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SMW

SWISS SOCIETY OF GASTROENTEROLOGY
SWISS VISCERAL SURGEONS
SWISS ASSOCIATION FOR THE STUDY OF THE LIVER
SWISS SOCIETY OF ENDOSCOPY NURSES AND ASSOCIATES

ANNUAL MEETING 2021

INTERLAKEN, SEPTEMBER 9–10, 2021

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ORAL PRESENTATIONS: GASTROENTEROLOGY & NGM

Systematic Assessment of Adult Patients' Satisfaction with Various Eosinophilic Esophagitis Therapies

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Background and aims: The treatment options for eosinophilic esophagitis (EoE) patients include drugs (proton pump inhibitors [PPIs], swallowed topical corticosteroids [STCs]), elimination diets, and dilation. Given the lack of data, we aimed to assess adult EoE patients' satisfaction with different EoE-specific treatment modalities.

Patients and methods: We evaluated therapy satisfaction recalled over a 12-month period using the validated Treatment Satisfaction Questionnaire for Medication that assesses effectiveness, side effects, convenience, and overall satisfaction. The score for each scale ranges from 0 (dissatisfied) to 100 (satisfied). To evaluate satisfaction with nonpharmacologic therapies, the questionnaire was modified and debriefed in three focus groups. The final questionnaire was sent to 147 patients.

Results: The patient response rate was 74%. In the last 12 months, 24, 75, 19, and 9% were treated with PPIs, STCs, elimination diet, and dilation, respectively. Patients identified the following considerations as important for therapy choice: effect on symptoms (89%), effect on esophageal inflammation (76%), side effects (69%), and ease of use (58%). Patients found STCs to be effective (83 points), convenient (83 points), and experienced no side effects when using this therapy. When using STCs alone (43%), overall patient satisfaction was high (86 points). Patients judged PPIs to be most convenient (89 points), STCs to be a bit less convenient (83 points), and diet to be most inconvenient (46 points) of the three therapies examined.

Conclusions: Adult EoE patients consider both therapy effect on symptoms and esophageal inflammation as important criteria when choosing EoE therapy and appear to be satisfied with STC use.

Budesonide Orodispersible Tablets Maintain Remission in a Randomized, Placebo-Controlled Trial of Patients With Eosinophilic Esophagitis

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Background and aims: It is unknown if swallowed topical corticosteroids are effective in maintaining long-term remission in patients with Eosinophilic Esophagitis (EoE).

Patients and methods: We performed a double-blind trial to compare the efficacy and safety of 2 dosages of a budesonide orodispersible tablet (BOT) vs placebo in maintaining remission of EoE. Maintenance of remission was defined as absence of clinical and histologic relapse and no premature withdrawal for any reason. 204 adults with EoE in clinical and histologic remission were randomly assigned to groups given BOT 0.5 mg twice daily (n = 68), BOT 1.0 mg twice daily (n = 68), or placebo twice daily (n = 68) for up to 48 weeks.

Results: At end of treatment, 73.5% of patients receiving BOT 0.5 mg twice daily and 75% receiving BOT 1.0 mg twice daily were in persistent remission compared with 4.4% of patients in the placebo group (P <.001 for both comparisons of BOT with placebo). Median time to relapse in the placebo group was 87 days. The frequency of adverse events was similar in the BOT and placebo groups. Morning serum levels of cortisol were in the normal range at baseline and did not significantly change during treatment. Clinically manifested candidiasis was suspected in 16.2% of patients in the BOT 0.5 mg group and in 11.8% of patients in the BOT 1.0 mg group; all infections resolved with treatment.

Conclusions: In a phase 3 trial, up to 48 weeks of treatment with BOT (0.5 mg or 1.0 mg twice daily) was superior to placebo in maintaining

remission of EoE. Both dosages were equally effective and well tolerated. EudraCT number; 2014-001485-99; ClinicalTrials.gov number, NCT02493335.

IL-20 Cytokine Signaling Reduces Epithelial Barrier Filaggrins in Eosinophilic Esophagitis

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Introduction: Epithelial barrier breaches contribute to eosinophilic esophagitis (EoE). Increased expression of the IL-20 cytokines IL-20, IL-19, IL-20 and IL-24 in TH2 diseases has been reported, yet their function in EoE remains unknown.

Methods: Combining RNA-sequencing (RNA-seq) and proteomics, we have investigated the effects of IL-20 cytokines on esophageal epithelial cells using patient-derived organoids and an EoE mouse model.

Results: EoE patients with active inflammation have increased IL-19, IL-20 and IL-24 expression and increased serum concentrations. Organoids stimulated with IL-20 cytokines showed decreased Filaggrin (FLG) and Filaggrin 2 (FLG2) levels. In agreement, EoE patients displayed reduced FLG and FLG2 expression. Topical corticosteroid treatment restored filaggrin expression, while reducing IL-20 cytokines. Complete abrogation of the IL-20 cytokine pathway in IL20rb^{-/-} animals attenuated EoE in an OVA-induced mouse model. In vitro, the IL-20 cytokines activated the STAT3 and MAPK pathway, but animals with an epithelium specific KO of Stat3 developed an aggravated EoE. Immunohistochemistry staining revealed a prominent decrease of Flg2 in the esophagus of Stat3fl/flKrt5cre mice. Consistently, pharmacological inhibition of STAT3 resulted in a more pronounced reduction of FLG and FLG2 than IL-20 cytokine stimulation.

Conclusion: Targeting IL-20 cytokines or the IL-20Rb chain could offer a novel strategy to prevent epithelial barrier breaches in EoE.

Epithelial GPR35 Protects from *Citrobacter Rodentium* Infection by Preserving Goblet Cells and Mucosal Barrier Integrity

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Background: Goblet cells secrete mucin to create a protective mucus layer against invasive bacterial infection and are therefore essential for maintaining intestinal health. The G protein-coupled receptor 35 (GPR35) is highly expressed in colonic epithelial cells, however, its importance in promoting the mucosal barrier is unknown.

Methods: We examined the relevance of Gpr35 to maintain both epithelial cells and gut microbiota homeostasis with single cell RNA sequencing (scRNA-seq) and 16S rRNA sequencing in mice lacking epithelial *Gpr35* (*Gpr35^{fl/fl}*).

Results: In a steady state, cell type-specific deletion of *Gpr35* in epithelial cells resulted in goblet cell depletion. We noted a transcriptional imbalance of genes involved in goblet cell maturation including *Muc2*, *Gfi1* and *Spdef*. Dysregulation of goblet cells was correlated with changes in the mucosa-associated bacterial communities. Mechanistically, scRNA-seq analysis indicated that signaling of epithelial Gpr35 is essential to maintain normal pyroptosis levels in goblet cells. *Gpr35^{fl/fl}* mice displayed increased susceptibility to *C. rod*-induced colitis as indicated by increased fecal bacterial abundance and dissemination of *C. rodentium* to the preapical tissues in the early phase of the infection.

Conclusion: Epithelial Gpr35 is a critical element for the function of goblet cell-mediated symbiosis between host and microbiota. It could deserve further interest as a therapeutic target of IBD.

Paneth cells regulate lymphangiogenesis in normal physiology and experimental portal hypertension

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Background and aims: The mesenteric lymphatic network contributes to the transport of fluid and intestinal mucosal associated immune cells along the gut-liver axis. We hypothesized that Paneth cells (PCs), as part of the intestinal innate immune system, regulate the development of lymphatic vessels and affect portal pressure in response to microbial-derived products.

Methods: Math1lox/lox VilCreERT2 or control mice were injected three doses of tamoxifen to induce depletion of PCs in the intestine. Portal hypertension was induced by partial portal vein ligation (PPVL). After 14 days, portal pressure was measured. Intestinal and mesenteric lymphatic vessels were identified by immunohistochemistry and quantified using Metamorph. The intestinal expression of specific genes involved in lymphangiogenesis was quantified using qPCR. Furthermore, intestinal crypts were isolated to culture organoids from mice with or without PCs. The organoids were then challenged with different microbial-derived products. Then human lymphatic microvascular endothelial cells (LECs) were cultured in the presence of conditioned media (CM). The lymphangiogenic activity of LECs was assessed using the tube formation and wound healing assays. Additionally, we quantified differentially expressed proteins in the CM collected from all different conditions with mass spectrometry-based proteomics and data were analyzed using MaxQuant.

Results: Depletion of PCs resulted in a significantly reduced portal pressure associated with lower density of lymphatic vessels in the intestine and mesentery as compared to PPVL mice with PCs. Several lymphangiogenic genes were significantly downregulated in the group of mice without PCs when compared to the control mice with PCs. Tube formation and wound healing responses were significantly decreased in LECs treated with CM from organoids without PC. In the absence of PCs, proteomic analyses revealed a significant downregulation of several proteins involved in lymphatic vessel development and morphogenesis, as well as in processes of lipid metabolism and transport.

Conclusion: In the absence of PCs, intestinal and mesenteric lymphangiogenesis was significantly decreased, and this was associated with an attenuation in portal hypertension. These findings suggest that PCs secrete lymphangiogenic signaling molecules in response to microbial-derived products, thereby regulating intestinal-mesenteric lymphatic vessels proliferation and portal pressure.

Timed microbial exposures in early-life modulate B cell repertoire and functional responsiveness

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Healthy mammals co-exist with a dense intestinal microbiota that profoundly shape host immune system. However, if and how maternal microbiota influence offspring immune system is less well defined. In this study we are addressing three facets of the impact of maternal microbial exposure on the key adaptive immune component - B cells of offspring. 1) whether maternal microbial exposure shapes the B cell differentiation and antigen receptor repertoire of offspring. 2) the means by which maternal microbiota involves in early B cell ontogeny in the fetal liver. 3) The consequent effects of altered B cell recognition possibilities on newborn immune responses.

To address the potential impact of the effect of the maternal microbiota we started by comparing the B cell populations in neonatal pups from maternal microbial exposed group and germ-free control. Germ-free pregnant mice were gavaged with reversible *E. coli* HA107 for four times during E5.5-E17.5 or left untreated as controls. Gestational colonisation caused increase of B1 population in neonates. Further analysis shows the preference of B1 determination in the absence of maternal microbial exposure occurred as early as embryonic day 14.5 in fetal liver. Evidences from previous studies indicate that B1 and B2 cells confer several fundamental physical, biological and functional differences. Given the altered B1/B2 ratio infers different adaptive immune responses of offspring to foreign antigens, we accessed the B cell repertoire, the VDJ recombination-formed antigen recognition capabilities of individual animal. B cell repertoire of offspring from group received microbial treatment during pregnancy showed minimal overlap with that of control germ-free group. These findings suggest B cell ontogeny in fetal liver during embryonic development might be impacted by the intestinal microbiota of pregnant mother. We then compared the haematopoietic stem cell (HSC) niche, the supporting mesenchymal cells in the fetal liver for B cell development before birth. Maternal microbial exposure significantly reduced HSC niche cell population. In addition, we measured the expression level of CXCL12, the key cytokine secreted by HSC niche cells in the fetal liver driving embryonic B cell development. CXCL12 was highly expressed at both RNA and protein levels in fetal liver of embryos collected from germ-free pregnant mums. This is consistent with elevated frequency of HSC niche cell population in fetal liver.

Collectively, we propose the maternal microbiota influences HSC niche function in fetal liver and concomitantly shapes the B cell ontogeny and pre-immune B cell repertoire of offspring. To advance our knowledge of the mechanisms that maternal microbiota impacts offspring B cell ontogeny, we will further address 1) how the niche cell function differs in the presence or absence of maternal microbial exposure. Regarding the high heterogeneous features of niche cells, we plan to perform single cell RNA sequencing on the niche cells from fetal liver and address the influence of maternal microbiota. 2) the HSC niche changes results from maternal microbiota mediated direct or indirect effects. To achieve this, we will sort HSC niche cells and HSCs from germ-free fetal liver, and in vitro co-culture them in the presence of bacterial lysis. 3) The physiological consequences of maternal microbiota to early-life B cell functions in offspring. We will study the B cell immune responses to systemic or mucosal antigen challenges during the early-life of pups right after weaning.

ORAL PRESENTATIONS: HEPATOLOGY I

A preclinical screening platform of patient-derived tumor organoids for drug discovery in hepatocellular carcinoma.

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Background: Hepatocellular carcinoma (HCC) is an aggressive cancer and a major cause of cancer-related deaths worldwide. Most HCCs are diagnosed at an advanced stage with limited treatment options and poor prognosis. The efficacy of currently available therapies differs greatly between patients, primarily due to pronounced inter- and intratumoral heterogeneity and the lack of biomarkers that predict treatment response. Classic cell culture assays fail in adequately representing patient's tumor biology and physiological conditions. Tumor organoids have recently emerged as a novel preclinical 3D *in vitro* system that recapitulates the diversity and complexity of tumors observed in patients. We established a robust screening platform based on patient-derived HCC organoids with the aim to identify novel compounds for the treatment of HCC.

Methods: A comprehensive biobank of HCC organoids was generated from HCC tissues obtained by needle biopsy and surgical resection. Semi-automated drug screening was performed in a 384-well plate format. Plates were coated with a hydrogel layer and cells were seeded on top to allow for organoid formation. A library of 2889 FDA-approved, investigational, and previously untested small-molecule compounds was screened on our HCC organoid biobank and hits were selected based on their activity profile.

Results: We report the identification of multiple compounds with strong activity against HCC cells using an organoid-based drug screening platform. Drug activity differed strongly between HCC organoid lines with compounds being highly active in all, only some, or individual lines, reflecting the heterogeneous drug response observed in patients.

Conclusions: Tumor organoids can be used to screen drugs with throughputs comparable to standard screening platforms but with the advantage of identifying hits based on physiologically relevant drug responses. Remarkably, the majority of hits resulting from the FDA library screen belong to drugs approved for indications other than cancer and thus open up new perspectives for drug repurposing.

Suppression of tumorigenicity 2 (ST2) serum level for the assessment of liver fibrosis

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Background: Liver fibrosis and cirrhosis are related to increased morbidity and mortality. Today's gold standard for assessing liver fibrosis remains liver biopsy. Alternatively, transient elastography (TE) and scores like the FIB4 and APRI can be used to estimate the fibrosis stage. The former is, however, available only through specialists and the latter require several serum parameters. Single serum biomarker for the assessment of liver fibrosis could facilitate outpatient care of patients suspected to suffer from advanced liver disease through general practitioners. A potential marker is soluble ST2 (sST2), which is related to hepatic stellate cell activation. We aimed to assess sST2 as a marker for liver fibrosis using patients treated for chronic hepatitis C.

Methods: Patients from the Swiss hepatitis C cohort study received treatment with direct-acting antivirals. sST2 was measured in plasma samples before and after therapy and correlated with reported values of TE, APRI and FIB-4.

Results: Overall, 176 patients were included with 126 having complete data sets pre- and post-treatment for compared data analyses. The median level of sST2 before treatment was 33.5 ng/ml and 28.4 ng/ml after treatment ($P < 0.0001$). A positive linear correlation between sST2 and

values for TE, APRI as well as FIB-4 was present with R^2 being in the range of 0.11 to 0.22. R^2 was highest for the correlation of sST2 with TE values and correlation generally improved after treatment.

Conclusion: In summary, the results of the study indicate that sST2 might be a suitable marker to assess liver fibrosis.

Development of a microscopy readout to characterize drug response in hepatocellular carcinoma organoids.

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Background: Hepatocellular carcinoma (HCC) is one of the most common causes of cancer-related deaths worldwide. Treatment options are limited for patients with advanced stage HCC and drug resistance is frequent. Current methods to assess drug sensitivity *in vitro* mainly rely on metabolic-based viability readouts. These readouts provide a very rapid and sensitive estimation of drug responses. But, they do not provide information at the cellular level such as whether a drug acts cytostatically or is cytotoxic. However, such information could likely be very valuable in guiding pre-clinical development of candidate drugs derived from large drug screens. Moreover, metabolic activity of cancer cells can change greatly depending on the culture conditions (e.g. normoxia or hypoxia). This can complicate interpretation of assays where drug sensitivity under different culture conditions is compared. Therefore, we developed a metabolic-independent microscopy approach to detect dead and live cells to assess drug sensitivity at the cellular level.

Methods: Patient-derived HCC organoids were cultured on a hydrogel layer in 384-well plates. The Live-or-Dye NucFix staining kit (Biotium) was implemented as a dead-cell marker together with Hoechst as a counterstain for all nuclei. Samples were fixed and image acquisition automated on a spinning disk confocal microscope. An analysis pipeline to assess number of living cells and the fraction of dead cells was developed using the QuPath software.

Results: We report the development of a metabolic-independent microscopy-based readout to assess drug sensitivity at the cellular level in HCC organoids. Our analysis pipeline produces reliable numbers for living cells and the fraction of dead cells, allowing for unbiased comparison of drug sensitivity between HCC organoid lines or culture conditions. Based on these parameters, we can also determine cytotoxic or cytostatic effects of a drug.

Conclusions: We believe that the microscopy-based readout for drug sensitivity will prove very useful for in depth drug response analysis and thus benefit the translation of *in vitro* results into clinical application.

Next-Generation Sequencing of Swiss Hepatitis E Virus Isolates Allows for Reconstitution of Functional Clones

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Background: Hepatitis E acquired in Switzerland is caused primarily by a specific hepatitis E virus (HEV) subtype which has been provisionally designated as 3s and recently assigned as a distinct group to 3h (3s[p]/h). Here, we analyzed HEV from patients with severe outcomes of hepatitis E by a newly developed next-generation sequencing (NGS) protocol and assembled subgenomic replicons as well as full-length clones.

Methods: Illumina RNA sequencing coupled with HEV-specific sequence enrichment was carried out on 24 plasma samples from patients with hepatitis E acquired in Switzerland and severe outcomes (severe acute hepatitis, acute-on-chronic liver failure and neurologic complications). Viral genomes reconstituted by DNA synthesis and molecular cloning were functionally characterized in cell culture.

Results: The entire HEV genomes from plasma of 24 patients could be sequenced successfully, confirming the predominance of subtype 3s(p)/h in Switzerland. The number of reads at each nucleotide position and overall coverage allowed to establish a consensus sequence for 17 genomes. Subgenomic replicons and full-length genomes derived from some of these replicated in cell culture. Functional clones are currently being further characterized, in particular for their ability to produce infectious virus.

Conclusions: A newly developed NGS protocol and DNA synthesis allowed to successfully reconstitute functional clones of Swiss HEV isolates. These represent a rare resource and should facilitate further studies on the molecular virology and pathogenesis of hepatitis E.

Heterogeneity of Peripheral Monocytes in Patients with Cirrhosis

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Background: In patients with cirrhosis, we recently discovered dysfunctional monocytic subsets (CD14+HLA-DR+AXL+, CD14+MERTK+, M-MDSC) prevail over regular monocytes, associated with reduced capacity to repel microbial challenge and infection susceptibility. The underlying signaling mechanisms remain unexplored. Transcriptome wide single cell RNA sequencing (scRNA Seq) is expected to enhance the understanding of immune cell differentiation processes.

Methods: Monocytes (20.000 cells/sample) from compensated (CC n = 4), decompensated (DC n = 4) cirrhosis patients and healthy controls (HC n = 4) were prepared for scRNA Seq (10x Technology) and analysed (>4000 cells/sample) using R/Bioconductor.

Results: Our preliminary scRNA Seq data revealed 6 distinct monocyte clusters. 4 clusters represent classical (CD14⁺⁺CD16⁻) monocytes, 2 representing intermediate (CD14⁺⁺CD16⁺) and non-classical (CD14⁺CD16⁺⁺) subsets. The cluster frequency of CD14⁺CD16⁺⁺-like monocytes was reduced in CC/DC while M- MDSC-like were increased compared to HC. Differentially expressed (DE) gene analysis revealed increased RNA expression of Cd52 (T-cell suppressor) and Ca²⁺ binding S100 family members on monocytes from CC/DC, while some MHC class II members were decreased. CD14⁺⁺CD16⁻ and CD14⁺⁺CD16⁺-like clusters showed increased *Commd4* (NF-κB downregulation) and decreased *Siglec5* (reduced inflammasome activity) in CC/DC. CD14⁺CD16⁺⁺ subset showed higher levels of *Ppargc1b* in CC/DC. *Timd4* (Kupffer Cell marker) was expressed in monocytes from cirrhosis only.

Conclusion: We identified 6 monocyte clusters, their prevalence differed between HC and CC/DC. DE Gene expression revealed abundance of immunomodulatory clusters in CC/DC.

Increasing prevalence of obesity among patients evaluated for liver transplantation in a Swiss tertiary referral center: a 10-year retrospective analysis

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Background and aims: NAFLD is the first cause of chronic liver disease in developed countries. We aimed to assess the trend in the prevalence of obesity, type 2 diabetes and NAFLD in patients undergoing liver transplantation (LT) evaluation and to assess whether obese patients were less likely to be listed or had an increased drop-out rate after listing.

Methods: We conducted a retrospective study of all consecutive patients who underwent a LT evaluation at a Swiss tertiary referring center between 2009 and 2020.

Results: 242 patients were included, 83% were male. The median age was 59 years (IQR, 51–64 years). The most common causes of end-stage liver disease were viral hepatitis (28%), alcoholic liver disease (21%) and NAFLD (17%). Obesity was present in 28% of our cohort, with a significant increase over time. Prevalence of diabetes followed this same trend (p = 0.02). The proportion of non-listed and listed obese patients was not different (21% vs. 30%, respectively; p = 0.3). When analyzing drop-out rates, there was no significant difference between obese and non-obese patients (36% vs. 32%; p = 0.9). HCC represented the primary indication for LT in approximately half of our cohort (46%), with increasing prevalence of NAFLD among patients with HCC (p = 0.03).

Conclusions: The prevalence of obesity and diabetes significantly increased over our study period. Obese patients had similar chances of being enlisted. The landscape of LT indications is shifting towards NAFLD, highlighting the urgent need to prevent NAFLD progression.

Increased serum levels of gut-derived MAIT cell stimulatory bacterial metabolites in patients with portal hypertension

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Background: Mucosal-associated invariant T (MAIT) cells represent the most abundant T cell type in human liver. They respond to bacterial metabolites derived from Riboflavin synthesis that are presented by MHC-like molecule MR1. The most potent stimulatory MAIT cell antigen (Ag) is 5-(2-oxopropylideneamino)-6-D-ribylaminoouracil (5-OP-RU). Recent murine studies showed that microbiota-derived Ag is necessary for intra-thymic development of MAIT cells, arguing for 5-OP-RU absorption from the gut. By analyzing sera of patients suffering from portal hypertension we investigated whether gut leakiness in humans may be associated with the presence of bacterial MAIT cell stimulatory Ags in circulation.

Methods: We examined MAIT cell stimulatory potential of peripheral blood serum obtained from 14 patients with a history of transjugular intrahepatic porto-systemic shunt (TIPSS), as compared to healthy subjects. Analogously, we analysed paired serum samples from portal and peripheral blood of 8 patients undergoing TIPSS. To detect MAIT cell ligands, Ag-presenting K562 cells overexpressing MR1 were exposed to serum and IFN-gamma release by MAIT cells was measured by ELISA. MR1 blocking antibodies were used to verify the MR1 dependence in MAIT cell activation. Serum Ag amounts were defined using control assays with 5-OP-RU added in the range of 0.006–25 pM.

Results: We found MR1-dependent MAIT cell stimulation by sera obtained from healthy subjects, corresponding to 5-OP-RU concentrations of 0.05–0.2 pM. Patients with a history of TIPSS showed significantly higher MAIT cell stimulatory potential than age- and sex-matched healthy control subjects. Sera from 4 out of 8 patients undergoing TIPSS strongly stimulated MAIT cells (1–2 pM 5-OP-RU equivalent) and portal serum was up to 3-fold more active than its peripheral counterpart.

Conclusions: We present first evidence for the presence of MAIT cell stimulatory gut bacterial metabolites in human blood. Our results provide rationale for the activated MAIT phenotype seen in human liver. Increased levels of gut-derived MAIT cell stimulatory ligands in the blood of TIPSS patients suffering from portal hypertension, associated with impaired intestinal barrier function, indicate that intrahepatic Ag-presentation may represent an important step in the development of liver disease. Measurement of circulating MAIT cell Ag levels could be considered as part of a diagnostic test panel for assessing gut integrity in the context of liver inflammation.

ORAL PRESENTATIONS: IBD AND BASIC SCIENCE

Biologicals and small molecule combotherapies: promising experience in refractory IBD patients

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Background: It has been hypothesized that combination of two biologics or with a small molecule could “break the ceiling” of the efficacy (~60%) of currently available biological therapies for IBD patients. The best combinations and their safety are, however, unknown.

Methods: A chart review of Inselspital, Bern University hospital, of IBD patients on combination therapy have been performed. Data on disease phenotype, previous treatment and efficacy and safety of the new combinations have been collected and studied to help moving forward the use of this armamentarium.

Results: Among 14 identified IBD patients (43% women, 8 ulcerative colitis, 6 Crohn’s disease) who received 17 combination therapies between September 2018 and April 2021. They suffered from steroid-dependency and half of them were refractory to at least two anti-TNF alpha agents. These treatments have been started after a median duration of disease of 4 years (range 1-31) for a mean period of combo treatment of 5 months (range 1–19), 6 were still ongoing. Various combotherapies and clinical response (arrows) are presented in Figure 1. A partial or complete response was observed in 11/17 therapies (65%) with a mean decrease of CRP of 11 mg/l (range -60 to 23) and calprotectin of 867 mcg/g (range 0–1745). Concerning the safety, we reported 2 infections (otitis media, skin mycosis) and 4 minor adverse events (tumefaction left parotide, eczema, 2x lymphopenia) when small molecules were involved.

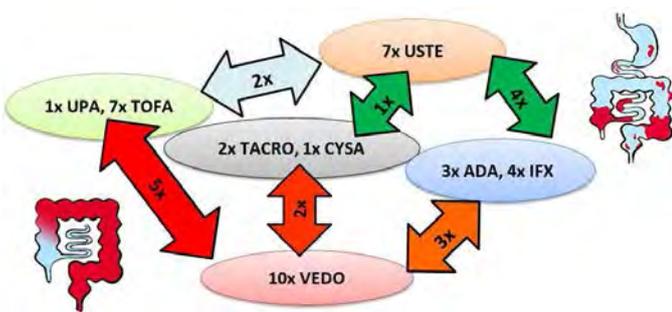


Figure 1. The best strategies seems to involve ustekinumab, anti-TNF agents and JAKs in Crohn’s patients with some minors adverse events, whereas vedolizumab and tofacitinib have been more safe when combined, but unsuccessful (40%) in refractory ulcerative colitis.

Conclusions: Ustekinumab combined with anti-TNF agents in Crohn’s disease is more effective than vedolizumab and tofacitinib in ulcerative colitis. Combining with small molecules increases the risk of lymphopenia and minor infections in severe refractory and steroid-dependent inflammatory bowel disease patients.

Prevalence and Impact of Alcohol Consumption and Cannabis Use on Inflammatory Bowel Diseases

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Background: There is little guidance regarding the impact of alcohol and cannabis on the clinical course of inflammatory bowel disease. The aim of this study was to assess the prevalence, sociodemographic characteristics and impact of alcohol and cannabis use on the clinical course of the disease.

Methods: We performed a retrospective analysis of prospectively collected data within the Swiss Inflammatory Bowel Disease Cohort Study with yearly follow-ups and substance specific questionnaires. We analyzed the prevalence of use, profile of users at risk for addiction and the impact of alcohol and cannabis on the course of disease.

Results: We collected data of 2828 patients included between 2006 and 2018, and analyzed it according to their completion of specific surveys on alcohol and cannabis use. The prevalence of patient-reported active use was 41.3% for alcohol and 6% for cannabis. Heavy drinkers were over-represented among retired, married smokers receiving mostly aminosalicylates and less immunosuppression. In ulcerative colitis patients, low-to-moderate drinking was associated with less extensive disease. Cannabis users were often students with ileal Crohn’s disease. A logistic regression analysis confirmed a risk of alcohol consumption in male workers >50 years, whereas cannabis use was only associated with nicotine consumption. Female gender, retirement and being married were protective factors regarding cannabis consumption.

Conclusions: A significant proportion of patients with inflammatory bowel disease consume alcohol or cannabis. Heavy alcohol consumption is most likely in male smokers >50 years, whereas young men with ileal disease rather use cannabis.

Regenerative therapy with SVF-PRP to treat complex perianal fistula

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Background: Curing complex anal fistula can be extremely challenging. This ongoing study investigates the healing rate of patients with complex anal fistula after regenerative therapy with autologous stromal vascular fraction derived mesenchymal stem cells and platelet-rich plasma (SVF-PRP).

Methods: Consecutive patients with complex anal fistula were prospectively followed for 12 months. MRI was performed before, and at 4 and 12 months after treatment with SVF-PRP. Complex fistulas were defined based on their relationship to the sphincter and patient factors such as multiple previous anal surgery and incontinence. Continence was assessed at each clinical evaluation prior and after SVF-PRP using the Vaizey score. Fistula were drained with setons for at least 6 weeks prior to SVF-PRP. SVF-PRP was standardized as follows: a lipoaspirate was harvested from subcutaneous abdominal fat, centrifugated twice and fractionated to yield SVF. PRP was obtained from peripheral blood. Fistulectomy was performed, the internal orifice closed and the excised external orifice left open. SVF-PRP was injected around the fistula.

Results: 14 patients (8 men and 6 women) were included between December 2019 and January 2021. Median age was 39 years with an interquartile range (IQR) of 32-49. 2 patients suffered from perineal Crohn’s disease and 12 had complex fistula of cryptoglandular origin. All were heavily pretreated. SVF-PRP fistula repair was performed at a median of 20.5 months (IQR 5-28) after the initial diagnosis with a median of 3 prior fistula surgeries (IQR 2-4). The median operation time was 82 minutes (IQR 74-96). All patients were discharged on postoperative day 1. The median follow up was 6 months (IQR 2–10). There was no deterioration in continence during follow-up. 1/14 patient developed an abscess and experienced an early failure within 6 weeks of SVF-PRP for an early success rate of 93%. All others patients were back to work and leisure activities with no limitations. At 4 months of follow-up, 9/10 patients were

clinically well with no active fistula at MRI. Last, 4/4 patients reached 12 months follow-up and demonstrated clinical and MRI complete healing.

Conclusion: SVF-PRP is a safe and promising tool in the broad armamentarium of treatments for complex perianal fistula.

Management of biliary obstruction in patients with newly diagnosed alveolar echinococcosis: a retrospective case-study

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Background: Alveolar echinococcosis (AE) is an orphan zoonotic liver disease of increasing concern in Switzerland. Most patients present in an advanced, inoperable stage and occasionally with symptomatic biliary stenosis. Oftentimes, biliary tract intervention is considered, but these are associated with a high risk of cholangitis and cyst infection. In this study, we aim to evaluate conservative management of biliary obstruction due to newly diagnosed AE.

Methods: We screened 220 AE patients participating in the Zurich Echinococcosis Cohort study from 2000-2020 for those presenting icteric at diagnosis. Patients with alternative reasons for hyperbilirubinemia, i.e. gall stone disease or cirrhosis, were excluded. Retrospective analysis included stage of the disease, location of biliary stenosis, bilirubin at diagnosis and after 1, 3, 6 months, biliary tract intervention or lack thereof, as well as occurrence of biliary complications during follow-up.

Results: We identified 15 patients that met in-/exclusion criteria. 2 patients received ERCP or PTCO within 4 weeks of diagnosis, both developed post-interventional cholangitis. 13 patients received benzimidazole treatment alone, completely relieving biliary obstruction within 6 months in all but 1 patient. 2 required biliary tract intervention during follow-up (median 54 months).

Conclusion: Biliary obstruction in the context of newly diagnosed AE can be treated by implementation of benzimidazole therapy alone. Biliary tract intervention should be reserved for those patients with insufficient response after 6 months or recurrence during follow-up.

Evaluation of a structured treatment discontinuation in patients with inoperable alveolar echinococcosis on long-term benzimidazole therapy

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Background: Alveolar echinococcosis (AE) is an orphan zoonosis of increasing concern in Switzerland. Most cases present in an advanced, inoperable stage that requires life-long benzimidazole therapy to slow parasite growth and stabilize the disease. In some patients, therapy may act parasitocidal and lead to serologically (Em18) and metabolically (PET) quiescent disease. It is disputed, whether these patients are truly cured and treatment can be discontinued.

Methods: Retrospective analysis of 34 inoperable AE patients who participated in a previous intervention study at our clinic to determine feasibility of benzimidazole treatment cessation. Of particular interest were AE recurrence or other reasons for retreatment. Additionally, volumetric measurement of AE lesions in sectional imaging was performed at baseline and last follow-up to determine subclinical lesion growth.

Results: 12 patients met criteria and stopped benzimidazole therapy for a median of 131 months. 11 patients showed no AE recurrence and stable or regressive AE lesions as determined by volumetric measurement. One patient developed progressive disease with persistently negative Em18 ELISA and only very slight FDG-uptake in delayed PET imaging.

Conclusion: Inoperable AE patients, who meet cessation criteria are taken off benzimidazole therapy, show favorable outcome in most cases. Close follow-up including sectional imaging to accurately assess lesions size is strongly advised.

Endocuff-assisted virtual chromo-colonoscopy for screening colonoscopy demonstrates high adenoma detection rate: Results of a prospective single center study

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Background: The adenoma detection rate (ADR) is inversely associated with the risk for interval colorectal cancer (CRC). An ADR >25% is therefore crucial for the effectiveness of CRC surveillance programs, and tools to improve the ADR especially in GI trainees are needed. Recent findings suggest that add-on devices such as Endocuff (EC) increase the ADR. Additionally, a recent meta-analysis indicates a significantly increased ADR using narrow band imaging (NBI), but only in patients with excellent bowel preparation. We aimed to evaluate the ADR in patients undergoing screening colonoscopy using the combination of EC and NBI.

Methods: We prospectively analyzed all patients undergoing EC-assisted screening colonoscopy at the Kantonsspital St. Gallen between February 2020 and February 2021. NBI was used for the duration of the withdrawal. Patients with a Boston bowel preparation score (BBPS) <8 and withdrawal time <6 minutes were excluded. Patients underwent colonic lavage with a split dose of Macrogol[®] over 2 days. Colonoscopies (PCF-H190, CF-HQ 190 AL, Olympus[®]; Tokyo, Japan) were performed by two experienced board-certified gastroenterologists (>4000 colonoscopies) and one trainee (<500 colonoscopies). ADR and sessile serrated lesion detection rate (SSLDR) were determined. Residual stool contamination in NBI colonoscopy of each bowel segment (right colon, transverse colon, and left colon) was assessed by each endoscopist using an additional modified NBI-BBPS score (1 point per segment if no residual pollution, ranging from 0-3).

Results: 272 patients (median age 60 years (IQR 54-58) and 52% male) with a modified NBI-BBPS of 3 in the majority of patients were included. Overall ADR and SSLDR were 55.1% and 12.5%, respectively. ADR and SSLDR did not significantly differ between experienced endoscopists and GI trainee (53.5% vs. 61%, $p = 0.375$, and 14.1% vs 6.8%, $p = 0.182$). A higher modified NBI-BBPS was not associated with a higher ADR or SSLDR, but a significant longer withdrawal time was observed in the trainee.

Conclusion: Screening colonoscopy using EC in combination with NBI is feasible achieving an excellent ADR of 55%. Particularly trainees seem to benefit from the combination of EC and NBI, resulting in an ADR comparable to the ADR of an experienced gastroenterologist.



Figure 1A-D. Bowel Boston Preparation Score (BBPS) of 3 (A, C) but categorized with NBI-BBPS 0 (B). No residual pollution in NBI (D), categorized NBI-BBPS 1.



Figure 2A-D. White light colonoscopy without polyp (A, C), NBI with sessile serrated lesions (B, D)

Management of nonfunctional pancreatic neuroendocrine tumors by endoscopic ultrasound guided radiofrequency ablation: a retrospective study in two tertiary centers

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Background: Recently, there has been growing interest in investigating endoscopic ultrasound guided radiofrequency ablation (EUS-RFA) in the management of small size non-functional pancreatic neuroendocrine tumors (nf pNETs).

Patients and methods: A bicentric retrospective study was performed including patients with histologically confirmed nf pNETs, consecutively treated by EUS-RFA between December 2015 and March 2021 at two tertiary referral centers.

Results: In 24 patients (mean age 65.7 years, 58% male) EUS-RFA was successfully performed. All patients had sporadic grade 1 lesions (mean size 14.2 ± 4.7 mm, 33% head/uncinulated process, 25% body, 42% tail). 8/24 lesions (33%) were found to be cystic. Mean hospital stay was 3.2 days. Complete treatment response was confirmed in 23/24 patients (96%) on follow-up imaging (median follow-up 11.5 months, range 1-36 months). Two patients had two EUS-RFA sessions until complete necrosis. One patient underwent secondary surgery. Histopathology of the resected specimen revealed 3 mm residual tumor tissue. Complications occurred in 9/24 patients (minor n = 4, major n = 5). Acute pancreatitis occurred in 4 patients and 1 patient had delayed pancreatitis due to stenosis of the main pancreatic duct.

Conclusion: EUS-RFA seems a promising treatment strategy in the management of small size nf pNETs with an excellent efficacy and a decent safety profile. Further evidence focusing on long term survival and recurrence is needed.

ORAL PRESENTATIONS: HEPATOLOGY II

Ubiquitous expression of HBsAg from integrated HBV DNA in patients with low viral load

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Background: Loss of serum hepatitis B surface antigen (HBsAg) is a hallmark of spontaneous and therapy induced resolution of HBV infection, since it generally reflects a profound decrease in viral replication. However, integrated HBV DNA can contribute to HBsAg expression independent of viral replication. The relative contributions of these two sources of HBsAg are not well understood. Specifically, it is not known whether actively transcribed HBV integration could spread throughout the entire liver.

Methods: The relative distribution of HBsAg and HBV RNA in liver biopsy tissue from HBe- patients was analyzed by immunohistochemistry (IHC) and in situ hybridization (ISH), respectively. Frozen biopsy tissue was used for molecular analysis of intrahepatic viral RNA, virus-host chimeric transcripts and viral DNA.

Results: IHC and ISH analysis revealed HBsAg and HBV RNA positivity in virtually all hepatocytes in the liver of some HBe- patients despite very low viremia. RT-qPCR and RNA-seq analysis confirmed high expression levels of HBV envelope coding RNAs. The amounts of the viral transcriptional template covalently closed circular (ccc)DNA, however, were too low to support the ubiquitous HBV RNA expression. In contrast, levels of total cellular HBV DNA were consistent with ubiquitous HBV integration. Finally, RNA-seq revealed the presence of many HBV-host chimeric transcripts with the potential for HBsAg expression.

Conclusions: Transcriptionally active HBV integration can extend to the entire liver in some HBe- patients. This can lead to ubiquitous HBsAg expression independent of HBV replication. In such patients, HBsAg is probably not a clinically useful surrogate marker for viral resolution or functional cure.

A Genome-Wide CRISPR/Cas9 Screen Identifies RAB5A as Host Factor of the Hepatitis E Virus Life Cycle

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Background: Hepatitis E virus (HEV) is a positive-strand RNA virus. Current understanding of the molecular mechanisms allowing for productive HEV infection is limited, especially with respect to host factors required for the viral life cycle. Hence, our study aims at identifying host factors required for HEV replication.

Methods: A genome-wide CRISPR/Cas9 screen was performed in permissive human cell lines harboring newly developed subgenomic HEV replicons allowing for positive and negative selection, followed by next-generation sequencing and bioinformatic analyses. Candidates were validated by siRNA-mediated gene silencing and CRISPR/Cas9-mediated gene knockout in cells transfected with subgenomic HEV replicons or infected with cell culture-derived HEV.

Results: The newly developed replicons and a library of 120,000 unique guide RNAs were employed in two separate screens, identifying 20 top host factor candidates. Validation yielded five host factors, including GBF1, which had been identified previously by a directed approach, and the Ras-related endosomal protein RAB5A. The expression level and functional activity of RAB5A and of well-characterized mutants thereof were found to modulate HEV RNA replication. Colocalization studies revealed close proximity of RAB5A and the HEV replicase.

Conclusions: We describe an innovative approach exploiting CRISPR/Cas9 to identify host factors of a noncytolytic virus. Future studies shall investigate the mechanisms by which the newly identified host factor RAB5A modulates HEV RNA replication. This work yields new insights into the HEV life cycle and the virus-host interactions required for productive infection.

Contrast-enhanced ultrasound improves CT-based detection of colorectal liver metastases modifying the therapeutic strategy: Results of a prospective study

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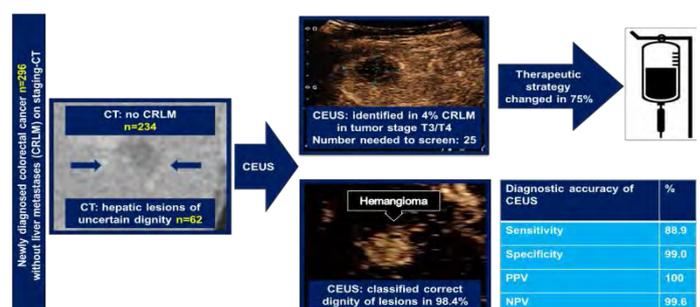
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Background and Aims: CT may miss up to 30% of cases of colorectal liver metastases (CRLM). We assessed the impact of contrast-enhanced ultrasound (CEUS) on the detection of CRLM and changes to the therapeutic strategy, and the accuracy of CEUS in differentiating unclear focal liver lesions (FLL) compared to staging-CT.

Methods: We prospectively analyzed all patients with newly diagnosed and histologically confirmed colorectal cancer (CRC) at our tertiary gastroenterological center between December 2015 and May 2019. CEUS was performed in a total of 296 patients without CRLM after staging-CT using the contrast agent (SonoVue®). Standard of reference was obtained by MRI or histology to diagnose CRLM missed by CT. Benign FLL were confirmed by MRI or follow-up CT (mean follow-up interval: 18 months).

Results: Eight additional CRLM were detected by CEUS (overall 2.7%; sensitivity 88.9%, specificity 99.0%, positive predictive value 100%, negative predictive value 99.6%). All patients with CRLM detected only by CEUS were in tumor stage T3/T4 (4.0% additionally detected CRLM). The number needed to screen to detect one additional CRLM by CEUS was 37 in all patients and 24.5 in T3/T4-patients. When results were reviewed by a board-certified radiologist and oncologist, the therapeutic strategy changed in 6 of these 8 patients. Among the 62 patients (20.9%) with unclear FLL after staging-CT, CEUS determined the dignity of 98.4% of the FLL.

Conclusion: CEUS detected overall 2.7% additional CRLM (including 4.0% in tumor stage T3/T4) with a significant impact on the oncological therapeutic strategy for 75% of these patients. Patients with tumor stage T3/T4 would particularly benefit from CEUS. We propose CEUS as the first imaging modality for CT-detected lesions of unknown dignity.



The G protein-coupled receptor MRGX4 is a novel receptor for bile salts expressed on sensory neurons

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Background: Mas gene-related G protein-coupled receptors (Mrg) represent a class of pruriceptors expressed on sensory neurons. Pruritus is a frequent symptom in various hepatobiliary disorders. The recent beneficial effects of ileal bile acid transport inhibitors in patients suffering from cholestatic pruritus have raised interest in bile salts as pruritogens. We hypothesized that cholephilic substances in serum of cholestatic patients may activate MRG receptors thereby causing pruritus.

Methods: Human and murine MRG receptors were cloned and stably expressed in HEK293 cells. Activation of MRG receptors in HEK293 or DRGs by cholephilic substances were measured by changes in cytosolic free calcium (Ca²⁺)_i using ratiometric fluorimetry. In mice scratch activity after intradermal pruritogen injection was quantified observer-independently measuring electric fields induced by implanted magnets. In 15 healthy volunteers itch intensity was quantified on a numeric rating scale after intradermal injection or focal application.

Results: We investigated the potential of human cholestatic serum and bile for activation of human and murine MRG receptors. Fractions containing bile salts resulted in rise of (Ca²⁺)_i in hMRGX4 expressing HEK cells but neither of other human or murine MRG isoforms nor cultures of freshly dissociated murine DRGs. Analyzing human bile salts revealed that certain bile salt species (referred to as hMRGX4-activating bile salt species) were capable of activating hMRGX4 while others did not. The EC₅₀ values ranged within the pathophysiological range of low micromolar concentrations. Intradermally injected bile salts did not cause significant scratching behavior in mice. In contrast, in humans focally applied or intradermally injected hMRGX4-activating bile salts caused significant itch intensity compared to non-hMRGX4 activating bile salts. Laser-doppler imaging indicated no widespread axon reflex erythema excluding relevant mast cells activation.

Conclusions: These data unravel a novel signaling pathway for bile salt subspecies that may contribute to cholestatic pruritus and may explain the differences between murine and human cholestasis. The hMRGX4 receptor represents a promising drug target to alleviate cholestatic pruritus.

When comparing the ICI group to the AILD group, centrilobular inflammation, together with endothelitis, were more frequent in the first (p = 0.067), whereas emperipolesis was present in 50% of the second and absent from the first (p = 0.007). Granulomas were present in 52% of ICI group liver biopsies and never found in the AILD group (p = 0.002). Plasma cells were the predominant inflammatory cells in the AILD group and were poorly represented in the ICI group (p = 0.006). Importantly, there was no statistically significant difference in the CD4/CD8 lymphocyte ratios, which were heterogeneous among the two groups.

Conclusions: Liver irAEs present with great variation both from clinical and immune-histopathological standpoints. Liver biopsy provides a clue to the diagnosis of hepatic irAEs and distinguishes these from AILD, reflecting different immunological mechanisms.

Transition to HBeAg-negative chronic hepatitis B virus infection is associated with reduced cccDNA transcriptional activity

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Background & Aims: HBeAg seroconversion during the natural history of chronic hepatitis B (CHB) is associated with a strong drop in serum HBV DNA levels and a reduction of intrahepatic covalently closed circular DNA (cccDNA) content. Of particular interest is the transition to HBeAg-negative chronic infection (ENCI). ENCI, previously known as inactive carrier state, is characterized by very low or negative viremia and the absence of liver disease. The molecular mechanisms responsible for the transition to ENCI and for the control of viral replication in ENCI are still poorly understood.

Methods: To identify which step(s) in the viral life cycle are controlled during the transition to ENCI, we quantified cccDNA, pre-genomic RNA (pgRNA), total HBV RNA and DNA replicative intermediates in 68 biopsies from patients in different phases of CHB.

Results: HBeAg seroconversion is associated with a reduction of cccDNA amounts as well as transcriptional activity. Silencing of cccDNA is particularly pronounced in ENCI, where there was ~46 times less pgRNA per cccDNA compared to HBeAg-negative CHB. Furthermore, a subgroup of patients with HBeAg-negative CHB can be characterized by reduced replication efficiency downstream of pgRNA.

Conclusions: The reduction in serum viral load during the transition to ENCI seems to primarily result from strong inhibition of the transcriptional activity of cccDNA which can be maintained in the absence of liver disease.

Immune Checkpoint Inhibitor-Associated Hepatitis: A Distinct Form of Immune-Mediated Liver Disease

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Background: Immune checkpoint inhibitors (ICI) have become a mainstay of advanced cancer treatment. We aimed to better characterize liver immune-related adverse events (irAEs) following ICIs and to compare them to classic autoimmune liver diseases (AILD), i.e. autoimmune hepatitis (AIH) as well as primary biliary cholangitis (PBC).

Patients and Methods: We retrospectively reviewed and compared the clinical, biological and liver histological features of two groups of patients: 1) Twenty-seven patients with irAEs (ICI group), twenty-six of whom presented grade three or above toxicities, and 2) Fourteen patients with AILD (AILD group; eleven AIH and three PBC patients).

Results: We observed three distinct clinical and histological liver injury patterns in the ICI group: a predominantly hepatic pattern with an inflammatory infiltrate consisting primarily of lymphocytes (56%), a predominantly cholangitic pattern (16%) and a mixed cholangiohepatic pattern (24%). Interestingly, 15% of ICI group patients presented a significant elevation of serological markers classically associated with AILD.

The HEV RNA-Dependent RNA Polymerase is Involved in RNA Replication and Virus Production

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Background: The hepatitis E virus (HEV) genome comprises three open reading frames (ORF). ORF1 is translated into a large protein corresponding to the viral replicase and including an RNA-dependent RNA polymerase (RdRp) domain. Here, we further investigated the structure and function of the HEV RdRp.

Methods: Sequence and nuclear magnetic resonance (NMR) structural analyses were combined with site-directed mutagenesis and functional characterization of subgenomic HEV replicons and full-length genomes.

Results: Sequence analyses across *Hepeviridae* family members identified a conserved predicted α -helix in the thumb subdomain of the HEV RdRp. NMR revealed an amphipathic α -helix extending from amino acid 1628 to 1644 of the ORF1 protein. Mutations on the hydrophobic side

of this helix impaired HEV RNA replication and resulted in the selection of a compensatory change in the RdRp palm subdomain. Importantly, some mutations on the hydrophilic side, including a mutant observed in patients with chronic hepatitis E who develop ribavirin resistance, did not affect or even increase HEV RNA replication but impaired infectious particle assembly and/or secretion.

Conclusions: Structure-function analyses identified a conserved amphipathic α -helix in the thumb subdomain of the HEV RdRp with a dual role in viral RNA replication and virus production. This study provides structural insights into a key segment of the ORF1 protein and describes the successful use of reverse genetics in HEV, revealing functional interactions between the RdRp thumb and palm subdomains. On a broader scale, it demonstrates that the HEV replicase, similar to those of other positive-strand RNA viruses, is also involved in virus production.

ORAL PRESENTATIONS: SURGERY

Primordial GATA6 macrophages function as extravascular platelets in sterile injury

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Background: Abdominal surgeries are life-saving operations. However, some patients develop intra-abdominal scars called peritoneal adhesions that cause significant morbidity and generate a significant burden for health care systems. The mechanism of adhesion formation is poorly understood and up to date no specific treatment exists.

Methods: Here we use intravital microscopy to explore how cavity macrophages that are suspended in the fluid phase (peritoneal fluid) can identify injury, how they migrate towards it and how this could affect post-surgical adhesion formation. We established a novel microscopy system that allows to image within the peritoneal cavity through the intact abdominal wall by using multi-photon excitation and a highly-sensitive non-descanned detection system.

Results: We show that cavity macrophages rapidly form thrombus-like structures in response to injury using primordial scavenger receptor (SRCR) domains. Aggregates of cavity macrophages physically sealed injuries and promoted rapid repair of focal lesions. In iatrogenic surgical situations, these cavity macrophages formed extensive aggregates that promoted the growth of intra-abdominal scar tissue termed peritoneal adhesions.

Conclusions: Peritoneal macrophage aggregation promotes healing of focal injuries but may cause detrimental scarring (adhesions) in response to extensive trauma. Thus, the inhibition of macrophage aggregation may provide a target to prevent adhesion formation after surgery.

Parenchymal-sparing hepatectomy for colorectal liver metastases reduces postoperative morbidity while maintaining equivalent oncologic outcomes compared to non-parenchymal-sparing resection

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Background: This study addresses the hypothesis that parenchymal-sparing hepatectomy for colorectal liver metastases (CRLM) reduces postoperative complications while ensuring similar oncologic outcomes compared to the standardized non-parenchymal-sparing procedures.

Methods: Clinicopathological data of patients who underwent liver resection for CRLM between 2012 and 2019 at a major hepatobiliary center in Switzerland were assessed. Patients were stratified according to the tumor burden score [TBS² = (maximum tumor diameter in cm)² + (number of lesions)²] and were dichotomized in a lower and a higher tumor burden cohort according to the median TBS. Postoperative outcomes, overall survival (OS) and disease-free survival (DFS) of patients following parenchymal-sparing resection (PSR) for CRLM were compared with those of patients undergoing non-PSR.

Results: During the study period, 153 patients underwent liver resection for CRLM. PSR was performed in 79 patients with TBS < 4.5, and in 42 patients with TBS ≥ 4.5. In patients with lower tumor burden (TBS < 4.5), PSR was associated with lower complication rate (15.2% vs. 46.2%, p = 0.009), shorter length of hospital stay (5 vs. 9 days, p = 0.006), equivalent 5-year OS (48% vs. 39%, p = 0.479), and equivalent 5-year DFS rates (DFS, 44% vs. 29%, p = 0.184) in comparison to non-PSR. For TBS ≥ 4.5, PSR resulted in lower postoperative complication rate (33.3% vs. 63.2%, p = 0.031), lower length of hospital stay (6 vs. 9 days, p = 0.005), equivalent 5-year OS (29% vs. 22%, p = 0.314), and equivalent 5-year DFS rates (29% vs. 22%, p = 0.896) compared to non-PSR.

Conclusions: PSR for CRLM is associated with lower postoperative morbidity, shorter length of hospital stay, and equivalent oncologic outcomes compared to non-PSR, independently from tumor burden. Our findings suggest that PSR should be considered as the preferred method for the treatment of curatively resectable CRLM, if allowed by tumor size and location.

Simultaneous Portal and Hepatic Vein Embolization achieves better liver hypertrophy and resectability than Portal Vein Embolization alone

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Background: The extent of liver resection for tumors is limited by the functional reserve of the future liver remnant (FRL). Therefore liver hypertrophy is induced by portal vein embolization (PVE). The novel PVE/HVE may have advantages over PVE alone.

Methods: Centers of the international DRAGON collaborative provided data on patients who had PVE/HVE or PVE on 2016–2019 (more than 5 PVE/HVE procedures in each single center was a requirement). Liver volumetry was performed using OsiriX MD software. Multivariable analysis was performed. C-statistics, regression, and Kaplan–Meier analysis were used.

Results: 39 patients underwent PVE/HVE and 160 underwent PVE alone. The PVE/HVE group had better hypertrophy than the PVE group (59 versus 48 % resp.; p=0.020) and increased resectability (90 versus 68%, p=0.007). Major complications (26 versus 34 % resp., p=0.550) and 90-day mortality (3 versus 16 % resp., p= 0.065) were comparable. Multivariable analysis confirmed that these effects were independent of confounders.

Conclusion: PVE/HVE leads to more liver hypertrophy and improved resectability compared to PVE and prospective studies are underway.

Long-term outcome of surgery for perianal Crohn's fistula

Background: Perianal fistulizing disease is a problem in patients with Crohn's disease (CD) because they often need repetitive surgeries. Among the available procedures, none of them proves to be superior. In addition, the long-term outcome of fistula Seton drainage is not well described. The aims of this study were to analyze the long-term healing and recurrence rates of perianal fistulas in CD patients.

Methods: Database analysis of a prospective Swiss cohort of patients with perianal CD.

Results: 365 patients with 576 interventions and a median follow-up of 7.5 years (0–12.6) were analyzed. 39.7% of patients required more than one surgery. The first surgical interventions were fistulectomies (58.4%), Seton drainage (26.9%), fistula plugs (2.2%) and combined procedures (9.9%). Fistulectomy patients required no more surgery in 67.6%, one additional surgery in 25.4% and more than one additional surgery in 7.7%. In these 3 groups of patients, after a median follow-up of 12.1 years, perianal fistula closure was achieved in 77.1%, 74.1% and 66.7%, respectively. In patients with Seton drainage as index surgery, 50.3% required no more surgery and over 75% achieved fistula closure after 10 years. 49.7% of patients with Seton required one or more surgeries. At median follow up of 7.5 years, closure rates were 64.2% and 60.5% in patients with one and more than one surgeries, respectively.

There was no difference in demographics in Seton patients with closed or not closed fistulas. Non-closure patients had a higher Crohn Disease Activity Index (33 vs. 6) and more anti-TNF medication (57.4% vs. 48.1%).

Conclusion: First line fistulectomies achieved the highest healing rates in perianal CD but 1/3 of patients require additional surgeries and 1/4 patients will remain with a fistula at 10 years. Initial seton drainage and concurrent medical therapy can achieve fistula closure in 75%. However, in 50% of patients more surgeries are performed with a seton staying in place up to 5 years and fistula closure in only 2/3 patients.

Neoadjuvant chemotherapy offers no survival benefit for cT2N0M0 gastric adenocarcinoma. A multicentric European study

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Background: According to current international guidelines, the optimal treatment of stage cT2N0M0 gastric adenocarcinoma consists of preoperative chemotherapy followed by surgery. Surgery first may be suggested in selected patients, especially if considered unfit for chemotherapy. The aim of the present study was to assess if cT2N0M0 patients treated with surgery first (S) had inferior overall and disease-free survival compared to those treated with neoadjuvant chemotherapy followed by surgery (CS).

Methods: A retrospective analysis was performed among 32 centers, including all consecutive patients with gastric adenocarcinoma operated between January 2007 and December 2017. Patients with cT2N0M0 stage were divided into two groups, surgery first (S) and neoadjuvant chemotherapy followed by surgery (CS). Clinico-pathological details, overall and disease-free survival were compared between the groups. Cox regression analysis was performed for long-term survival.

Results: Among the 2131 included patients, 202 (9.5%) had cT2N0M0 disease: 68 (33.7%) were placed in the CS group and 134 (66.3%) in the S group. CS patients were younger (mean age 62.7±12.8 vs 69.8±12.1 years, $P < 0.001$) with WHO status 0 in 60.3% versus 34.5% in S patients ($P = 0.006$). The CS group had more proximal tumors, undergoing more frequently total gastrectomy (70.6% CS vs 45.5% S, $P = 0.001$). The median number of resected lymph nodes was similar (22 vs 20.5, $P = 0.74$). R0 resection margins were obtained in 97.1% CS vs 95.5% S patients ($P = 0.72$). Adjuvant chemotherapy was more often administered in CS patients (75.8% versus 29.8% in S, $P < 0.001$). Recurrence occurred in 30.9% in CS and 18.1% in S ($P = 0.04$), predominantly as distant metastases (81% CS vs 75% S, $P = 0.76$). Overall 5-year survival was similar between CS (74.4%, 95%CI 58.1 – 85.1) and S groups (66.7%, 95%CI 54.4–76.5, $P = 0.73$), as was 5-year disease-free survival (DFS) (64.6%, 95%CI 48.4–76.9 for CS vs 62.8%, 95%CI 50.7–72.6 for S, $P = 0.82$). Perioperative chemotherapy was not associated with OS or DFS in multivariate analysis.

Conclusions: Patients with cT2N0M0 gastric adenocarcinoma did not present a survival or recurrence benefit if treated with CS compared to S. In accordance with esophageal cT2N0 tumors, surgery first might be a valid treatment option for these patients.

Extended Lymph Node Resection Versus Standard Resection for Pancreatic Head and Periampullary Adenocarcinoma: A Cochrane Systematic Review

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Background: Lymph node (LN) involvement is an important predictor of survival after partial pancreaticoduodenectomy (PD). At present, standard lymphadenectomy (SLA) with resection of LN stations no. 5, 6, 8a, 12b1-2, 12c, 13a, 13b, 14a, 14b, 17a, and 17b is recommended for this procedure by the International Study Group on Pancreatic Surgery (ISGPS) and extended lymphadenectomy (ELA) is discouraged. However, a systematic review that compares the outcomes of SLA with ELA within the established analytical framework of the Cochrane Collaboration has not been performed to date.

Methods: A Cochrane systematic review was conducted to identify all RCTs comparing PD with ELA versus PD with SLA for patients with periampullary or pancreatic cancer. The following electronic databases were reviewed: Cochrane library; MEDLINE; PubMed and EMBASE. The methodological quality of the included studies was assessed using the Cochrane risk of bias criteria and the quality of evidence using GRADE.

Results: Seven RCTs were included with 843 patients (421 ELA and 422 SLA). Definitions of LN stations and SLA/ELA varied widely in the RCTs. No difference in overall survival (1- and 3-years after surgery) was seen between groups. Mortality and morbidity (pancreatic fistula, delayed gastric emptying, postoperative bleeding) rates were similar between groups. Operative time was longer following ELA (mean difference 50min; $P = 0.001$). Total amount of blood loss (mean difference 137 ml; $P = 0.03$) and transfusion requirements (mean difference 0.15 units; $P < 0.00001$) were increased for ELA. More LN were retrieved during ELA (mean difference 11 nodes; $P < 0.00001$).

Conclusion: There is no indication for routine ELA in PD.

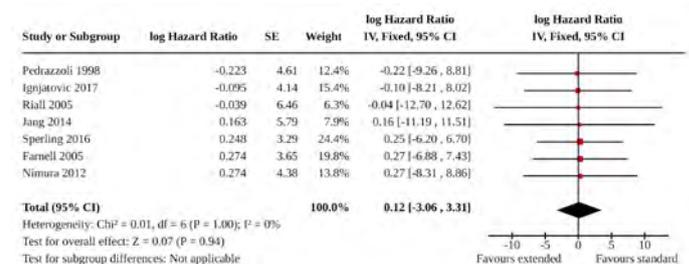


Figure: Forest plot of comparison: 1 Extended vs standard lymph node resection, outcome: 1.1 Overall survival.

Effects of structured intraoperative briefings on patient outcomes: A multicentric before and after study

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Background: Surgeries require close collaboration by surgeons, anesthesia providers and nurses. Aim of this study was to determine whether intraoperative briefings influence patient outcomes.

Methods: In a controlled trial with before-and-after design (nine-month baseline and nine-month intervention), intraoperative briefings were introduced in four general-surgery centers; including 8256 adult patients. During the operation, main surgeons briefed the surgical team using the StOP? protocol about the progress of the operation (Status), next steps (Objectives), possible problems (Problems), and were encouraged to ask

questions (?). Primary outcome: surgical site infections, Secondary outcomes: mortality, unplanned reoperations, and length of stay.

Results: End-point data were available for 7745 (93.8%) patients. Adjusted intention-to-treat analyses showed no differences for surgical site infections between baseline (9.75%) and intervention (9.59%); (adjusted absolute difference (AD) -0.15% , 95% confidence interval (CI) -1.45 to 1.14 ; odds ratio (OR) 0.92 , CI 0.83 to 1.15 ; $P = 0.797$), but reductions in mortality (1.59% vs. 1.05% ; AD -0.54% , CI -1.039 to -0.033 ; OR 0.60 , CI 0.39 to 0.92 ; $P = 0.018$), unplanned reoperations (6.44% vs. 4.79% ; AD -1.66% , CI -2.69 to -0.62 ; OR 0.72 , CI 0.59 to 0.89 ; $P = 0.002$), and long hospital stays (21.64% vs. 19.82% ; AD -1.82% , CI -3.48 to -0.15 ; OR 0.87 , CI 0.77 – 0.98 ; $P = 0.024$).

Conclusions: The intervention yielded no change in surgical site infection rates, but a reduction in mortality, unplanned reoperations, and length of stay. Short yet flexibly structured intraoperative briefings should be considered during surgery.

POSTER: GASTROENTEROLOGY – CLINICAL

G1

Mapping of aetiologies and clinical presentation of acute colitis: results from a prospective cohort study in a tertiary centre

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Background: Our objective was to describe the aetiologies of acute colitis and to identify patients who require diagnostic endoscopy.

Methods: Patients with symptoms of gastrointestinal infection and colonic inflammation on CT were prospectively included. Those immunosuppressed, with history of colorectal cancer or inflammatory bowel disease (IBD) were excluded. Microbiological analysis of the stools was performed using PCR assays BD-Max and FilmArray GI panel, faecal calprotectin was determined. Patients with negative BD-Max underwent colonoscopy.

Results: One hundred and seventy-nine patients were included. Patients with infectious colitis (n = 103, 57.5%) were positive for *Campylobacter* spp (n = 57, 55.3%), *Escherichia coli* spp (n = 8, 7.8%), *Clostridium difficile* (n = 23, 22.3%), *Salmonella* spp (n = 9, 8.7%), viruses (n = 7, 6.8%), *Shigella* spp (n = 6, 5.8%), *Entamoeba histolytica* (n = 2, 1.9%) and others (n = 4, 3.9%). Eighty-six patients underwent colonoscopy, which was compatible with ischaemic colitis in 18 patients (10.1%) and IBD in 4 patients (2.2%). Faecal calprotectin was elevated in all patients, with a mean concentration of 1922.1±2895.6 µg/g, and was the highest in patients with IBD (8511±9438.4 µg/g, p <0.001). After exclusion of patients with infectious aetiology, a faecal calprotectin >625 µg/g allowed identifying patients with IBD with an area under ROC curve of 85.1%.

Conclusion: Computed tomography-proven colitis was infectious aetiology in 57.5% of patients. Ischaemic colitis (10.1%) and IBD (2.2%) were seldom represented. No colorectal cancer was found.

G2

Evaluation of 30-Day Mortality in Patients undergoing Endoscopy or Liver Biopsy in a Tertiary Hospital: A 3 Year Survey

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Background: Mortality in patients undergoing invasive procedures in gastrointestinal centers is not well characterized in the literature. Our aim was to describe patients who died 30 days after an endoscopic procedure or a liver biopsy.

Methods: This retrospective observational monocentric study depicted all patients who died within 30 days after an endoscopic procedure or a liver biopsy between January 2017 and December 2019.

Results: Out of the 19'989 procedures performed, 267 patients died within 30 days after a total of 383 (1.91%) endoscopies (244 gastroscopies, 53 colonoscopies, 24 echoendoscopies, 17 ERCP, 6 PEG) and liver biopsies (37 transjugular, 2 transcutaneous). Median age was 70 (IQR 61–79) and 184 (68,6%) were male. Median Charlson Index was 5 (IQR 3–7) and ASA score was 3 (IQR 3–4). Most frequent indications were suspicion of GI bleeding (n = 161;42.04%), suspicion of GI cancer or tumoral staging (n = 56;14.62%) and suspicion of biliary obstruction (n = 29;7.57%). Major causes of death were progression of underlying malignancies (n = 68;25.47%), liver failure (n = 30;11.24%) and GI bleeding (n = 26;9.74%). Due to STEMI, 2 deaths were direct complication of procedure.

Conclusions: Thirty-day mortality after endoscopy or liver biopsy is low. Patients were mostly elderly male with multiple co-morbidities. Malignancies were the major cause of death.

G3

Systematic Review of Outcome Measures in Adult Eosinophilic Esophagitis Treatment Trials and Observational Studies

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Background and aims: This systematic review aims to identify the outcomes measures that were assessed in observational studies reporting effects of different eosinophilic esophagitis (EoE) treatments (topical corticosteroids, diet and dilation) over the last 20 years in adult EoE patients.

Methods: We searched MEDLINE and EMBASE for prospective and retrospective studies (cohorts/case series, randomized open-label, case-control) evaluating the use of EoE treatments. Results: We included 69 studies that met inclusion criteria. Thirty-five, 17, and 17 studies reported on effects of topical corticosteroids, diets, and dilation, respectively. EoE-associated endoscopic findings (either as absence/presence or assessed using Endoscopic Reference Score) were evaluated in 24/35 studies of topical corticosteroids, 11/17 studies of dietary therapy, and 9/17 studies of dilation. Esophageal eosinophil density was recorded in 32/35 studies of topical corticosteroids, 17/17 studies of dietary therapy, and 11/17 studies of dilation. Patient-reported outcomes were not uniformly used (in 14 studies of topical corticosteroids, 8 studies of diet, and 3 studies of dilation), and most of the tools used were not validated for use in adults with EoE.

Conclusions: Despite the lack of an agreed set of core outcomes that should be universally reported in observational studies in adult EoE patients, endoscopic appearance of EoE-associated findings as well as esophageal eosinophil density are commonly reported in studies evaluating the use of various EoE-specific treatments. Standardization of outcome reporting and data supporting the use of various outcomes are needed to facilitate the quality of evidence synthesis and comparisons of interventions in meta-analyses in therapeutic trials in adults with EoE.

G4

Development of a Core Outcome Set for Therapeutic Studies in Eosinophilic Esophagitis (COREOS)

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Background and aims: Endpoints used to determine treatment efficacy in eosinophilic esophagitis (EoE) have evolved over time. With multiple novel therapies in development for EoE, harmonization of outcomes measures will facilitate evidence appraisal when comparing different treatments. We aimed to develop a core outcome set (COS) for controlled and uncontrolled studies of pharmacologic and dietary interventions in adult and pediatric patients with EoE.

Methods: Candidate outcomes were generated from systematic literature reviews and direct patient engagement interviews and surveys. Consensus was established using an iterative Delphi process, with items voted on using a 9-point Likert scale and with feedback from other participants to allow score refinement. Consensus meetings were held to ratify the outcome domains of importance and the core outcome measures. Stakeholders were recruited internationally and included adult and pediatric gastroenterologists, allergists, pathologists, and methodologists.

Results: The COS consists of four outcome domains for controlled and uncontrolled studies: histopathology, endoscopy, patient-reported symptoms, and EoE-specific quality of life (QoL). A total of 69 stakeholders (response rate 95.8%) prioritized 42 outcomes in a two-round Delphi process and the final ratification meeting generated consensus on 33 outcome measures. These included measurement of the peak eosinophil count, EoE Histology Scoring System in controlled trials, EoE Endoscopic Reference Score, and patient-reported measures of dysphagia and QoL.

Conclusions: This interdisciplinary collaboration involving key global stakeholders has produced a COS that can be applied to adult and pediatric studies of pharmacologic and dietary therapies for EoE, which will facilitate meaningful treatment comparisons and improve quality of data synthesis.

G5

Long-Lasting Dissociation of Esophageal Eosinophilia and Symptoms Following Dilation in Adults with Eosinophilic Esophagitis

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Background and aims: Esophageal dilation improves dysphagia but not inflammation in eosinophilic esophagitis (EoE) patients. We investigated if dilation modifies the association between symptoms and esophageal eosinophil count (eos/hpf). **Methods:** Adults enrolled in a multisite, prospective Consortium of Gastrointestinal Eosinophilic Disease Researchers OMEGA observational study (NCT02523118) completed the symptom-based EoE activity index (EEsAI) and underwent endoscopy with biopsies. Patients were stratified based on dilation status as absent, performed ≤ 1 and > 1 year before endoscopy. Assessments included Spearman's correlations of the relationship between symptoms and eos/hpf and linear regression with EEsAI as the outcome, eos/hpf as predictor, and interaction for dilation and eos/hpf.

Results: Amongst 100 patients (n = 61 male, median age 37 years), 15 and 40 patients underwent dilation ≤ 1 year and > 1 year before index endoscopy, respectively. In non-dilated patients, association between eos/hpf and symptoms was moderate (Rho = 0.49, p-value < 0.001). In patients dilated ≤ 1 and > 1 year before index endoscopy, this association was abolished (Rho = -0.38, p-value = 0.157 for ≤ 1 year and Rho = 0.02, p-value = 0.883 > 1 year); for 10 eos/hpf increase, the predicted EEsAI changed by -1.64 (p-value = 0.183) and 0.78 (p-value = 0.494), respectively. Dilation modifies association between symptoms and eos/hpf (p-value = 0.005 and p-value = 0.187 for interaction terms of eos/hpf and dilation ≤ 1 year and > 1 year before index endoscopy, respectively).

Conclusions: In non-dilated EoE adults, eos/hpf correlates modestly with symptoms; this correlation was no longer appreciated in dilated patients, and the dilation effects lasted longer than one year. Dilation status should be considered in studies evaluating EoE treatment and for clinical follow-up.

G6

2021 Update on the Swiss Eosinophilic Esophagitis Cohort

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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 (EoE) 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: Patients are included using validated online instruments for capture of symptoms, EoE-specific quality of life, endoscopic and histologic activity. A follow-up visit is performed once a year. A biobank (located at CHUV) stores biopsies and blood samples. In addition to patients with EoE, samples of patients with gastro-esophageal reflux disease (GERD) and esophagus-healthy controls are collected. SEECs is supported by the Swiss National Science Foundation. Approval from the major Swiss IRB's has been granted.

Results: As of May 2021, 527 patients with EoE, 39 with GERD, and 40 esophagus-healthy controls have been included. Recruitment performance is on track with anticipated 70 EoE patients per year. Biosamples

have been provided to collaborators for evaluation of novel therapeutic approaches. Seven papers were published with SEECs data and several projects are ongoing.

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.

G7

Technical feasibility, clinical effectiveness, and safety of esophageal stricture dilation using BougieCap in adults with Eosinophilic Esophagitis

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Background and aims: BougieCap (Ovesco Endoscopy AG, Tübingen, Germany) is a new device that allows optical and tactile feedback during stricture dilation of the upper gastrointestinal tract. We evaluated the technical feasibility, clinical efficacy, and safety of a one-time esophageal stricture dilation using BougieCap in adults with eosinophilic esophagitis (EoE).

Patients and methods: EoE patients prospectively included in the Swiss EoE Cohort were dilated with BougieCap in case of the presence of esophageal strictures (diameter ≤ 14 mm) and stricture-related symptoms. Symptoms were assessed before and two weeks after a single dilation session using the validated EEsAI PRO instrument (score ranges from 0–100 points).

Results: Fifty patients (70% male, median age 41 years, median disease duration of 4 years, 50% treated with swallowed topical corticosteroids, 10% with proton pump inhibitors, 14% with combined swallowed topical corticosteroids plus proton pump inhibitors, 14% with elimination diet, 12% without anti-eosinophil therapy) were evaluated. Endoscopic bougienage was technically successful in 100%. Median esophageal diameter increased from 12 mm (IQR 12–13) to 16mm (IQR 16–16, p < 0.001). Median symptom severity dropped from 32 points (IQR 27–41) to 0 (IQR 0–10, p < 0.001) at 2 weeks post dilation. In one patient the BougieCap was temporarily lost after stricture dilation in the hypopharynx but could be retrieved.

Conclusions: In adults with EoE, endoscopic treatment of esophageal strictures using BougieCap is technically feasible, safe and offers significant symptomatic improvement in the short term.

G8

Increasing incidence of microscopic colitis in a population-based cohort study in Switzerland

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Background and aims: Population-based epidemiologic data regarding the frequency and natural history of microscopic colitis (MC) are scarce. We aimed to evaluate the clinical presentation at diagnosis, incidence and prevalence, and natural course of microscopic colitis in Cantons of Vaud and Fribourg, Switzerland. **Patients and methods:** Cantons of Vaud and Fribourg lie in the French speaking, Western part of Switzerland. As of 12/2017, both cantons together had a population of 1,109,230 inhabitants. After having identified patients through databases of all Pathology institutes (n = 6) serving both cantons, we performed a chart review in practices of gastroenterologists in charge.

Results: We included 218 patients with MC, whereof 123 had lymphocytic colitis (LyC) and 95 collagenous colitis (CC). Annual incidence of MC significantly increased from 0.09/100,000 inhabitants in 1994 to 1.71/100,000 inhabitants in 2017 (p = 0.025). The prevalence of MC, LyC, and CC in 2017 was 19.7/100,000, 11.1/100,000, and 8.6/100,000, respectively. Median duration of follow-up was 4 years (IQR 2–7, range 1–22 years). A total of 62% of patients had a mild disease (defined as less than one flare per 12 months), 28% had moderate disease activity (defined as at least one flare per 12 months), and 10% had chronic on-

going disease. Stopping the offending agent (eg. statins, PPI) was significantly associated with a mild disease course (OR 3.13, $p = 0.013$) in logistic regression modeling.

Conclusions: The incidence and cumulative prevalence of MC shows a steady increase in Western part of Switzerland. Roughly two thirds of patients were characterized by a mild disease course.

G9

German Translation and Validation of The IBD-Control Questionnaire

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Background: Patient Reported Outcome Measures (PROMs) serve as an instrument to measure treatment success. Because the IBD-Control questionnaire has not yet been published in German, the translation and validation of the IBD-Control was necessary before use.

Methods: We have translated the English original version of the IBD-Control questionnaire into German in a state-of-the-art procedure of "forward-backward translation" and validated the translated IBD Control questionnaire with 154 patients with Crohn's disease or with ulcerative colitis.

Results: Translation and professional health care experts have contributed to the German translation of the IBD-Control. Spearman's Rho revealed high consistency between the IBD-Control-8-Subscore and the IBD-Control-VAS-Score ($r = 0.632$). The disease activity in the past 6 months highly correlated with the IBD-8 subscore ($r = 0.640$) as well with the IBD-Control-VAS-Score ($r = 0.622$). The IBD-Control-8-Subscore highly correlated with the Harvey Bradshaw Index ($r = -0.620$) and the partial Mayo Score ($r = -0.679$) as well as the IBD-Control-VAS-Score with the Harvey Bradshaw Index ($r = -0.484$) and the Mayo Score ($r = -0.435$), showing sufficient construct validity. The result is the German version of the IBD-Control, the IBD-Control-D, a highly accepted questionnaire for the assessment of PROMs in IBD patients.

Conclusion: The German translation of the IBD-Control, the IBD-Control-D is a valid instrument for measuring the subjective feeling of illness and treatment outcome.

G10

Endoscopic management of disconnected pancreatic duct syndrome: experiences from a tertiary referral center

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Background and aims: Disconnected pancreatic duct syndrome can lead to development of fluid collections, ascites, chronic pancreatitis, and associated chronic pain. Surgical treatment is associated with high morbidity. We aimed to evaluate the technical and clinical success rate of endoscopic management for disconnected pancreatic duct syndrome.

Methods: Retrospective analysis (2015–2021) of endoscopically treated patients who presented with disconnected pancreatic duct syndrome at our center. We evaluated clinical success (defined by lack of subsequent need for radiological or surgical treatment) and technical success.

Results: Thirty patients were analyzed (median age 53.5 ± 19.3 years). Etiologies were pancreatic surgery (40%), necrotic pancreatitis (40%) and abdominal trauma (20%). Duct rupture was mainly located at the isthmus (46%) and tail (40%). 2/3 of patients developed one or multiple fluid collections. Various endoscopic procedures were applied: retrograde trans-papillary duct drainage (26%), endosonographic ultrasound-guided transmural fluid collection drainage (20%), association of both techniques (36%) or a pancreaticogastrostomy (16%). Technical success was achieved in all cases with no major complication. Five patients (16%) underwent surgery. After endoscopic treatment, 86% of patients were free from pain, 23% were treated for diabetes, and 36% for pancreatic exocrine dysfunction. No recurrence of disconnected pancreatic duct syndrome was observed in patients benefitting from exclusive endoscopic treatment.

Conclusion: Management of disconnected pancreatic duct syndrome is challenging and complex. Endoscopic management had a high technical and clinical success rate in our center.

G11

Outcome of nonfunctioning pancreatic neuroendocrine tumors after initial surveillance or surgical resection: a single center observational study

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Background: Current guidelines consider observation a reasonable strategy for low grade non-functional pancreatic neuroendocrine tumors (nf pNET) ≤ 2 cm. Pancreatic surgery in contrast carries a high risk of morbidity and mortality.

Patients and methods: Data of patients with histologically confirmed nf pNETs ≤ 2 cm, managed at a single tertiary referral center between 2002 and 2020, were retrospectively reviewed.

Results: 39 patients (mean age 62.1 years, 56% male), with 43 lesions (mean size 12.7 ± 3.9 mm; 32 grade 1 (G1) and 7 grade 2 lesions (G2)) have been managed by careful surveillance. Progression was observed in 15 lesions (35%, mean follow-up 47 months) and 6 of them (6/39, 18%) underwent secondary surgery; 3 patients had lymph node metastasis on the resected specimen. Pancreatic surgery was followed by pancreatic fistula in 2/6 patients, one of them died. No disease related death or metastasis was observed in patients with ongoing surveillance. In contrast, 14 patients (mean age 59 years, 64.3% female, mean size of lesions 11.4 ± 3.1 mm) underwent pancreatic surgery immediately after diagnosis. Surgery associated complication rate was 57.1% (8/14). 13/14 patients remained recurrence free (median follow-up 67 months). Recurrent metastatic disease was observed in one patient 3 years after pancreaticoduodenectomy.

Conclusion: There is growing evidence for malignant behavior in a subgroup of patients with small nf pNETs. Pancreatic surgery is associated with significant morbidity. There is need for less invasive ablation strategies.

G12

Endoscopic ultrasound-guided radiofrequency ablation for pancreatic insulinoma: experience in two tertiary centers

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Background: Insulinoma is the most frequent functional neuroendocrine tumor of the pancreas and endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) a novel and promising ablation technique.

Methods: Data of patients with pancreatic insulinoma < 2 cm, treated by EUS-RFA at two tertiary referral centers, were retrospectively reviewed.

Results: Between 2017 and 2020, seven patients were included (6/7 female; mean age 66 years). Lesion size ranged between 8 and 20 mm. EUS-RFA was feasible in all patients (100%), achieving clinical success with immediate hypoglycemia relief after only one single treatment session. Complete response was confirmed by cross-sectional imaging in 6/6 patients. All patients remained asymptomatic and recurrence free until the end of follow-up as confirmed by high resolution imaging (median 21 months; range 3–38). Three patients had minor complications. A 97-year-old multimorbid patient developed a retrogastric collection 15 days after intervention. Respecting her decision, she did not receive any further treatment and died one month after EUS-RFA.

Conclusion: Management of pancreatic NETs < 2 cm by EUS-RFA seems effective with an acceptable safety profile. As malignant disease progression is rare, EUS-RFA should be considered as first line treatment for selected small size insulinomas. Yet, further evidence focusing on long term survival and recurrence is needed.

G13**Sex impacts endoscopic and histological disease activity but not symptoms or quality of life in adults with eosinophilic esophagitis: a nationwide prospective cohort study**

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Background: Eosinophilic esophagitis (EoE) has a strong male predominance that appears at least partially due to genetic susceptibility. However, data regarding gender and sex-related differences in patients with EoE are scarce.

Methods: We analyzed prospectively collected data from adults enrolled into the Swiss EoE cohort study (SEECs). Patients with and without dilation in the past 12 months completed patient-reported EoE activity index (EEsAI) and EoE-specific QoL (EoE-QoL-A) and underwent endoscopy with biopsies. We used linear regression with EEsAI or EoE-QoL-A as the outcome, eosinophils per high power field, rings and strictures, current therapy use, and disease duration as predictors.

Results: A total of 261 patients (77% male, median age at diagnosis 35.6 years, median disease duration 10.7 years) were seen during 379 visits. Men had a longer diagnostic delay (62.5 vs. 35 months, $p = 0.015$), had higher endoscopic disease activity (EREFS median 3.0, IQR 1.0-6.0 vs. EREFS median 2.0, IQR 0.0-4.0, $p = 0.001$), more micro-abscesses (24% vs. 12.7%, $p = 0.042$) and more often fibrosis of the lamina propria (mild/moderate 73.7% vs. 58.7%, severe 9.7% vs. 6.5%, $p = 0.034$) than women. When adjusting for objective measures of disease activity, disease duration and current therapy use, we did not observe differences in EEsAI or EoE-QoL-A between women and men.

Conclusions: Men with EoE had higher endoscopic and histologic disease activity than women. However, adjusting for these objective markers we did not identify differences in symptom severity or EoE-specific QoL between men and women with EoE.

G14**Odynophagia and retrosternal pain in patients with eosinophilic esophagitis – rather indicative of disease activity than side effect of therapy**

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Background: Dysphagia for solids is the hallmark symptom in eosinophilic esophagitis (EoE). However, patients may present with less frequent complaints, including odynophagia and retrosternal pain. While both symptoms are well described as a consequence of viral or candida esophagitis and following dilation, there is paucity of data regarding their overall prevalence and potential implications in patients with EoE.

Methods: All adult patients enrolled into the Swiss EoE cohort study (SEECs) were analyzed. Odynophagia was defined by either painful symptoms in the prior 7 days reported in the physician questionnaire or pain associated to swallowing reported in the patient questionnaire. Retrosternal pain was defined by pain independent of food ingestion in the last 7 days reported in the physician questionnaire. Demographics, EoE-related symptoms, histologic and endoscopic activity were compared between EoE patients with vs. without odynophagia and/or retrosternal pain.

Results: A total of 474 patients (75.2% male patients, 67% with atopic disease) were analysed of which 110 (23.2%) patients experienced odynophagia and 64 (13.5%) patients retrosternal pain. Only a minority of 24 (5%) of patients complained about both symptoms. Patients with odynophagia had higher symptom severity (Visual analog scale 0–10) in the last 7 days (assessed by physician and patient questionnaire 2.0 vs. 1.0, <0.001 and 2.0 vs. 1.0, $p <0.001$, respectively), higher EREFS score (median 3.0 vs. 2.0, $p = 0.006$), higher histologic activity and a lower quality of life (median 18 vs. 14, $p = 0.001$) compared to patients without odynophagia. Sex, age at diagnosis, EoE specific treatment, complications such as candida or viral esophagitis and disease duration did not differ between the groups. In patients with retrosternal pain a higher symptom severity could be demonstrated (assessed by physician and patient questionnaire 2.0 vs. 1.0, $p = 0.001$ and 2.0 vs. 1.0, $p <0.001$, respectively). However, there was neither a difference in endoscopic/histologic disease activity nor in quality of life according to presence or absence of retrosternal pain.

Conclusion: Our data show that odynophagia and swallowing-independent retrosternal pain are, in addition to the well-known dysphagia, frequently occurring symptoms in EoE.

G15**Technical and clinical efficacy of endoscopic management of chronic calcifying pancreatitis and its complications.**

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Background and aims: Obstruction of the main pancreatic duct (MPD) in chronic calcifying pancreatitis (CCP) may cause major and life-threatening complications. Recent endoscopic techniques using a duodenoscope or an endoscopic ultrasound (EUS) allow to treat strictures of the MPD or common bile duct (CBD). We aimed to evaluate the technical and clinical success rate of endoscopic management of patients with obstructive and symptomatic CCP.

Methods: Retrospective analysis (2016 to 2020) in a single, tertiary university center of endoscopically treated patients with CCP. The primary outcome was clinical success (defined as pain $\leq 2/10$ on a Visual Analog Scale [VAS]). Secondary outcomes were technical success, adverse events (AE) rate, mortality, and rate of repetitive endoscopic interventions.

Results: 54 patients were analyzed (74.1% of male; median age of 57.3 years old) with a mean follow up of 15.53 \pm 9.48 months. Etiologies for CCP were alcohol/tobacco consumption (60.1%), obstructive and biliary disease (22.2%) and idiopathic forms (16.7%). 44.4% (24/54) patients had concomitant treatment of both MPD and CBD strictures. Technical success was achieved in 94.5% with an overall clinical success of 91.8%, for an average of 5 sessions per patient (range 3–16) and a mean treatment duration of 16.87 \pm 11.33 months. Minor and major AE rates were 6.9% and 0.3%, respectively; all were treated conservatively. Mortality rate was 7.4% during the observation period. None of the fatalities were due to endoscopic procedures. No relapse was observed and no endoscopic re-intervention was required after the initial endoscopic treatment was considered to be completed.

Conclusion: Endoscopic ductal decompression therapy is an effective treatment for patients with symptomatic CCP and offers an excellent safety profile.

G16**Efficacy and safety of endoscopic ultrasound guided drainage of pseudocysts and walled off necrosis after failure of percutaneous drainage.**

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Background and aims: Endoscopic Ultrasound (EUS)-guided drainage of pancreatic fluid collections (PFC) is regarded as gold standard. However, data concerning salvage EUS drainage after initial percutaneous drainage

are limited. The purpose of our study was to evaluate the clinical outcomes and safety of EUS-guided drainage of pancreatic collections after failure of percutaneous drainage.

Methods: This retrospective study was conducted in a single, tertiary university center from August 2013 to January 2020. Patients were included in case of presence of PFC following pancreatitis requiring EUS-guided drainage after failure of percutaneous drainage.

Results: Twenty-two patients with PFC after acute pancreatitis were included (median age 66.5 years old \pm 17.25 years): 4/22 (18.2%) had a pancreatic pseudocyst and 18/22 (81.8%) presented with a walled-off necrosis. Seventy-six interventions were performed among the 22 patients. Lumen-apposing metal stents were used in 5/22 (22.7%) and double pigtail plastic stents in 17/22 (77.3%) of interventions with a median number of 3 interventions per patient (range 1 to 7). Technical success rate was 98.7% with an overall, clinical success of 81.8%. Procedure related adverse events rate was 9.1% including one bleeding and one pancreatic fistula. Two non-procedure related deaths occurred.

Conclusion: EUS-guided drainage of pancreatic fluid collections was clinically effective and safe in a high proportion of patients after failure of radiological percutaneous management.

G17

Higher Educational Level in Patients with Eosinophilic Esophagitis: A Comparative Analysis

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Background: Eosinophilic Esophagitis is a chronic-inflammatory gastrointestinal disease with a high prevalence in younger, atopic males. In our clinical practice we observed a striking preponderance of patients having a high educational background. The purposes of this study were, first to assess the level of education of Eosinophilic Esophagitis patients; and second to compare the findings to patients with inflammatory bowel disease, another chronic immune-mediated condition of the gastrointestinal tract, and with the Swiss General Population.

Methods: Using a validated questionnaire, we assessed the educational level of adult patients who have attended Swiss Eosinophilic Esophagitis Clinics in the past. Additionally, the educational level of the parents was assessed as well. We calculated the proportions of patients and parents who have obtained a higher educational level. Data from the Swiss Inflammatory Bowel Disease Cohort Study and from the Swiss General Population served as confirmation and as comparison, respectively.

Results: 277 successfully contacted patients (response rate 69.1%; mean age 51.1 years, 73% male) participated. A significantly higher proportion of surveyed Eosinophilic Esophagitis patients had a high ISCED level (66.8%, $p < 0.001$) compared to inflammatory bowel disease patients ($n = 2534$; 34.2%, $p < 0.001$) and to the Swiss General Population ($n = 6'066'907$; 30.5% $p < 0.001$).

Conclusion: Our analysis confirms the clinical observation that Eosinophilic Esophagitis patients have a significantly higher educational level compared to the general population and to patients with other chronic inflammatory diseases of the gastrointestinal tract. As a limitation, this impressive finding remains on a purely descriptive level.

G18

Food-induced Immediate Response of the Esophagus – a newly identified Syndrome in Patients with Eosinophilic Esophagitis

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Background: Dysphagia is the main symptom of adult EoE. We describe a novel syndrome, referred to as "Food-induced Immediate Response of the Esophagus" (FIRE), observed in EoE patients.

Methods: FIRE is an unpleasant/painful sensation, unrelated to dysphagia, occurring immediately after esophageal contact with specific foods. EoE experts were surveyed to estimate the prevalence of FIRE, characterize symptoms and identify food triggers. We also surveyed a large group of EoE patients enrolled in the Swiss EoE Cohort Study (SEECs) for FIRE

Results: Response rates were 82% (47/57) for the expert- and 65% (239/368) for the patient-survey, respectively. Almost 90% of EoE experts had observed the FIRE symptom-complex in their patients. Forty percent of EoE patients reported experiencing FIRE, more commonly in patients who developed EoE symptoms at a younger age (mean age of 46.4 vs. 54.1 years without FIRE; $p < 0.01$) and in those with high allergic comorbidity. FIRE symptoms included narrowing, burning, choking and pressure in the esophagus appearing within 5 minutes of ingesting a provoking food that lasted less than 2 hours. Symptom severity rated a median 7 points on a visual analogue scale from 1–10. Fresh fruits/vegetables and wine were the most frequent triggers. Endoscopic food removal was significantly more commonly reported in male patients with vs. without FIRE (44.3% vs. 27.6%; $p = 0.03$).

Conclusions: FIRE is a novel syndrome frequently reported in EoE patients, characterized by an intense, unpleasant/painful sensation occurring rapidly and reproducibly in 40% of surveyed EoE patients after esophageal contact with specific foods.

G19

Acute esophageal necrosis (AEN): A case report

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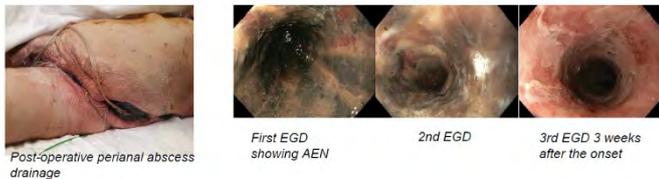
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Background: Acute esophageal necrosis (AEN) is a rare clinical entity characterized by a diffuse, circumferential, black-appearing esophageal mucosa, mostly seen in shock and low-flow states like sepsis.

Methods: We present a case of acute esophageal necrosis

Results: A 73 years-old man underwent a perianal abscess surgery in January 2019 and was then discharged. Two weeks later, the patient was readmitted after developing septic shock. A CT-Scan showed necrotic fasciitis of the left inguinal region and flank, originating from a recurrence of the perianal abscess. He was immediately operated (perianal

abscess drainage, necrosectomy and fasciotomy). Broad spectrum antibiotic therapy was started. The patient then presented upper digestive bleeding. An EGD showed AEN, and a duodenal ulcer. Treatment with proton pump inhibitors and parenteral nutrition was started. The patient's condition improved and a control EGD showed gradual recovery. He was eventually discharged at day 24.



Conclusions: The treatment of AEN is to treat the triggering pathology and supportive care. Complications include stenosis, strictures, perforation and mediastinitis. Despite aggressive treatment, overall mortality approaches 32%.

G20

A survey based assessment of management of Esophageal Food Impactions in the US and Europe

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Background: Consensus has not been achieved on optimal approaches for the management of esophageal food impaction (EFI) in patients with eosinophilic esophagitis (EoE). We set out to better understand current approaches across relevant healthcare providers.

Methods: We developed and administered a web-based survey (RED-Cap) to European and US endoscopists, recruited via email by different societies of Gastroenterology in Europe and the US. The survey consisted of 38 questions (6 questions about socio-demographical characteristics, 3 about prehospital care, 23 about in-hospital and endoscopic management and 6 about follow-up after EFI).

Results: Of the total 308 respondents, 99% were gastroenterologists (78% adult and 22% pediatric gastroenterologists) and 1% were otolaryngologists, other surgeons or allergist. Most respondents rarely treated patients with EoE (46% treated 0–1 EoE patients per month ("less experienced, LE"), 39% treat 2–10 ("moderately experienced, ME") and 15% treat >10 EoE patients per month ("very experienced, VE"). Endoscopists agreed that in the setting of acute EFI, patients should avoid induced vomiting (84% agreement), that no medication was necessary (85% agreement), and patients should seek medical attention at an emergency room (ER) (66% agreement) within 1–2 h (41%). For patients in the ER, most endoscopists did not recommend routine blood analysis (62% agreement), gastrografin swallow (81% agreement), CT-scan (77% agreement), ECG (64% agreement) or X-Ray (66% agreement). Although there was high agreement (62%) that endoscopy should be performed as soon as possible, 27% of the pediatric gastroenterologists recommended waiting 6 hours after the last meal (until the stomach was empty). The majority recommended monitored anesthesia care (46%, vs. conscious sedation with disoprivan (32%), midazolam (6%), fentanyl with midazolam (4%), or other medications given without an anesthesiologist (3%). Pediatric gastroenterologists and endoscopists with more EoE-experience were more likely to recommend monitored anesthesia care and pre-procedural endotracheal intubation.

Significantly more adult gastroenterologists (48%) recommended attempting to gently push the food bolus into the stomach, compared to pediatric providers (19%, $p < 0.001$). Fewer than half (43%) of all respondents recommended taking esophageal biopsies; those recommending biopsies were more experienced with EoE (25% vs. 52% vs. 77%, $p < 0.001$; LE vs ME vs VE) and were more likely to be pediatric gastroenterologists (32% vs. 79%, $p < 0.001$; adult vs peds). 70% agreed that first follow-up post ED visit should occur within one month after EFI.

Conclusion: The considerable practice variation in the management of EFI in patients with EoE provides a rationale for the creation of consensus practice guidelines.

G21

Endoscopic ultrasound-guided pancreatic duct drainage: a single center observational study

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Background and aims: Pancreatic duct (PD) obstruction can cause pain and atrophy of the pancreatic parenchyma. Endoscopic placement of pancreatic stents by endoscopic retrograde pancreatography is the first-line treatment. In some patients, the classic transpapillary approach cannot be performed. Endoscopic ultrasound-guided PD drainage (EUS-PDD) is a promising alternative technique to treat PD obstruction. We aimed to evaluate technical and clinical success of EUS-PDD.

Methods: Data of patients who underwent EUS-PDD in our center between 2018 and 2021 were retrospectively reviewed. Technical success was defined as successful stent placement in PD. Clinical success was defined as pain ≤ 2 on the Numerical Rating Scale (NRS, 0–10) and no recurrence of obstructive pancreatitis post procedure.

Results: 38 patients (mean age 55.6 years, 71.1% male) were included. Indications of EUS-PDD were chronic calcifying pancreatitis in 71.1% of patients (74.1% due to alcohol abuse). Other indications included anastomotic stenosis or rupture of PD. Technical success was achieved in 89.5% of patients. Clinical success was 90.9%. Remaining pain NRS >2 occurred in 9.1% of patients and obstructive pancreatitis recurrence in 9.1%. Three patients had pancreatitis recurrence, which was of alcoholic origin. Adverse event occurred in 11 patients (29.7%). Among them, 9 patients were treated by a new endoscopic procedure, 1 patient by surgical procedure and 1 patient by hybrid endoscopic and surgical treatment.

Conclusion: EUS-PDD had a high technical and clinical success rate in our center. It is therefore a good minimally invasive alternative to avoid pancreatic surgery in patients with failed endoscopic retrograde pancreatography.

G22

Esophageal radiofrequency ablation, an effective treatment for lichen planus associated dysplasia?

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Background: Esophageal lichen planus (ELP) is a chronic idiopathic inflammatory disorder that may lead to symptomatic stenosis and squamous cell carcinoma. Current mainstay treatments include immunosuppressant therapy (mainly corticosteroids) and balloon dilatations. A search of computerized medical databases did not identify any patient with ELP treated by radiofrequency ablation (RFA). However, both laser and RFA therapies have shown clinical and histologic improvement in patients with vulvar and oral lichen planus. Therefore, in the absence of alternative treatments, we assessed the performance of RFA in a 68-year-old female presenting with a high grade dysplasia (HGD) of the remaining lichen planus following the surgical esophagectomy of a squamous cell carcinoma of the esophagus.

Methods: We used a RFA BARRX Trough-the-scope (TTS) device to ablate HGD localizations, at the upper part of the esophagus above the esogastric anastomosis.

Results: A total of 5 sessions of RFA were performed with a 6–12 weeks interval. After 2 sessions no evidence of residual dysplasia was detected in the esophagus. Due to the occurrence of a new lichenoid lesion, we performed 3 additional sessions. The biannual endoscopic follow-up showed a reepithelialization of the treated mucosa and did not show any recurrence of dysplasia. No complications of RFA were observed following the treatment.

Conclusions: In this case study, radiofrequency ablation was demonstrated to be an effective and safe treatment for ELP associated dysplasia.

G23**Management of Groove Pancreatitis – a single center case series**

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Background/Aims: The diagnosis and management of groove pancreatitis (GP) is challenging and a matter of controversy. GP is a rare, chronic condition involving inflammation of the pancreas in the anatomic space of the pancreatic groove located between the C-loop of the duodenum and the head of the pancreas. Diagnosis is based on clinical/lab signs of pancreatitis, radiology and endosonography. There is significant overlap with chronic pancreatitis and infiltrative processes such as pancreatic ductal adenocarcinoma or duodenal carcinoma. In this case series we report the outcomes of 11 patients diagnosed with GP in our center.

Methods: A retrospective review of all patients undergoing pancreatotomy for pancreatitis between 2011 and 2021 was performed. 11 patients (3 female, mean age:57 yrs; mean BMI

27) with clinical, radiologic and endoscopic confirmation of GP were identified.

Results: All patients had signs of an acute pancreatitis (lipase/amylase elevated), pain and history of nicotine and alcohol use. Conservative treatment including parenteral/enteral nutrition, pain medication, antibiotics, nicotine and alcohol abstinence was initiated in all patients. Due to pain and duodenal obstruction (1pt), 6 patients underwent pancreaticoduodenal resection (PD). The time from diagnosis of GP to surgery was 9 ± 4 months. Pancreatic exocrine functional insufficiency was observed in 4/6 patients preoperatively and 5/6 postoperatively. All 6 patients experienced a resolution of pancreatitis and significant improvement in pain. Of the 5 patients not undergoing PD 3 had relapsing symptoms and persistence of abdominal pain.

Conclusions: Conservative treatment is successful in 50% of patients with GP. For patients with on-going symptoms, PD is a safe procedure leading to long-term symptom control.

POSTER: HEPATOLOGY – CLINICAL

H1

Management of hepatocellular adenoma (HCA) in a tertiary care hospital: a multidisciplinary team experience

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Background/Aim: Due to a potential risk of hemorrhage or malignant transformation, hepatocellular adenoma (HCA) represents a challenge with regards to diagnostic and therapeutic procedures. We describe the management of patients addressed at our multidisciplinary team (MDT) meeting for HCA.

Methods: In the period from 2013 to 2021, 45 patients (mean age: 39.7 yrs, M/F: 6/39) were addressed to our MDT of the CHBP for the management of known (n = 13) or suspected HCA (n = 32). At every meeting consultations (median number/patient: 2 [1-6]), recommendations were made based on the input of radiologists, pathologists, surgeons, oncologists and gastroenterologists, regarding both diagnostic procedures (imaging, biopsy) and management strategies (surgery, interventional radiology, follow-up imaging).

Results: Diagnosis of HCA was excluded in 4 patients based on radiology. In the remaining 41 patients, a total of 85 recommendations were made by the MDT, including 44 propositions related to diagnosis and 41 to management strategies (see Table for detailed description). Additional imaging studies allowed a conclusive diagnosis in 2 patients. A nodule biopsy was recommended in 29 patients. Nine were unsuccessful in 9 (failure, refusal) allowing a definite histological diagnosis in 69% (20/29) of cases, including additional sequencing analysis in 9 patients. Propositions for management included follow-up imaging after cessation of oral contraceptives (n = 21), surgery (n = 6), or interventional radiology (bland embolization (n = 13) or radiofrequency (n = 1)).

Diagnostic recommendations (=44)			Recommendations for management (=41)		
strategy	n	Definite diagnosis	strategy	n	Full realization n
radiology	15	2	Follow-up imaging	21	21
biopsy	29	20	Interventional radiology	14	6
incl.sequencing	9		surgery	6	4

Conclusion: This real life experience illustrates the added value of a MDT consultation regarding HCA in keeping with recent developments in both diagnostic and therapeutic strategies.

H2

Evolution of health-related quality of life in patients surviving an episode of alcoholic hepatitis

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Background: Quality of life (QoL) measured by individual physical and psychosocial perception is underestimated compared to classical clinical determinants in decompensated liver disease. We studied changes in QoL in patients surviving an episode of severe alcoholic hepatitis (AH) exploring potentially targetable factors.

Methods: We included 51 patients with severe AH (mean age 54 years, M/F 37/14, MELD 18.3 + 2.8, Maddrey's score 45.5) treated with standard of care including steroids in 75% of cases. The validated QoL questionnaire EQ-5D-3L (self-rated perception of physical + mental aspects) was applied at time of hospital stay and repeated at 3 month thereafter in survivors. Factors with potential influence on QoL (MELD changes, steroid response status, control of ascites, psychiatric comorbidity, alcohol abstinence/relapse) were also measured.

Results: At baseline, QoL was impaired compared to an age/gender matched population. At follow-up visit, MELD has improved (p <0.001), ascites was clinically persistent in 33%, and 31% had returned to alcohol

use. A moderate improvement in QoL (p <0.03) affected mostly the pain/discomfort related domain, without correlation to MELD changes. (Table: Predictors of improvement in QoL: uni- and multivariate analysis; OR: odds ratio)

Variable	Univariate		Multivariate	
	OR	p-value	OR	p-value
MELD improvement	2.70 (0.79-9.6)	0.11	-	-
Steroid response	0.71 (0.17-2.62)	0.62	-	-
Ascites control	1.38 (0.44-4.38)	0.58	-	-
No psychiatric comorbidity	1.61 (0.52-5.31)	0.42	-	-
Alcohol abstinence	3.47 (1.06-12)	0.04	3.84 [1.12-14.2]	0.035

Conclusion: Patients with AH and decompensated chronic liver disease report a poor QoL. The hepatic recompensation on the mid-term is associated with an improved QoL, with sustained alcohol abstinence as an independent predictor. Treatment of alcohol use disorders is a major challenge in the management of patients surviving an episode of AH.

H3

Gut microbiota and malnutrition in patients with alcoholic liver disease: a longitudinal study.

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Background: Cross-sectional studies demonstrate dysbiosis in cirrhosis. This longitudinal prospective study aimed to evaluate nutritional status and gut microbiota changes during follow-up (FU) in patients with alcoholic hepatitis (AH) and alcoholic cirrhosis (AC).

Methods: We included 10 patients with severe AH and 12 patients with AC without recent exposition to antibiotics. The following data were collected at baseline and at 3 and 6 months of FU: MELD score, C-reactive protein (CRP), anthropometric measurements, body composition (bioimpedance analysis expressed as phase angle), and gut microbiota by metagenomics of stool samples. Data are presented as median (lower and upper quartile) and compared at baseline and FU with non parametric tests. Permanova and Shannon diversity index estimate were used for microbiota comparisons.

Results: At baseline all patients were actively drinking alcohol. Age and nutritional parameters did not differ between groups but patients with AH had a higher MELD score, CRP and severity of portal hypertension (all p <0.05). During FU, 7 AH patients and 4 AC patients became alcohol abstinent. A statistically significant improvement in MELD and nutritional parameters over time was restricted to AH patients (see Table, *p <0.05 vs baseline, Friedman test).

Variables	Baseline	3 month	6 month
Phase angle, (degree)	4.1 [3.1-4.9]	4.9 [4.1-5.9]	5.1 [4.6-5.6]*
Mid-arm circumference (mm)	293 [255-320]	310 [275-340]	328 [295-360]*
Skinfold thickness (mm)	14.9 [10.5-24.3]	19.8 [12.1-25.5]	27.8 [16-31]*

No significant changes in overall microbiota structure were observed between time points, neither in AH nor in AC patients. However, in patients with AH, the relative abundance of some typically oral species belonging to genera *Streptococcus*, *Actinomyces*, and *Fusobacterium* significantly decreased during FU.

Conclusions: An improvement in nutritional parameters and changes in oral bacterial species affects only patients with AH. Future studies should evaluate the impact of alcohol abstinence on nutrition and gut dysbiosis in patients with alcoholic liver disease (supported by FLAGS foundation)

H4**Adherence and motivation for follow-up care in patients with hepatitis C cure: A mixed-methods study**

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Background and Aims: Clinical guidelines recommend post-treatment follow-up (FUP) in patients who achieved sustained virological response (SVR) if they have advanced liver fibrosis/cirrhosis, comorbidities or risk of re-infection. Our aims were 1) to evaluate patient's adherence to FUP recommendation and 2) to explain their motivations for FUP.

Method: With an explanatory mixed-methods design, we first evaluated quantitative FUP data from patients who achieved SVR24 with direct-acting antivirals from 2015-2019 (n = 270). Second, we conducted qualitative interviews to explain patient's motivation for FUP (n = 12).

Results: Of patients with SVR24, 146 (54%) required FUP, for HCC surveillance 68 (25%), comorbidities 29 (11%), or risk behaviors 12 (4%). Lost-to-FUP were 37 (14%). Of these, 15 (6%) with advanced fibrosis and 13 (5%) with comorbidities. In FUP not matching recommendation were 70 of 124 (26%) patients. Motivation can be explained in 1) Patients following the recommendation (109/146) as *Following my HCP's advice*. They just describe HCPs advice and seldom a medical reason as FUP-motivation; 2) In patients in FUP without recommendation (70/124) as *Maintaining the liver care*. They describe the liver as their focus of care over years and the FUP was important to maintain control by ongoing assessments of liver health.

Independent of recommendation (179/270) important motivation was *Taking on illness related work*. Patients describe with cure, they were challenged by management of comorbidities, adapting behaviours and social issues.

Conclusion: Adherence with FUP is generally high, interestingly almost a third of patients were in FUP without an indication according to recommendation. This was explained by the wish for ongoing liver control. From the patient's perspective, many show ongoing self-care needs and this highlights the need to include patients' perspectives into FUP decision making and the provision of prolonged self-management support for some.

H5**Therapy adaption by dose titration of obeticholic acid in a 57-year-old female patient with PBC and advanced liver fibrosis**

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Background: PBC can progress despite first-line therapy with ursodesoxycholic acid (UDCA) with inadequate biochemical response to UDCA treatment generally being considered at highest risk for disease progression. In addition, more recent data demonstrate that the presence of advanced liver fibrosis (F3/F4) is an independent predictor of transplant-free survival in PBC. Thus, individual risk stratification and eventual early adaption of therapy seems pivotal to improve long-term outcomes. For patients with inadequate response to UDCA, current guidelines recommend add-on therapy with the FXR agonist obeticholic acid (OCA).

Case report: A 57-year-old female patient with PBC who had been treated with UDCA (2x500 mg/day) for 12 years presented with markedly increased cholestasis parameters (ALP >1.5xULN, GGT 334U/L). Ultrasound was suggestive of liver cirrhosis w/o presence of ascites and elastography indicated increased liver stiffness (ARFI, median: 1.55m/s, IQR: 0.42). Liver biopsy confirmed chronic low-grade hepatitis and cholangitis with bridging fibrosis and incomplete cirrhosis (Ishak stage 5). Based on these clinical findings, add-on therapy with OCA was initiated (5 mg/day; 10/2018). After one month of OCA therapy, treatment was

well tolerated and cholestasis parameters improved, but remained elevated (11/2018; Tab. 1). Based on the patient's high risk for disease progression, OCA dose was therefore increased to 10 mg/day (12/2019). This led to a further marked decrease of ALP and GGT values. In addition, bilirubin levels decreased and were stabilized within the normal range (Tab. 1).

Conclusions: Incomplete biochemical response to UDCA and/or presence of advanced fibrosis put patients at high risk for disease progression. Add-on therapy with OCA and subsequent dose titration to 10 mg/day can improve biochemical response and further increase therapeutic effect. In the present case, this led to a clinically meaningful improvement and stabilization of liver function tests and was well tolerated.

Date	ALP [U/l]	AST [U/l]	ALT [U/l]	GGT [U/l]	Alb [g/l]	Bili [mg/dl]
01/2018	351	51	28	334	N/A	0,7
11/2018	213	46	25	118	43,0	0,8
09/2019	207	50	24	71	43,1	0,9
12/2019	221	53	27	91	42,0	1,0
03/2020	123	68	37	42	43,8	0,9
10/2020	105	43	12	33	41,7	0,7

H6**Integrated thoraco-laparoscopic approach with parenchymal-sparing resection of a hepatocellular carcinoma located in the hepatic dome**

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Background: Laparoscopy is commonly used for resection of liver tumours. However, access to lesions located in the hepatic dome is difficult and adequate exposure often requires a laparotomy even for small tumours. This video presents a novel minimally-invasive approach that integrates laparoscopy and thoracoscopy in a parenchymal-sparing resection of a hepatocellular carcinoma (HCC) in segment VIII of the liver.

Methods: A 71-year-old man with a single HCC 3.2 cm in diameter located in the liver dome and Child A5 cirrhosis (Barcelona Clinic Liver Cancer, BCLC stage A) due to alcohol-related liver disease was referred for surgical treatment. The patient was placed in a 45° left lateral decubitus position with double-lumen tube intubation. Four trocars were inserted in the abdomen and one trans-diaphragmatic trocar was placed through the 8th intercostal space allowing adequate triangulation. The resection was performed using a 3D optical system, intraoperative ultrasonography, Cavitron Ultrasonic Surgical Aspirator (CUSA), a Thunderbeat device, clips and bipolar forceps. After chest tube insertion the trocar entry point in the diaphragm was closed with 2 single-button sutures.

Results: Operating time was 279 minutes with 150 ml blood loss. The recovery was uneventful and the patient discharged on the 4th postoperative day. Final pathology showed tumour free margins.

Conclusions: A limited liver resection for tumours in the hepatic dome via a minimally-invasive approach integrating thoracoscopy and laparoscopy is feasible and can be performed safely in selected patients. The integrated approach offers a superior exposure of tumours located in cranial liver segments and facilitates resection.

H7

Primary sclerosing cholangitis and chronic inflammatory bowel disease: post liver transplant evolution

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Background: Primary sclerosing cholangitis (PSC) is associated in most cases with inflammatory bowel disease (IBD) and the only curative option is liver transplantation (LT) in case of advanced disease. The evolution of the disease according to presence or absence of associated inflammatory bowel disease (IBD) is less studied. In this retrospective study we assessed factors associated with post-LT outcomes in PSC including the role of IBD.

Method: We conducted a retrospective study of patients who underwent LT due to PSC in our institution. We collected baseline and follow-up variables. Continuous variables are reported as median [IQR] and categorical as n (%). Statistical testing was performed using Wilcoxon and Fisher exact test respectively.

Results: We identified 29 patients with PSC who underwent LT in Geneva University Hospitals between 1989 and 2020 (2.8% of total LT). Out of 29 included patients, there were 10 women (34.5%), median age was 52 y [44-57y], 4 patients (18%) were <18 y old at time of liver transplantation. Median follow-up was 5 years (2–10). 21 patients (72%) had IBD, of which 17 had UC (81%) and 4 had Crohn's disease (19%). Concerning IBD treatment, the most common therapy pre-LT was 5-ASA (n = 8, 38%), in 6/17 (35%) ulcerative colitis (UC) and 2/4 (50%) Crohn's disease (CD) patients, followed by Azathioprine in 4 patients (19%). No patient had any biological treatment before LT. Of the UC patients, 4 required colectomy, 3 due to neoplastic disease and 1 due to inflammatory activity. There was no significant difference in the main composite outcome (recurrence of PSC; re-LT or death) in patients with IBD vs without IBD (43% vs 38% respectively, p = 1.00) during follow-up. However corticosteroid therapy after LT was significantly associated with the composite outcome (75% vs 12% in patients with and without post-LT corticosteroid therapy, p = 0.001).

Conclusion: In a single-center retrospective cohort of PSC undergoing LT we found that 72% of PSC patients had underlying IBD, but presence of IBD was not associated with worse outcomes post LT. However corticosteroid therapy after LT was associated with a higher risk of poor outcomes. Main limitations include a small sample size and a single center cohort so we aim to further explore these questions in a multicentric approach across additional transplant centers.

H8

Low baseline but not delta cortisol relates to 28-day transplant-free survival in acute liver failure syndromes

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Background: There is an ongoing controversy on diagnosis, clinical, prognostic and therapeutic impact of adrenal insufficiency (AI) in patients with acute liver failure syndrome. **Methods:** We studied 28-day transplant-free survival (TFS) in relation to different definitions of AI, cortisol concentrations at baseline (BL) and treatment with glucocorticoids (GC) in patients with ALF (n = 30) and ACLF (n = 34). Admission cortisol levels

at BL and following short synacthen test (SST) were assessed and circulating monocytes were studied phenotypically. GC treatment was based on clinical judgement.

Results: In ALF, BL cortisol <387nM indicated TFS (sensitivity 83%, specificity 53%), accordingly patients with AI defined by low BL cortisol had higher TFS compared to patients without AI. GC treatment improved TFS only in patients with AI defined by BL cortisol <414 nM. In ACLF, BL cortisol <392 nM correlated with TFS (sensitivity 80%, specificity 61%), yet detection of AI did not affect TFS. Patients with AI defined by BL cortisol <275 nM benefitted from GC treatment. In both, ALF and ACLF, TFS did not differ when AI definition was based on SST results. High BL cortisol correlated with HLA-DR_{low} expression on monocytes.

Conclusions: Low BL cortisol indicated TFS and thus may serve as a prognostic marker in ALF/ACLF. This finding was affirmed by the correlation of cortisol and HLA-DR_{low}, previously associated with poor outcome. Patients with BL cortisol <414 nM in ALF and <275 nM in ACLF, respectively, benefitted from GC treatment suggesting cortisol assessment can be applied for treatment guidance. Conducting an SST was dispensable.

H9

Belimumab in Autoimmune Liver Diseases with associated Sjögren's Syndrome

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Background: B cell-activating factor (BAFF) levels are elevated in autoimmune hepatitis (AIH) and primary biliary cholangitis (PBC). About 20% of patients with PBC and 5% with AIH have a Sjögren's syndrome (SjS). PBC and SjS have many features in common. Belimumab (anti-BAFF) shows positive effects in SjS.

Methods: Retrospective analysis on treatment response to belimumab in three female patients with AIH and/or PBC with SjS. Patient 1: 52y, with AIH (F2), PBC and SjS. Indication: active AIH with intolerance to standard treatment; belimumab since 01/20. Patient 2: 72y, with PBC (F3) and SjS. Indication: refractory PBC; belimumab since 11/20. Patient 3: 54y, with PBC (F2, ductopenia), SjS and erosive rheumatoid arthritis.

Indication: refractory PBC; belimumab since 11/20.

Results: Patient 1: AIH in remission under belimumab monotherapy. Patient 2: PBC in remission 6 months after treatment start. Patient 3: Cholestasis stable. Slight decrease of mildly elevated transaminases and almost normalization of IgM. The effects on SjS were overall encouraging in all patients.

Conclusions: These preliminary findings indicate belimumab as a promising treatment option in AIH and PBC, with so far no safety concerns.

Our study shows how the occurrence of different autoimmune diseases can guide us to further personalize treatment and highlights the strengths of a tight collaboration between hepatology and rheumatology.

H10

IMbrave150: updated efficacy and safety by risk status in patients (pts) receiving atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) as first-line treatment for unresectable hepatocellular carcinoma (HCC)

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Background: Based on the Ph III IMbrave150 trial (NCT03434379), atezo+bev has been approved globally and is standard of care for pts with unresectable HCC without prior systemic therapy. With an additional 12 mo of follow-up from the primary analysis (median, 15.6 mo), atezo+bev showed consistent clinically meaningful benefit and safety (Finn ASCO GI 2021). Here, we report results of updated analyses considering high-risk factors.

Methods: Pts were randomized 2:1 to receive atezo 1200 mg IV q3w + bev 15 mg/kg IV q3w or sor 400 mg PO BID until loss of clinical benefit

or unacceptable toxicity. High-risk situation was defined as tumor invasion of the portal vein and/or the portal vein branch contralateral to the primarily involved lobe (Vp4), and/or bile duct invasion and/or tumor occupancy of $\geq 50\%$ of liver.

Results: In the ITT population, 64 (19%) pts with atezo+bev and 37 (22%) pts with sor were defined as high risk. 10 pts had bile duct invasion, 73 had Vp4-invasion and 31 had liver tumor occupancy of $\geq 50\%$. 9 pts in the atezo+bev arm and 4 pts in the sor arm had 2 high-risk factors. OS, PFS and ORR all favored atezo+bev over sor, in both non-high-risk and high-risk patients. In safety-evaluable pts, Grade 3/4 treatment-related AEs (TRAEs) occurred in 122 (45%) of 269 non-high-risk and 21 (35%) of 60 high-risk atezo+bev pts. Grade 5 TRAEs occurred in 5 (2%) non-high-risk and 1 (2%) high-risk atezo+bev pt.

Conclusions: Efficacy benefit was seen with atezo+bev vs sor regardless of high-risk features. HRs remained similar despite the numerical differences in median OS between non-high-risk and high-risk pts. The overall safety data in the atezo + bev arm were comparable between non-high and high-risk pts and in line with the known safety profile of each drug.

POSTER: HEPATOLOGY - BASIC/TRANSLATIONAL

H1

Assessment of circadian sleep-wake rhythms in non-alcoholic fatty liver disease (NAFLD)

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Background: Non-alcoholic fatty liver disease (NAFLD) has become the most common chronic liver disease in industrialised nations. The circadian rhythm may play a role in its pathophysiology. Actigraphy objectively quantifies sleep-wake rhythms and physical activity and has not been assessed in NAFLD. We aim to better understand the chronobiology of NAFLD patients in regards to a potential role in its pathophysiology and future therapy.

Methods: We intended to assess sleep-wake rhythms by actigraphy (ActTrust, Condor) in relation to non-invasive parameters of circadian rhythm (cortisol, melatonin), markers of liver disease and the immune responses in NAFLD patients compared to healthy controls (HC). Two weeks of Actigraphy were succeeded by single standardised sleep hygiene counselling, and continued for subsequent 2 weeks.

Results: Waking after sleep onset (WASO) was significantly higher and sleep efficiency was lower in NAFLD compared with HC ($p < 0.05$). Data from questionnaires showed that patients with NAFLD slept shorter and woke up earlier compared with HC ($p < 0.05$). HC drank more coffee than patients with NAFLD and cirrhosis ($p < 0.05$). Coffee consumption correlated negatively with fibrosis in NAFLD. HLA-DR expression on monocytes was reduced in NAFLD and cirrhosis, as was CCR7 and CD32 ($p < 0.05$). MERTK, Tyro3, CD163 and CCR7 expression negatively correlated with sleep time. Single sleep hygiene counselling didn't improve metabolic or hepatic parameters in patients with NAFLD.

Conclusions: Subjective and objective sleep assessment differed, objectively patients with NAFLD had more waking up episodes and less effective sleep. Data from questionnaires showed that NAFLD patients

woke up earlier and slept shorter. Sport and coffee consumption appeared protective.

H2

Defining the Host Interactome of the Hepatitis E Virus Capsid Protein by Proximity Labeling

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Background: Hepatitis E virus (HEV) is the most common cause of acute viral hepatitis worldwide. The viral genome harbors three open reading frames (ORF). The ORF2 protein corresponds to the viral capsid. Here, we aimed to define the host interactome of the HEV capsid protein.

Methods: Transposon-mediated random insertion was exploited to identify functional insertion sites in the HEV capsid protein. Full-length viral genomes with in-frame insertions of the TurboID biotin ligase in the capsid protein were characterized by immunofluorescence and immunoblot analyses as well as functional assays. Biotinylated capsid-proximal proteins were identified by streptavidin-mediated pull-down and mass spectrometry (MS).

Results: Transposon-mediated random insertion and sequencing of viable genomes identified functional insertion sites in the N- and C-terminal parts of the HEV capsid protein. TurboID inserted into four of these sites retained biotin ligase activity and was tolerated in terms of viral genome replication as well as capsid secretion. MS identified 496 host proteins that were significantly enriched in the proximity of the capsid protein. The role of selected candidate host proteins in the HEV life cycle is currently being investigated.

Conclusions: Identification of functional insertion sites enabled tagging of the HEV capsid protein with biotin ligase and proximity labeling. Investigation of interacting host proteins should allow to decipher the different functions of the capsid protein and yield new insights into the pathogenesis of hepatitis E.

POSTER: SURGERY - CLINICAL

S1

Does fluorescence angiography reduce the incidence of anastomotic leak in colorectal surgery: a systematic review and meta-analysis of randomized controlled trialsJ. Meyer^{1,2}, H. Joshi², N. Buchs¹, F. Ris¹, R. J. Davies²*1 Digestive Surgery, Geneva University Hospital, Geneva, Switzerland; 2 Colorectal Unit, Addenbrooke's Hospital, Cambridge NHS Foundation Trust, Cambridge, United Kingdom***Background:** Observational studies have shown that fluorescence angiography (FA) decreases the incidence of anastomotic leak (AL) in colorectal surgery, but high-quality pooled evidence is lacking.**Methods:** MEDLINE, Embase and CENTRAL were searched for RCTs assessing the effect of intra-operative FA versus standard assessment of bowel perfusion on the incidence of AL of colorectal anastomosis. Pooled relative risk (RR) and pooled risk difference (RD) were obtained using models with random effects.**Results:** Two-hundred forty-eight articles were screened, 245 were excluded and 3 were kept for inclusion. The three included RCTs compared assessment of the perfusion of the bowel during confection of a colorectal anastomosis using FA versus standard practice. In meta-analysis, FA was significantly protective against anastomotic leak (3 RCTs, 964 patients, RR: 0.67, 95%CI: 0.46 to 0.99, I2: 0%, p = 0.04). The incidence of AL was non-significantly decreased by 4 percentage points (95%CI: -0.08 to 0, I2: 8%, p = 0.06) when using FA.**Conclusion:** The effect of FA on prevention of AL in colorectal surgery exists but is potentially of small magnitude.

S2

Current practice of fluorescence angiography during colorectal surgery in Switzerland: a cross-sectional surveyJ. Meyer¹, B. Schiltz¹, A. Balaphas¹, M. Carvello², A. Spinelli², C. Toso¹, F. Ris¹, N. Buchs¹*1 Digestive surgery, Geneva University Hospital, Geneva, Switzerland; 2 Colorectal Surgery, Humanitas Hospital, Milano, Italy***Objective:** The indications and modalities of use of fluorescence angiography (FA) are still not well defined in colorectal surgery.**Methods:** An online survey composed of 35 question was carried out among Swiss colorectal surgeons.**Results:** Sixty-seven participants were included in the survey. Forty-six participants (68.7%) were using FA on a regular basis. When performing a bowel anastomosis, participants relied mostly on FA (56.7%) to take the final decision regarding assessment of bowel perfusion. FA was reported to be mostly used in both elective and emergency surgery procedures (89.1%), and to check both bowel anastomosis and perfusion of end segments (67.4%). FA was mostly used on the external wall of the bowel but was reported to be also used endoscopically by 45.6% of participants. FA was used in 100% of patients by 51.1% of participants for right colectomy, 50% for segmental transverse colectomy, 71.7% for left colectomy, 77.5% for rectal surgery and 42.9% for ileo-anal pouch creation.**Conclusion:** Although FA is gaining increasing popularity in colorectal surgery, its indications and modalities of application remains subject to heterogeneity and deserve to be better standardized.

S3

Pre-operative iron allows correction of anaemia before abdominal surgery: A systematic review and meta-analysis of randomized controlled trialsJ. Meyer^{1,2}, R. Cirocchi³, S. Di Saverio⁴, F. Ris², J. Wheeler¹, R. J. Davies¹*1 Colorectal Unit, Cambridge NHS Foundation Trust, Cambridge, UK; 2 Digestive Surgery, Geneva University Hospital, Geneva, Switzerland; 3 Department of General Surgery and Surgical Oncology, Hospital of Terni, Terni, Italy; 4 General Surgery, Ospedale di Circolo Fondazione Macchi, Varese, Italy***Objective:** Our aim was to determine if pre-operative iron allows correction of haemoglobin concentration and decreased incidence of peri-operative blood transfusion in patients undergoing major abdominal surgery.**Methods:** MEDLINE, Embase and CENTRAL were searched for RCTs written in English and assessing the effect of pre-operative iron on the incidence of peri-operative allogeneic blood transfusion in patients undergoing major abdominal surgery. Pooled relative risk (RR), risk difference (RD) and mean difference (MD) were obtained using models with random effects. Heterogeneity was assessed using the Q-test and quantified using the I2 value.**Results:** Four RCTs were retained for analysis out of 285 eligible articles. MD in haemoglobin concentration between patients with pre-operative iron and patients without pre-operative iron was of 0.81 g/dl (3 RCTs, 95% CI: 0.30 to 1.33, I2: 60%, p = 0.002). Pre-operative iron did not lead to reduction in the incidence of peri-operative blood transfusion in terms of RD (4 RCTs, RD: -.13, 95% CI: -0.27 to 0.01, I2: 65%, p = 0.07) or RR (4 RCTs, RR: 0.57, 95% CI: 0.30 to 1.09, I2: 64%, p = 0.09).**Conclusion:** Pre-operative iron significantly increases haemoglobin concentration by 0.81 g/dl before abdominal surgery but does not reduce the need for peri-operative blood transfusion. Important heterogeneity exists between existing RCTs in terms of populations and interventions. Future trials should target patients suffering from iron-deficiency anaemia and assess the effect of intervention on anaemia-related complications.

S4

A systematic review of scores predicting anastomotic leak in colorectal surgeryA. Litchinko, A. Balaphas, I. Uhe, C. Toso, N. Buchs, F. Ris, J. Meyer
*Digestive Surgery, Geneva University Hospital, Geneva, Switzerland***Objective:** Predicting the risk of anastomotic leak (AL) is of importance to define the optimal surgical strategy in colorectal surgery. Our objective was to perform a systematic review of existing scores in the field.**Methods:** Medline was searched for observational studies reporting scores predicting AL after colorectal anastomosis. Studies reporting only validation of existing scores and/or scores based on post-operative variables were excluded. PRISMA recommendations were followed. Qualitative analysis was performed.**Results:** One hundred and eighty-eight articles were identified. One hundred and seventy-nine articles were excluded after title/abstract and full-text screening, leaving 9 studies for analysis. Scores included the Colon Leakage Score, the modified Colon Leakage Score, the REAL score, www.anastomoticleak.com and the PROCOLE score. Four studies (44.4%) included more than 1'000 patients and one extracted data from existing studies (meta-analysis of risk factors). Scores included the following pre-operative variables: age (44.4%), gender (77.8%), ASA score (66.6%), BMI (33.3%), diabetes (22.2%), respiratory comorbidity (22.2%), cardiovascular comorbidity (11.1%), liver comorbidity (11.1%), weight loss (11.1%), smoking (33.3%), alcohol consumption (33.3%), steroid consumption (33.3%), neo-adjuvant treatment (44.9%), anticoagulation (11.1%), hematocrit (22.2%), total proteins (11.1%), WBC (11.1%), albumin (11.1%), distance from anal verge (77.8%), hospital size (11.1%), bowel preparation (11.1%), indication for surgery (11.1%). All scores also included the following peri-operative variables: emergency surgery (22.2%), surgical approach (22.2%), duration of surgery

(66.6%), blood loss/transfusion (55.6%), additional procedure (33.3%), operative complication (22.2%), wound contamination class (1.11%), mechanical anastomosis (1.11%) and experience of the surgeon (11.1%). Five studies (55.6%) reported the area under the curve (AUC) of the scores, and 4 (44.4%) included a validation set.

Conclusion: Existing scores are heterogeneous in the identification of variables allowing to predict AL. A majority of the scores was calculated from small cohorts of patients which, considering the low incidence of AL, might lead to miss potential significant predictors of AL. AUC is seldomly reported. We recommend that new scores to predict the risk of AL in colorectal surgery to be based on large cohorts of patients, to include a validation set and to report the AUC.

S5

The BiLe Trial: Presentation of a national multicentric randomized controlled trial for the prevention of bile leakage after liver resection

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Background: Bile leakage is a frequent complication after liver resection. Strategies leading to a reduction of the rate of this complication are valuable. Results of several non-randomized trials, a unique monocentric randomized trial (RCT) of low quality as well as meta-analyses suggest that the intraoperative application of the white test could be a promising strategy to reduce the postoperative occurrence of bile leakages. We propose to conduct a national multicentric RCT with primary endpoint rate of postoperative bile leakage with and without the intraoperative performance of the white test as described by Nadalin et al. 2008.

Methods: The BiLe trial is an investigator-initiated randomized controlled, parallel group, double-blinded, multicentric, superiority trial in 4 Swiss centres (Aarau, Lugano, St. Gallen and Lucerne). A total of 210 patients undergoing a resection of at least 2 liver segments are randomly allocated intraoperatively to either the intervention (intraoperative white test) or the control group (white gauze on the liver resection surface). Randomization and data collection are performed with SecuTrial. Both the cantonal ethics committees of all participating centres and Swissmedic approved the study.

Results: The primary outcome is the comparison of the postoperative bile leakage rate in both groups within 30 days after liver resection. Secondary outcomes are operative and postoperative complication, including severity grade of the bile leakage, rate of ERCP, interventional drainage, morbidity, intensive care unit (ICU) stay, and mortality.

Conclusions: Patient recruitment started on March 1st. Study duration is expected to be 3 years without interim analyses. The results of the BiLe-Trial will be submitted to a peer-reviewed journal regardless of the outcome.

S6

Bias of Meta-analyses: Influence on treatment recommendation for small hepatocellular carcinoma

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Background: Beside hepatic resection (HR) and transplantation, radiofrequency ablation (RFA) has evolved from a palliative tool to a curative treatment modality for small hepatocellular carcinoma (HCC). Two Cochrane reviews compare outcome after HR versus RFA for small HCC (Weis et al., 2013 and Majumdar et al., 2017). Both authors conclude that there was no evidence of a difference in all-cause mortality at maximal follow up between surgery and RFA. By including only low risk of bias trials HR seemed more effective than RFA regarding overall survival (HR 0.56, 95% CI [0.40; 0.78]) in the meta-analysis of Weis et al. Aim of this article was to assess the validity of the randomized controlled trials (RCT) included in both Cochrane reviews and to investigate the impact of their results on current guidelines.

Methods: The validity of the RCT included in both Cochrane reviews was analyzed using the CONSORT checklist.

Results: The meta-analysis of Weis et al. 2013 included a total of 3 studies. One of them (Feng et al.) was not included in the meta-analysis of Majumdar et al. 2017, which included a total of 4 studies. One of them (Lee et al.) was available only as abstract. Four studies (Chen, Huang, Feng, Fang) could be further assessed for validity and revealed several inconsistencies. Unclear or not adequate randomization, missing blinded setup, conflict of interest and lacking intention-to-treat analysis were the most common findings.

Conclusion: The validity of the included studies is a prerequisite for the validity of the meta-analyses. The authoritative value of guidelines is generally recognized and recommendations often are based on results of Cochrane reviews. We suggest an improved critical appraisal of the validity of single studies and meta-analyses.

S7

ERCP & laparoscopic cholecystectomy as a rendez-vous procedure: is it worth the effort?

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Background: Several clinical studies show shortened length of hospital stay (LOS) performing laparoscopic cholecystectomy (LC) and endoscopic retrograde cholangiopancreatography (ERCP) in a rendez-vous procedure (RVP) for treatment of choledocholithiasis. Our aim was to analyse potential benefits of a one-year cohort for both patients and hospital.

Methods: This retrospective single-center study included all patients undergoing LC and ERCP in 2019. Patient records and procedure specific data were assessed.

Results: 62 patients underwent LC and ERCP either as separated procedures within one (group EC-H1, n = 14) or two admissions (group EC-H2, n = 41) or in a RVP (group RVP, n = 7). Total procedure time was shorter in group RVP compared to group EC-H1 with significantly shorter total time of involvement anaesthetist (233 vs 297 min, p = 0.02). Group EC-H1 had significantly longer total procedural time (162 min vs 123 min, p = 0.01), a significantly increased duration of narcosis (226 min vs 194 min, p = 0.03) and significantly longer total time in procedure room (265min vs 226min, p = 0.02) in comparison to group EC-H2. There were no significant differences between group RVP vs group EC-H2 regarding all parameters. LOS, costs and post-interventional complication rate were lowest in group RVP compared to group EC-H1 vs EC-H2.

Conclusion: Despite an extra organizational effort, the RVP provides clear benefits for both the patient and the hospital (LOS).

S8

Preoperative hiatal hernia in oesophageal adenocarcinoma; does it have an impact on patient outcomes?

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Background: Uncontrolled gastroesophageal reflux and the often-associated hiatal hernia (HH) are frequently encountered in oesophageal adenocarcinoma patients. Previous data suggest unfavourable long-term oncologic outcomes in the presence of a HH, but the evidence remains scarce. The aim of this study was to assess the potential impact of preoperative HH on histologic response after neoadjuvant treatment (NAT), as well as on overall and disease-free survival.

Methods: All patients operated for an adenocarcinoma of the oesophagus or gastro-oesophageal junction (GOJ) between 2012-2018 were assessed. Baseline endoscopy and CT-scan images were retrospectively

reviewed to identify the presence of a clinically significant HH (≥ 3 cm). Response to neoadjuvant treatment (Mandard TRG grade), postoperative outcomes and survival were compared between HH and non-HH patients. Categorical variables were compared with the χ^2 or Fisher's test, whereas continuous ones with the Mann-Whitney-U test. Survival analyses were performed with the Kaplan-Meier method and log-rank test.

Results: Overall, 101 patients were included (84.1% male, median age 63 years); among them, 33 (32.7%) had a HH ≥ 3 cm at diagnosis of oesophageal cancer. There were no significant baseline differences in demographics and tumour stages between the two groups. NAT was used in 80.9% of non-HH versus 81.8% HH patients ($P = 0.910$), most often chemoradiation (57.4% in non-HH versus 63.6% in HH patients, $P = 0.423$). Surgical approach and postoperative complication rates were similar in all patients. Good response to NAT (TRG 1-2) was observed in 36.4% of non-HH, versus 32.4% of HH patients ($P = 0.297$), whereas R0 resection was achieved in 90.9% vs 94.1% of patients respectively ($P = 0.551$). Overall survival was comparable between HH (median 28 mo, 95%CI 22-NA) and non-HH patients (median 41mo, 95% CI 29-NA) ($P = 0.605$). Disease-free survival was also similar (median 18 mo, 95%CI 12-NA for HH, vs 34mo, 95%CI 14-NA for non-HH patients, $P = 0.283$).

Conclusions: A clinically significant HH is encountered in almost a third of patients with oesophageal adenocarcinoma. However, in our study, it was not associated with a worse response to NAT, nor did it lead to a worse overall and disease-free survival.

S9

Irrigation with passive drainage to reduce clinically-relevant pancreatic fistulas after major pancreatic resections

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Background: We aim to illustrate a technique to reduce clinically relevant post-operative pancreatic fistula (CR-POPF) in high-risk patients after distal (DP) and proximal (PD) pancreatectomy. We compare our results with data retrieved from the literature.

Methods: Only patients harbouring high-risk stigmata for POPF development were included in the study. Twelve high-risk DP received irrigation and passive drainage of the pancreatic stump for 2 postoperative days (POD). Similarly, 34 high-risk PD received perianastomotic irrigation and passive drainage until POD 2. Biochemical tests carried out on the drained fluid allowed progressive reduction of irrigation flow and subsequent removal of the irrigation-drainage system.

Results: In the DP group we experienced only 1 (8.3%) grade B POPF. Data retrieved from the literature, instead, report a CR-POPF rate ranging from 11.2 to 59% for the same high-risk categories. In the PD group we encountered 2 (5.8%) grade B and 3 (8.9%) grade C POPFs. Once again, the likelihood of CR-POPF development after PD in the high-risk population reported in other studies ranges from 67 to 100%. In our case series, all grade B POPF were managed with radiologic drainage of the fluid collection, while grade C POPF required reoperation. The post-operative course after the reoperation was uneventful in all cases. No POPF-related deaths occurred in both groups. The median length of hospital stay was 13 and 17 days in the DP and PD groups, respectively.

Conclusions: Irrigation with passive drainage of the pancreatic stump after DP or perianastomotic area after PD seems an interesting approach for CR-POPF rates reduction in high-risk patients.

S10

RefluxStop™, a novel device to address Gastroesophageal Reflux Disease: Short-term results

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Background: To report safety, feasibility, and patient's functional short-term outcome of novel RefluxStop anti reflux operation.

Methods: All patients ($n = 20$) who received laparoscopic anti reflux surgery (LARS) by implantation of the RefluxStop device, from September

2018 to November 2020 in a university hospital, were included for retrospective analysis. Incidence of adverse device-effects and procedure-related adverse events were reported as primary endpoint. Feasibility was assessed reporting operation duration and rate of conversion to open surgery. Subjective and objective data were reported as functional outcome parameters.

Results: Median follow up was 8 (1–30) months. No serious adverse device related events occurred. One patient (5%) presented with stenosis at the gastroesophageal junction on x-ray during follow up. The stenosis was endoscopically not significant but still treated by balloon dilation. No further major complications (Clavien-Dindo \geq III) occurred during follow-up. Median duration of surgery was 85 (59–188) minutes. No conversion from laparoscopic to open surgery occurred. There was significant reduction in the mean of total gastro-oesophageal reflux disease (GERD) – health related quality of life score between baseline and 6-weeks after surgery (for $n = 12$) with 23.9 and 4.3 ($p < 0.001$) as well as between baseline and 6 months after surgery (for $n = 10$) with 24.9 and 4.4 ($p < 0.001$), respectively. The success rate for complete control of a given symptom varied from 40 to 92% after 6 months and the success rate for improvement of any GERD-symptom from 60 to 100%, respectively. Fifty-four per cent had absence of any side effect (dysphagia, bloating, and diarrhoea) 6 months after LARS. Newly developed or worsening side effects were found in 31% 6 months after LARS.

Conclusions: RefluxStop procedure seems to be a safe operation with promising short-term results. For high-level recommendation, further studies looking for long-term results and randomized comparisons to the standard anti reflux procedures like Nissen or Toupet fundoplication are required.

S11

Laparoscopic resection of hepatic alveolar echinococcosis

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Introduction: Alveolar echinococcosis remains a very rare disease requiring complete radical resection for definitive treatment. While open approaches are common, safety and efficacy of laparoscopic approaches remain unknown.

Methods: This is a single-center, retrospective cohort study with patients undergoing liver resections for alveolar echinococcosis at the Department of Visceral Surgery and Medicine, Bern University Hospital from December 2002 to December 2019. Postoperative outcomes of patients following laparoscopic hepatectomy for alveolar echinococcosis were compared with those of patients undergoing open hepatectomy.

Results: A total of 70 patients underwent liver resection for alveolar echinococcosis. Laparoscopic hepatectomy was performed in 18 patients and open hepatectomy in 52 patients. While there were no significant differences in terms of gender, age and diagnostic tools, all patients of the LH cohort were staged P1 (100%) in contrast to only 39% in the OH cohort ($p < 0.05$). All patients undergoing laparoscopic hepatectomy were treated by atypical liver resections in comparison to the open hepatectomy cohort with 64% major liver resections and 36% atypical resections. Laparoscopic hepatectomy was associated with shorter mean operation time (122 minutes vs. 245 minutes, $p < 0.05$), lower overall complication rate (6% vs. 46%, $p < 0.05$), lower major complication rate (0% vs. 12%, $p = 0.599$) and shorter length of hospital stay (4.5 days vs. 13 days, $p < 0.05$). There were no significant differences in disease-free survival (0% vs. 14%, $p = 0.368$) and overall survival (100% vs. 97%, $p = 0.688$) in a mean observed follow-up of 22 and 58 months, respectively.

Conclusion: Laparoscopy is a feasible and safe approach for selected patients with alveolar echinococcosis without impact on disease recurrence.

S12

Robot-assisted pancreaticoduodenectomy: a hybrid minimally-invasive approach

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Background: There is currently plenty of evidence from high-volume pancreatic centres about the safety and feasibility of robot-assisted pancreaticoduodenectomy (RPD). However, it is unclear whether the utilisation of this minimally-invasive technology for pancreaticoduodenectomy (PD) is safe and practicable in the Swiss health-care system. This video presents a hybrid minimally-invasive PD approach that combines robot-assisted and conventional laparoscopy.

Methods: A 66-year old woman with histologically-proven periampullary carcinoma was referred for surgical treatment. Preoperative assessment has shown no radiologic sign of invasion of the main visceral vessels or distant metastases and a standard vascular anatomy. The resection phase was performed using conventional laparoscopy with a 3D optical system. Utilizing the same trocar entry points, the da Vinci Xi system was docked and the pancreatic and the biliary anastomoses were performed. The gastro-enterostomy was done in a standard surgical fashion using a small epigastric incision through which the specimen was earlier retrieved.

Results: Total operative time was 563 minutes (hereof resection phase 248 minutes, docking 16 minutes, console time 169 minutes). Total blood loss was 200 ml. The recovery was uneventful and the patient was discharged on the eighth postoperative day. Final pathology showed a periampullary carcinoma (pT2) with 18 retrieved lymph nodes (pN0) and tumour free margins (R0).

Conclusions: In selected patients, RPD seems feasible and can be performed safely using a hybrid approach that combines robot-assisted and conventional laparoscopy. Robot-assisted technology facilitates the reconstruction phase of the Whipple's procedure. Prospective multi-centre studies conducted in Switzerland are key to ensuring RPD meets the high-quality standards of open and laparoscopic PD in this health-care system.

S13

Rate of local recurrence in a cohort of 125 patients treated with Transanal Total Mesorectal Excision due to Rectal CancerPozza Gioia^{1,2}, Gloor Severin^{1,3}, Troller Rebekka¹, Adamina Michel^{1,4}

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Background: Transanal Total Mesorectal Excision (TaTME) is an alternative to conventional TME owing to its reported superior ability to achieve clear resection margins in low rectal cancers. Yet, nationwide Norwegian data claimed a 12-month local recurrence rate of up to 10%, a three-fold increase compared to conventional TME, questioning the oncological safety of TaTME.

Methods: Consecutive patients affected by rectal cancer treated with TaTME were prospectively included. Patients who required a partial mesorectal excision were excluded. Perioperative outcomes were reported as median & interquartile range (IQR). Data were independently audited and certified.

Results: 125 patients (88 men: 37 women) with a low or middle rectal cancer (7 cm to anal verge, IQR 5-9) underwent TaTME. Age and body mass index were 65 years (IQR 56-76) and 26 kg/m² (IQR 23-29). 87 (70%) patients had neoadjuvant radiochemotherapy. Surgery time was 357 minutes (IQR 303-435). 1 patient (0.8%) required a conversion to laparotomy. Performing TaTME in a 2-team technique saved 94 minutes or 19% of operating time (p <0.005, t-test one-team (n = 52, 420 minutes, IQR 349-494) vs. 2-team (n = 73, 326 minutes, IQR 285-372). 30-day morbidity amounted to 36% of minor complications (Dindo Clavien I-II) and 25% of major complications (Dindo Clavien III-V), including 11 anastomotic leaks (9%) and 3 reoperations (3%). Most of the leaks could be managed endoscopically. Median length of hospital stay was 10 days (IQR 8–14). Median follow-up was 45 months (IQR 25-67; range 13-95). Dissection of the mesorectum was excellent (Quirke 1 incomplete mesorectal excision rate: 1.6%) with 100% clear margins (distal margin 16mm, IQR 10-30; circumferential margin 10mm, IQR 5–15). Median T stage was 3 (IQR 2-3). 24 patients had positive lymphnodes (median 27, IQR 21-38). Local recurrence occurred in 7 (6%) patients and development of metachronous metastasis occurred in 36 (29%) patients. This led to a 5-year disease-free survival of 56% and a 5-year overall survival of 86%.

Conclusion: TaTME for low and middle rectal cancer is safe, feasible, and can lead to high quality of rectal cancer resection specimen, acceptable major morbidity and anastomotic leakage rate, to the expenses of a longer surgery time.

POSTER: SURGERY - BASIC/TRANSLATIONAL

S1

Amelanotic melanoma of the anal marginC. Maurus¹, C. Dumont¹, L. Parmentier², C.A. Apestegui¹, M. Matter⁴ and G. Berthod³

1 General surgery, 2 dermatology, 3 oncology, CHVR; 4 Visceral surgery, CHUV

Aim: We describe the diagnostic and therapy of an anal margin amelanotic melanoma.

Method: A 71 years old female patient presented with a mildly itching mass at the anal margin, detected about 3 months before, not responding to an over the counter "hemorrhoid ointment".

Results: The exam showed a rosy exophytic nodular tumor of about 1x1 cm at the anal margin with an irregular surface, and a R0-resection was performed. Histology showed an ulcerated amelanotic melanoma, pT4 Clark IV Breslow 5.2, mitotic index >10/mm². The classical melanoma

markers were positive; KIT, NRAS and BRAF as well as GIST-markers were negative. No synchronous distant metastases were detected by PET-CT and cerebral MRI. Because of the high-risk histological profile, the initial scar was re-resected with a security margin of 2 cm (histology: tumor-free), and sentinel lymph node excision (left inguinal and sciatic nerve region) was negative. The patient was included into a Pembrolizumab (anti-PD1) vs Placebo study, initially receiving placebo treatment. Two years later, generalized perianal melanosis was excised circumferentially, and a gluteal metastasis resected. The patient received anti-PD1, and local radiotherapy was started.

Conclusion: Anal margin amelanotic melanoma is rare, therefore resection and histologic examination are crucial for diagnosis.

The treatment needs to be interdisciplinary. Surgical options include large excision, metastasectomy and abdomino-perineal amputation.

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