepatic CD4 T cells was reversed after PD-L1 blockade.

#### Conclusion

The results of this study demonstrate that inhibition of both, PD-1 and PD-L1 reduces the extent of AE infection via modulation of hepatic Treg and CD8 T cells. These findings suggest that the use of checkpoint inhibitors potentially may alter the clinical course of AE infection.

PS17

### First experience of robotic-assisted (da Vinci Xi) surgery for giant hiatal hernias and comparison to laparoscopy

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**Background:** Since July 2015 we perform robotic-assisted surgery to repair giant hiatal hernias with the da Vinci Xi. To evaluate feasibility and quality of this approach we analyzed perioperative results of the last 18 months and compared them to a laparoscopic group.

**Methods:** Retrospective analysis of prospectively collected data Jul 2015 - Dec 2016. We included all patients with type III or IV hiatal hernia according to Hill classification. In 19 patients (12 female, 7 male) the robotic system was used for hernia repair (Rob-G), 15 (10 female, 5 male) patients were treated laparoscopically (Lap-G). Hiatal hernia repair was done with or without mesh augmentation, fundoplication and/or gastropexy.

**Result:** Average age was 70,6 years (58-84) in the Rob-G and 71,2 years (30-91) in the Lap-G (p=n.s). Mean operating time (MOT) was 246 min (± 133) in the Rob-G and 173 min (± 137) in the Lap-G (p=0.00048). Mesh augmentation was performed in 17 Rob-G and 3 Lap-G patients. In the Rob-G 16 whereas in the Lap-G 13 funduplications were carried out. Gastropexy was applied 17 times in the Rob-G and 13 times in the Lap-G. Morbidity in Rob-G was 10% , in Lap-G 7% (Clavien-Dindo III). Length of hospital stay was statistically not different with 9,5 days in Rob-G and 9 days in Lap-G.

**Conclusion:** Analysis of our results showed that using the da Vinci Xi System is safe, feasible and equivalent to the laparoscopic technique. We attribute the longer MOT to larger hernias with mesh augmentation more frequent in the Rob-G. That and the fact still being in the learning curve we expect the MOT in the Rob-G to shorten in the near future.

PS19

### Percutaneous image-guided stereotactic microwave ablation (PISMA) for non-colorectal liver metastases

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Prof. Daniel Candinas, MD, Vanessa Banz, MD PhD  
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PS18

**Background:** PISMA is increasingly performed for the treatment of hepatocellular carcinoma (HCC) and within clinical trials for colorectal liver metastases (CRLM). Due to its minimal invasiveness and safety, its use for the treatment of other liver metastases is discussed. The aim of this study was to analyze PISMA for non-CRLM treated in our institution during the last two years.

**Methods:** Retrospective study of patients undergoing PISMA for non-CRLM in our institution from January 2015 to April 2017. HCC, CRLM or benign lesions, as indicated by imaging and/or biopsies were excluded. Follow-up included clinical and 3-monthly imaging in addition to the regular oncologic follow-up.

**Results:** 23 interventions were performed in 19 patients as recommended by the interdisciplinary tumorboard decision. Ten patients were women (52.6%), mean age was 58.4yrs (range 7-79). Thirty-eight metastatic lesions were treated in the given time period including fifteen neuroendocrine tumors (NET), nine breast cancer, six sarcoma, two non-small cell lung cancer, three duodenal-, one papillary-, one prostate- and one renal cell carcinoma. Median follow-up was 7.7 months with ablation site recurrence of 5.2% (2/38). Intrahepatic disease progression was found in 8/19 patients (42%). We observed four (17.4%) complications, three Clavien-Dindo grade I and one grade IIIa.

**Conclusion:** In our experience PISMA is technically feasible and safe for non-CRLM, particularly in the setting of NET liver metastases. PISMA results in good short-term local tumor control with low recurrence rates at the site of ablation using a minimally invasive technique. However, the long-term oncological benefits still need to be evaluated in a much larger patient cohort.



The numbers refer to the pages of this supplement.

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